

Geroscience

Different association of GDF15 and FGF21 with glycemic status and aging in the context of obesity

Laura Salmón-Gómez · Victoria Catalán · Beatriz Ramírez · Maite Aguas-Ayesa · Amaia Rodríguez · Sara Becerril · Jorge Baixauli · Sonsoles Gutierrez-Medina · Carmen Mugueta · Inmaculada Colina · Carolina M. Perdomo · Camilo Silva · Javier Escalada · Gema Frühbeck · Javier Gómez-Ambrosi

Corresponding author:

Javier Gómez-Ambrosi, PhD
Metabolic Research Laboratory
Clínica Universidad de Navarra
Irunlarrea 1
31008 Pamplona
Spain
Phone: +34 948 425600 (ext. 806567)
e-mail: jagomez@unav.es

Supplementary Table 1. Analysis of the correlation between GDF15 and anthropometric and biochemical variables, unadjusted and after adjusting by age, BMI, BF% or age and BMI.

Variable	Serum GDF15		Serum GDF15 adjusted by age		Serum GDF15 adjusted by BMI		Serum GDF15 adjusted by BF%		Serum GDF15 adjusted by age&BMI	
	r	P value	r	P value	r	P value	r	P value	r	P value
Sex	-0.118	<0.05	-0.136	<0.05	-0.080	0.147	-0.224	<0.001	-0.105	0.058
Age	0.545	<0.001	-	-	0.552	<0.001	0.527	<0.001	-	-
Body weight	0.149	<0.01	0.241	<0.001	-0.048	0.385	0.102	0.065	0.095	0.088
BMI	0.200	<0.001	0.226	<0.001	-	-	0.120	<0.05	-	-
Body fat (%)	0.155	<0.01	0.063	0.253	0.064	0.250	-	-	-0.084	0.127
Waist circumference	0.274	<0.001	0.250	<0.001	0.192	<0.001	0.216	<0.001	0.112	<0.05
Hip circumference	0.108	<0.05	0.175	<0.01	-0.132	<0.05	0.003	0.961	-0.045	0.419
WHR	0.310	<0.001	0.181	<0.001	0.229	<0.001	0.298	<0.001	0.102	0.065
WHtR	0.312	<0.001	0.231	<0.001	0.301	<0.001	0.255	<0.001	0.060	0.280
SBP	0.318	<0.001	0.133	<0.05	0.267	<0.001	0.287	<0.001	0.054	0.329
DBP	0.272	<0.001	0.126	<0.05	0.195	<0.001	0.227	<0.001	0.050	0.366
Glucose	0.249	<0.001	0.111	<0.05	0.224	<0.001	0.247	<0.001	0.053	0.340
Glucose 2-h OGTT	0.303	<0.001	0.216	<0.001	0.256	<0.001	0.279	<0.001	0.152	<0.01
Insulin	0.159	<0.01	0.187	<0.001	0.078	0.161	0.123	<0.05	0.118	<0.05
Insulin 2-h OGTT (μ U/mL)	0.168	<0.001	0.128	<0.05	0.115	<0.05	0.137	<0.05	0.086	0.121
HOMA	0.193	<0.001	0.203	<0.001	0.123	<0.05	0.166	<0.01	0.136	<0.05
QUICKI	-0.200	<0.001	-0.150	<0.01	-0.111	<0.05	-0.164	<0.01	-0.065	0.244
TyG index	0.218	<0.001	0.150	<0.01	0.193	<0.001	0.227	<0.001	0.097	0.081
Triglycerides	0.114	<0.05	0.102	0.065	0.095	0.087	0.125	<0.05	0.076	0.172
Cholesterol	0.062	0.223	-0.067	0.224	0.109	<0.05	0.067	0.227	-0.024	0.670
LDL-cholesterol	0.071	0.164	-0.028	0.608	0.109	<0.05	0.090	0.103	-0.002	0.973
HDL-cholesterol	-0.096	0.060	-0.194	<0.001	-0.053	0.342	-0.140	<0.05	-0.126	<0.05
Uric acid	0.217	<0.001	0.194	<0.001	0.144	<0.01	0.219	<0.001	0.144	<0.01
ALT	0.150	<0.01	0.168	<0.01	0.106	0.056	0.160	<0.01	0.138	<0.05
AST	0.243	<0.001	0.193	<0.001	0.210	<0.001	0.235	<0.001	0.185	<0.001
AST/ALT ratio	-0.023	0.646	-0.059	0.288	0.023	0.677	-0.042	0.445	0.003	0.960
GGT	0.197	<0.001	0.171	<0.01	0.185	<0.001	0.218	<0.001	0.151	<0.01
Adiponectin	-0.030	0.571	-0.126	<0.05	0.012	0.824	-0.052	0.347	-0.085	0.123
Leptin	0.027	0.601	-0.010	0.859	-0.064	0.247	-0.154	<0.01	-0.094	0.089
FGF21	0.340	<0.001	0.317	<0.001	0.301	<0.001	0.323	<0.001	0.254	<0.001
Adipoq/Lep ratio	-0.036	0.504	-0.010	0.871	0.056	0.346	0.098	0.097	0.081	0.171
GDF15/Adipoq ratio	0.625	<0.001	0.631	<0.001	0.619	<0.001	0.645	<0.001	0.613	<0.001
FGF21/Adipoq ratio	0.280	<0.001	0.308	<0.001	0.252	<0.001	0.276	<0.001	0.262	<0.001
FGF21/Lep ratio	0.310	<0.001	0.251	<0.001	0.269	<0.001	0.333	<0.001	0.224	<0.001
PON1	-0.024	0.646	0.082	0.138	0.035	0.523	0.034	0.536	0.103	0.062
MDA	-0.067	0.197	-0.066	0.230	-0.053	0.343	-0.052	0.349	-0.074	0.184

GDF15, growth differentiation factor 15; BMI, body mass index; BF%, body fat percentage WHR, waist-to-hip ratio; WHtR, waist-to-height ratio; SBP, systolic blood pressure; DBP, diastolic blood pressure; HOMA, homeostatic model assessment; QUICKI, quantitative insulin sensitivity check index; TyG index, triglycerides, and glucose index; ALT, alanine aminotransferase; AST, aspartate aminotransferase; GGT, gamma-glutamyl transferase; Adipoq, adiponectin; Lep, leptin; PON1, paraoxonase-1; MDA, malondialdehyde. Data are Pearson's correlation coefficients and associated *P* values. For correlation with gender, male = 1 and female = 2 was used. Significant correlations are highlighted in bold.

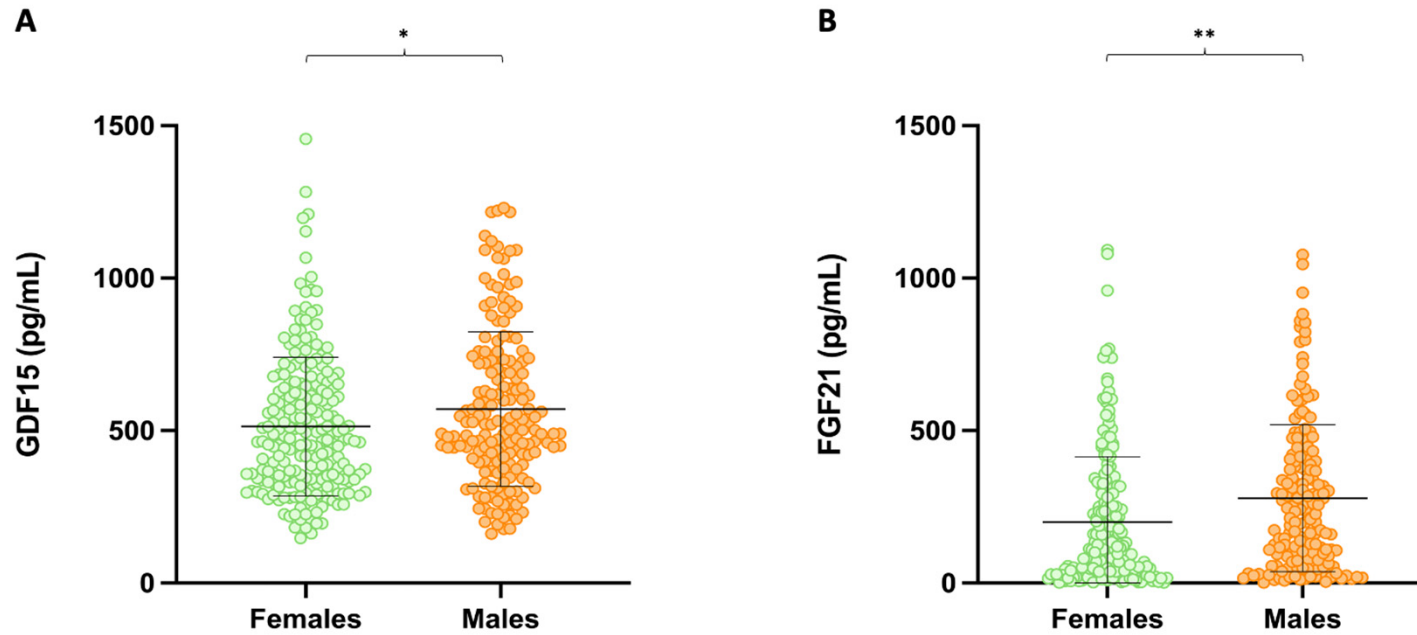
Supplementary Table 2. Analysis of the correlation between FGF21 and anthropometric and biochemical variables, unadjusted and after adjusting by age, BMI, BF% or age and BMI.

Variable	Serum FGF21		Serum FGF21 adjusted by age		Serum FGF21 adjusted by BMI		Serum FGF21 adjusted by BF%		Serum FGF21 adjusted by age&BMI	
	r	P value	r	P value	r	P value	r	P value	r	P value
Sex	-0.171	<0.01	-0.151	<0.01	-0.099	0.080	-0.272	<0.001	-0.177	<0.05
Age	0.146	<0.01	-	-	0.177	<0.01	0.130	<0.05	-	-
Body weight	0.336	<0.001	0.342	<0.001	0.068	0.232	0.286	<0.001	0.128	<0.05
BMI	0.358	<0.001	0.332	<0.001	-	-	0.289	<0.001	-	-
Body fat (%)	0.167	<0.01	0.126	<0.05	-0.031	0.589	-	-	-0.090	0.117
Waist circumference	0.410	<0.001	0.368	<0.001	0.194	<0.001	0.343	<0.001	0.163	<0.01
Hip circumference	0.272	<0.001	0.255	<0.001	-0.094	0.096	0.181	<0.01	-0.058	0.317
WHR	0.318	<0.001	0.268	<0.001	0.204	<0.001	0.317	<0.001	0.155	<0.01
WHtR	0.409	<0.001	0.345	<0.001	0.176	<0.01	0.340	<0.001	0.084	0.143
SBP	0.171	<0.01	0.119	<0.05	0.074	0.190	0.139	<0.05	0.003	0.957
DBP	0.153	<0.01	0.107	0.060	0.056	0.326	0.123	<0.05	0.004	0.939
Glucose	0.398	<0.001	0.328	<0.001	0.303	<0.001	0.343	<0.001	0.266	<0.001
Glucose 2-h OGTT	0.463	<0.001	0.401	<0.001	0.356	<0.001	0.405	<0.001	0.318	<0.001
Insulin	0.271	<0.001	0.254	<0.001	0.141	<0.05	0.229	<0.001	0.148	<0.01
Insulin 2-h OGTT (μ U/mL)	0.153	<0.01	0.137	<0.05	0.088	0.120	0.133	<0.05	0.058	0.313
HOMA	0.320	<0.001	0.283	<0.001	0.184	<0.01	0.266	<0.001	0.186	<0.01
QUICKI	-0.332	<0.001	-0.295	<0.001	-0.197	<0.001	-0.291	<0.001	-0.174	<0.01
TyG index	0.386	<0.001	-0.295	<0.001	0.343	<0.001	0.387	<0.001	0.317	<0.001
Triglycerides	0.263	<0.001	0.369	<0.001	0.260	<0.001	0.290	<0.001	0.255	<0.001
Cholesterol	-0.019	0.715	0.274	<0.001	0.076	0.178	-0.005	0.930	0.042	<0.470
LDL-cholesterol	-0.033	0.528	-0.047	0.404	0.043	0.452	-0.007	0.904	0.012	0.830
HDL-cholesterol	-0.199	<0.001	-0.237	<0.001	-0.125	<0.05	-0.248	<0.001	-0.146	<0.05
Uric acid	0.218	<0.001	0.219	<0.001	0.141	<0.01	0.249	<0.001	0.094	0.101
ALT	0.184	<0.001	0.173	<0.01	0.128	<0.05	0.194	<0.001	0.140	<0.05
AST	0.178	<0.001	0.154	<0.01	0.151	<0.01	0.183	<0.01	0.148	<0.01
AST/ALT ratio	-0.174	<0.001	-0.172	<0.01	-0.086	0.131	-0.177	<0.01	-0.111	0.053
GGT	0.244	<0.001	0.243	<0.001	0.232	<0.001	0.280	<0.001	0.218	<0.001
Adiponectin	-0.261	<0.001	-0.287	<0.001	-0.203	<0.001	-0.306	<0.001	-0.235	<0.001
Leptin	0.066	0.212	0.069	0.212	-0.062	0.258	-0.097	0.079	-0.068	0.219
GDF15	0.340	<0.001	0.317	<0.001	0.301	<0.001	0.323	<0.001	0.254	<0.001
Adipoq/Lep ratio	-0.238	<0.001	-0.244	<0.001	-0.114	0.055	-0.176	<0.01	-0.111	0.060
FGF21/Adipoq ratio	0.854	<0.001	0.857	<0.001	0.837	<0.001	0.856	<0.001	0.841	<0.001
FGF21/Lep ratio	0.721	<0.001	0.763	<0.001	0.771	<0.001	0.831	<0.001	0.765	<0.001
GDF15/Adipoq ratio	0.432	<0.001	0.369	<0.001	0.341	<0.001	0.398	<0.001	0.316	<0.001
PON1	-0.043	0.426	-0.019	0.738	-0.021	0.715	-0.027	0.641	-0.020	0.731
MDA	-0.064	0.232	0.003	0.961	0.010	0.857	0.001	0.981	0.037	0.521

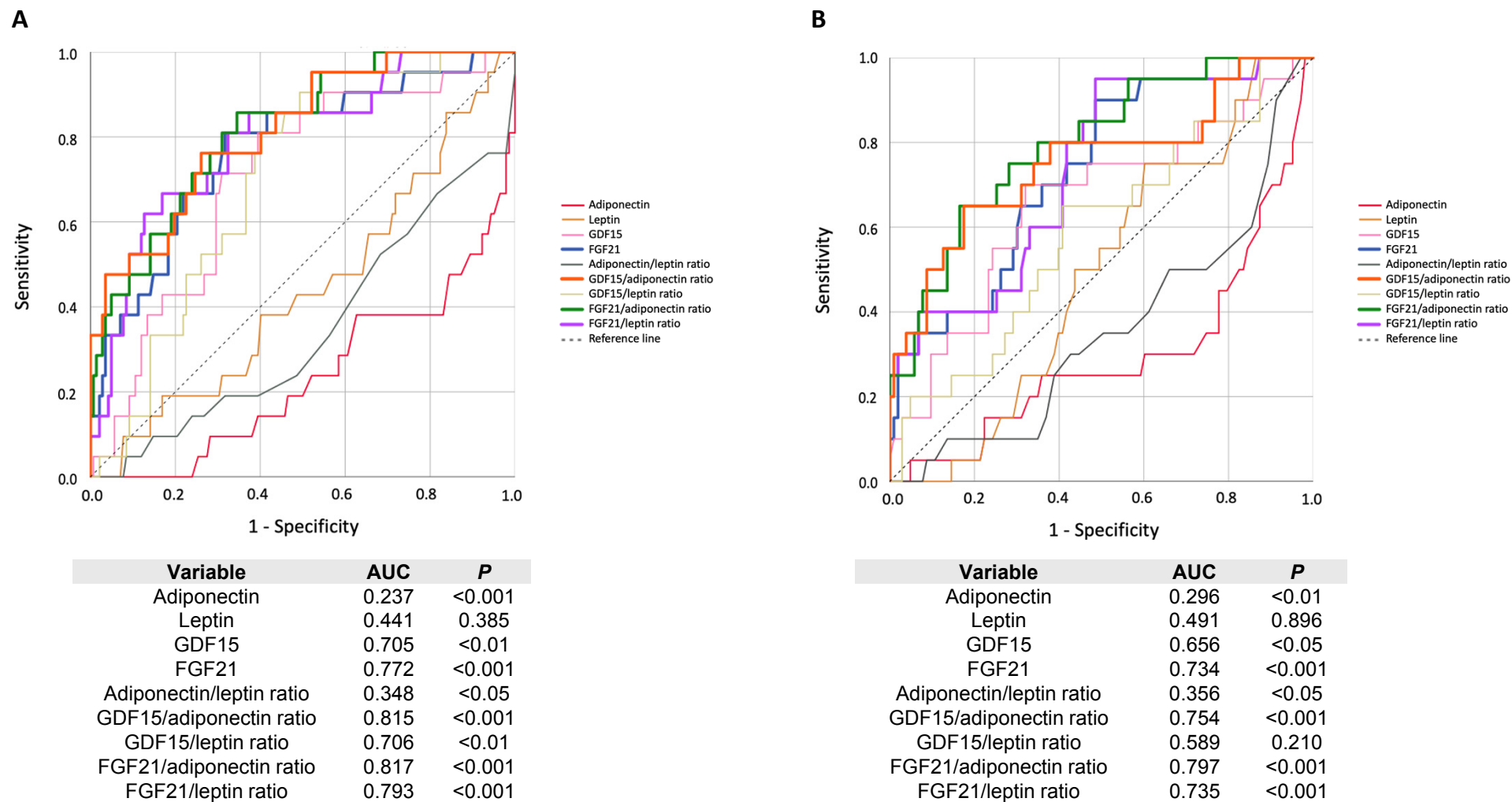
FGF21, fibroblast growth factor 21; BMI, body mass index; BF%, body fat percentage WHR, waist-to-hip ratio; WHtR, waist-to-height ratio; SBP, systolic blood pressure; DBP, diastolic blood pressure; HOMA, homeostatic model assessment; QUICKI, quantitative insulin sensitivity check index; TyG index, triglycerides, and glucose index; ALT, alanine aminotransferase; AST, aspartate aminotransferase; GGT, gamma-glutamyl transferase; GDF15, growth differentiation factor 15; Adipoq, adiponectin; Lep, leptin; PON1, paraoxonase-1; MDA, malondialdehyde. Data are Pearson's correlation coefficients and associated *P* values. For correlation with gender, male = 1 and female =2 was used. Significant correlations are highlighted in bold.

Supplementary Table 3. Area under the curve (AUC) obtained in the receiver operating characteristic (ROC) analysis to detect the presence of type 2 diabetes.

Variable	AUC	<i>P</i>
Adiponectin	0.268	<0.001
Leptin	0.438	0.204
GDF15	0.683	<0.001
FGF21	0.760	<0.001
Adiponectin/leptin ratio	0.359	<0.01
GDF15/adiponectin ratio	0.779	<0.001
GDF15/leptin ratio	0.642	<0.01
FGF21/adiponectin ratio	0.807	<0.001
FGF21/leptin ratio	0.762	<0.001



Supplementary Figure 1. Serum levels of (A) GDF15 and (B) FGF21 depending on sex. Statistical differences between groups were analyzed by unpaired Student's *t* tests. **P*<0.05 and ***P*<0.01.



Supplementary Figure 2. Receiver operating characteristic (ROC) curves of Adiponectin, Leptin, GDF15 and FGF21, and of Adiponectin/Leptin, GDF15/Adiponectin, GDF15/Leptin, FGF21/Leptin and FGF21/Adiponectin ratios to predict T2D with their AUC and *P* values in (A) women and (B) men.