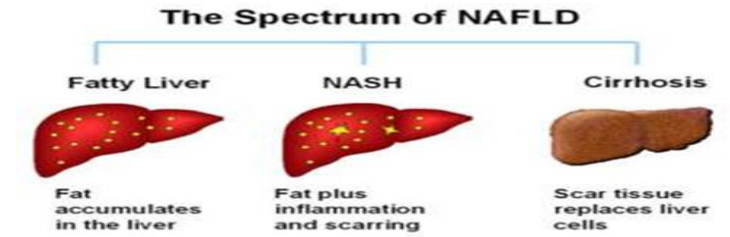
TITLE

ASSOCIATION OF BILIRUBIN WITH LIVER FIBROSIS AND REMISSION OF DIABETES IN MORBID OBESITY PATIENTS UNDERGOING TO BARIATRIC SURGERY

Authors, co-authors, institution

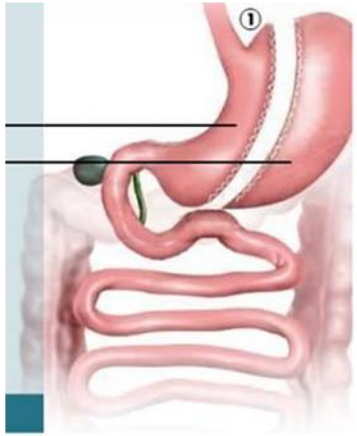


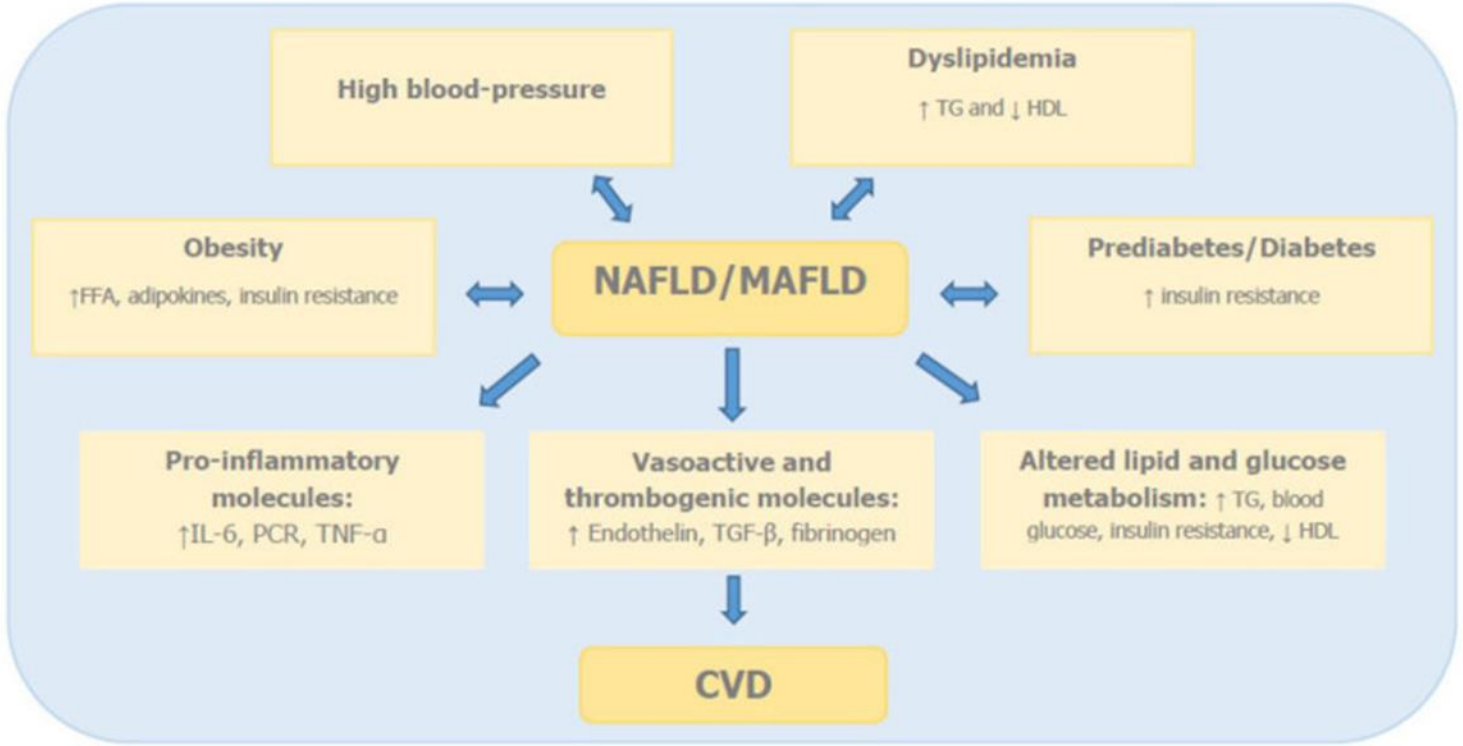
Unidad de Cirugía Endocrina y Metabólica
Hospital Clínico Universitario
"Virgen de la Vitoria". Málaga

Dr. Ocaña Wilhelmi

[ ] I have no potential conflict of interest to report

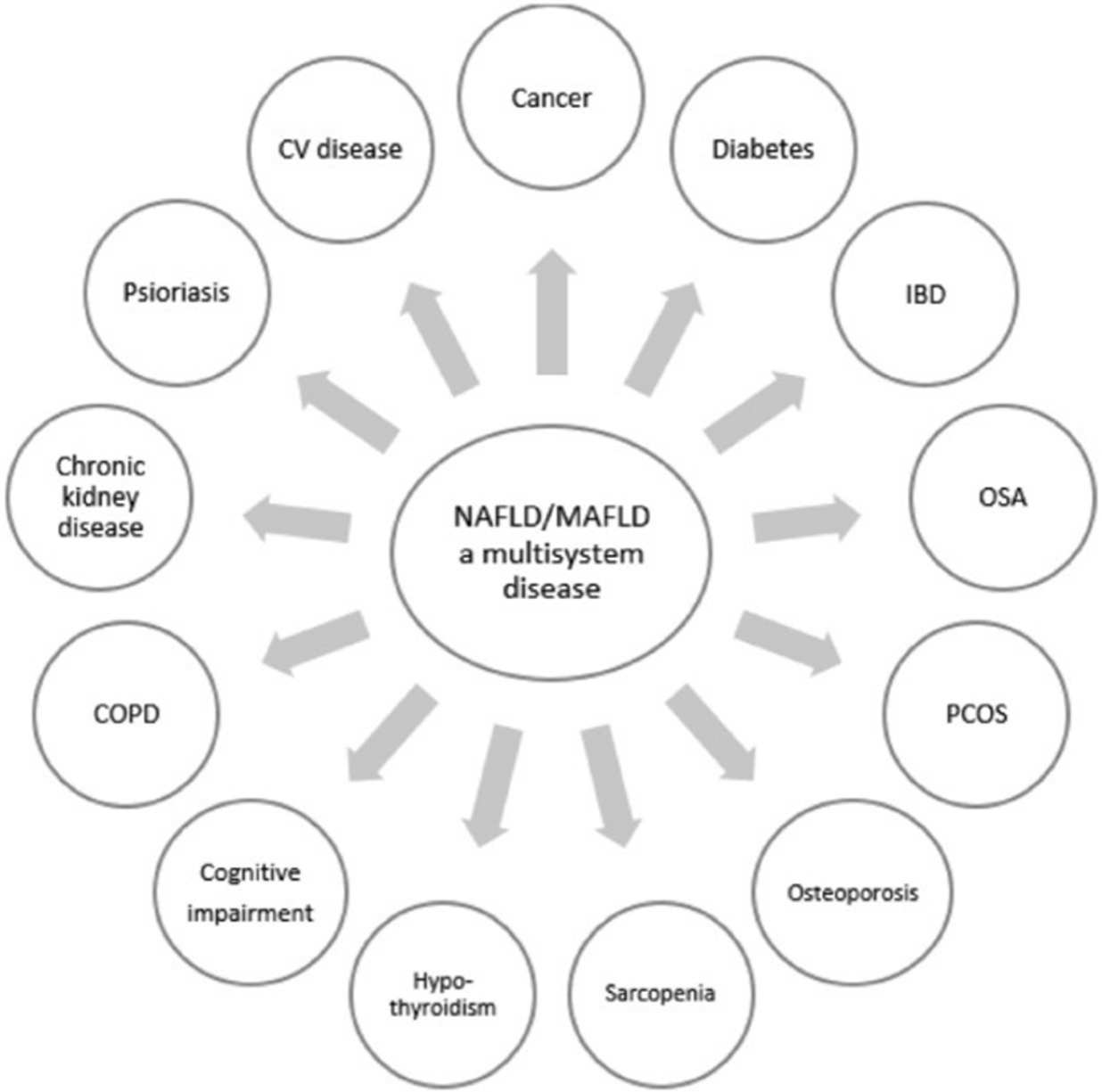
Currently, bariatric surgery (BS) is the most effective treatment for obesity and its comorbidities, such as type 2 diabetes mellitus (T2DM). Factors that improve T2DM post-intervention have been identified, such as young age, short duration of the disease, good glycemic control, and no use of insulin. However, little is known about the effect of other factors, such as metabolic dysfunction-associated fatty liver disease (MAFLD) or its association with bilirubin on the improvement of T2DM.

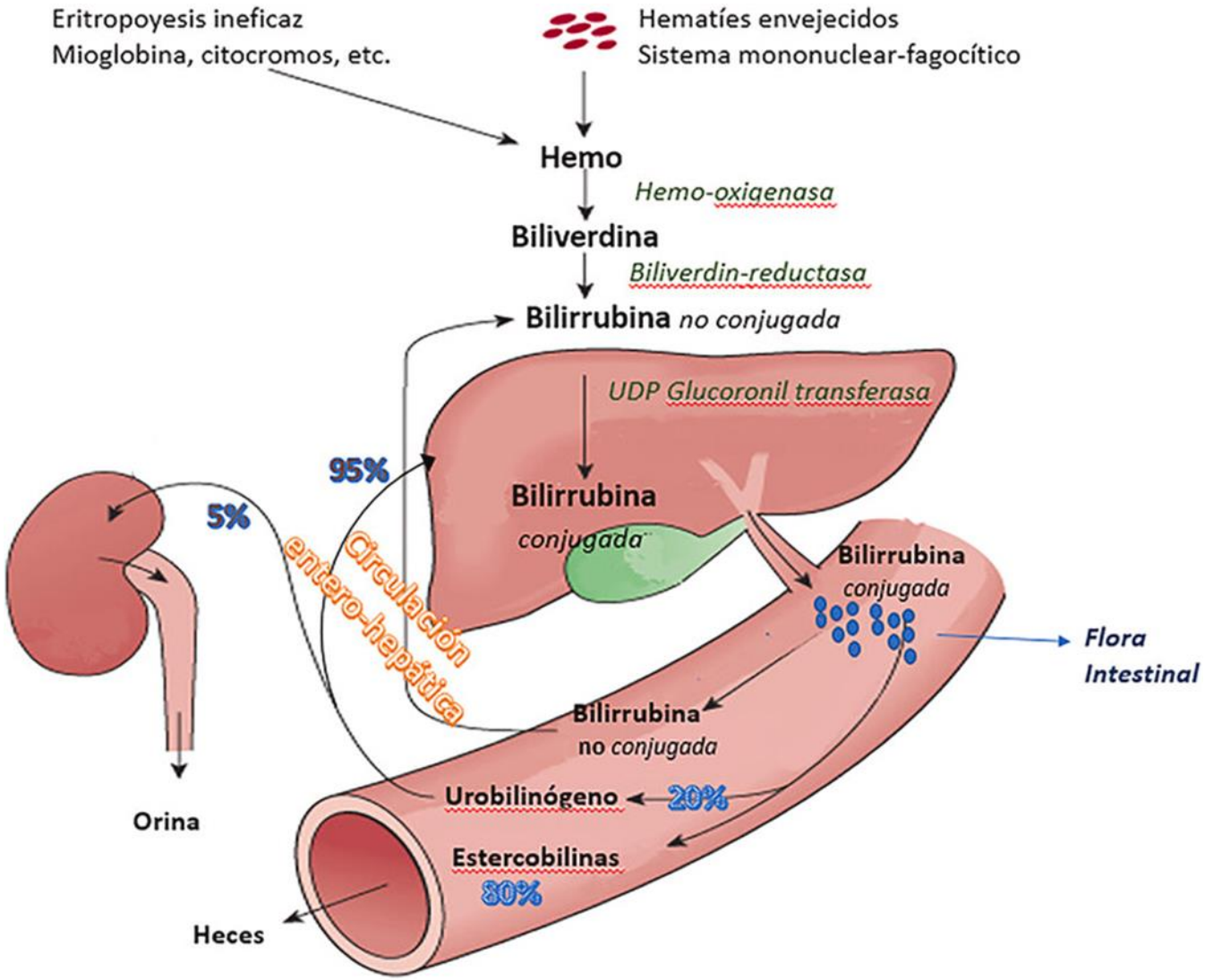




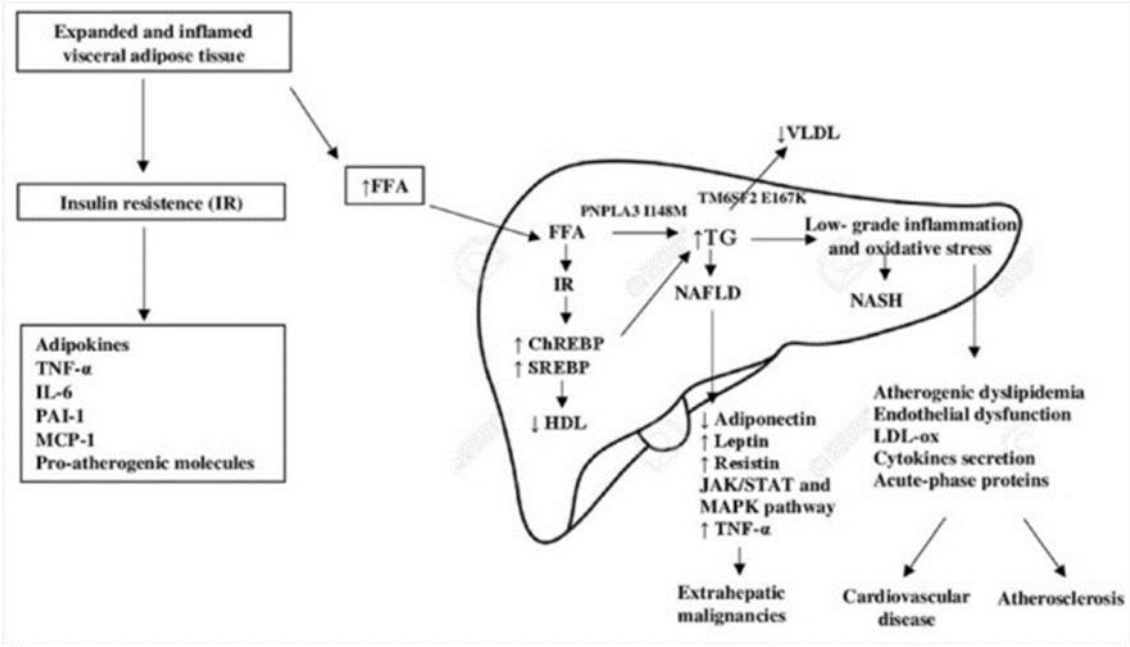
.- There appears to be a bidirectional relationship between cardiovascular risk factors and MAFLD, such that the presence of non-alcoholic fatty liver disease predicts the development of metabolic disorders (mainly hypertension and DM2), and vice versa (metabolic syndrome, hypertriglyceridemia, hypertension, carbohydrate intolerance and DM2 predispose to MAFLD).

Pipitone RM, Ciccioli C, Infantino G, La Mantia C, Parisi S, Tulone A, Pennisi G, Grimaudo S, Petta S. MAFLD: a multisystem disease. Ther Adv Endocrinol Metab. 2023 Jan 28;14:20420188221145549. doi: 10.1177/20420188221145549. PMID: 36726391; PMCID: PMC9885036.





Bilirubin is widely known as an end product of heme metabolism, so it is a physiological breakdown product of blood metabolism and under normal conditions is efficiently processed and eliminated by the liver.



.- Association of low bilirubin concentrations with cardiovascular diseases, DM2, metabolic syndrome and obesity.

.- Other authors also agree that patients with metabolically healthy obesity have higher levels of bilirubin compared to the metabolically unhealthy obesity group.

.- Total bilirubin and direct bilirubin levels are inversely related to the appearance of metabolic syndrome and MAFLD.

AIM OF THIS STUDY

Primary objective:
.- The primary objective of this study is to examine which indicators or parameters linked to MAFLD could have a connection with the reversal of type 2 diabetes in the short term (12 months) after undergoing bariatric surgery.

Specific Objectives:
.- To evaluate the effect of bariatric surgery on anthropometric and biochemical levels, as well as on the improvement of liver fibrosis and remission of type 2 diabetes after surgery.
.- To examine the connection between carbohydrate metabolism and MAFLD in patients with morbid obesity before undergoing bariatric surgery.
.- To evaluate which factors associated with liver and carbohydrate metabolism are associated with remission of type 2 diabetes and improvement of liver fibrosis in morbidly obese patients after bariatric surgery.Enviar comentariosPaneles lateralesHistorialGuardado

STUDY DESIGN:

.- Prospective study in patients with morbid obesity (BMI>40kg/m2), aged between 18 and 65 years, who underwent vertical gastrectomy at the Hospital Clínico Universitario de Málaga, during the years 2021 and 2022.

.- Subsequently, the remission and non-remission of DM2 was evaluated after the follow-up period (1 year) according to the remission criteria stipulated by the American Diabetes Association (ADA) expert consensus of 2009.

.- Exclusion criteria: Patients under 18 years of age and over 65 years of age, those with other types of liver disease, those with contraindications for bariatric surgery and those men who consumed more than 30g/alcohol per day, and those women who consumed more than 20g per day were excluded.

Tipo de Remisión	Criterio de Remisión	Confirmación
Remisión Parcial	Hiperglucemia por debajo de los límites de diagnóstico de diabetes (HbA1c no diagnóstica de diabetes (< 6,5%) y glucemia plasmática en ayunas 100-125 mg/dl) en ausencia de tratamiento farmacológico	Al menos un año de duración
Remisión Completa	Niveles normales de glucemia (HbA1c en rango de la normalidad (< 6 %) y glucemia plasmática en ayunas < 100 mg/dl) en ausencia de tratamiento farmacológico	Al menos un año de duración

Criterios de remisión de la DM2 estipulados por el consenso de expertos de la American Diabetes Association (ADA) de 2009

RESULTS:

.- After one year of BC, we observed significant changes in multiple anthropometric and biochemical variables.

.- Something similar occurred with the liver scores, which improved significantly.

.- The percentage of change was significant and greater than 30% for TG, insulin and HOMA-IR; and for the fibroscan, LAP, NAFLD-FS and FLI scores. Of the 24 patients, 45.8% presented a remission of DM2 at one year, compared to 54.2% who continued to be diabetic one year after surgery.

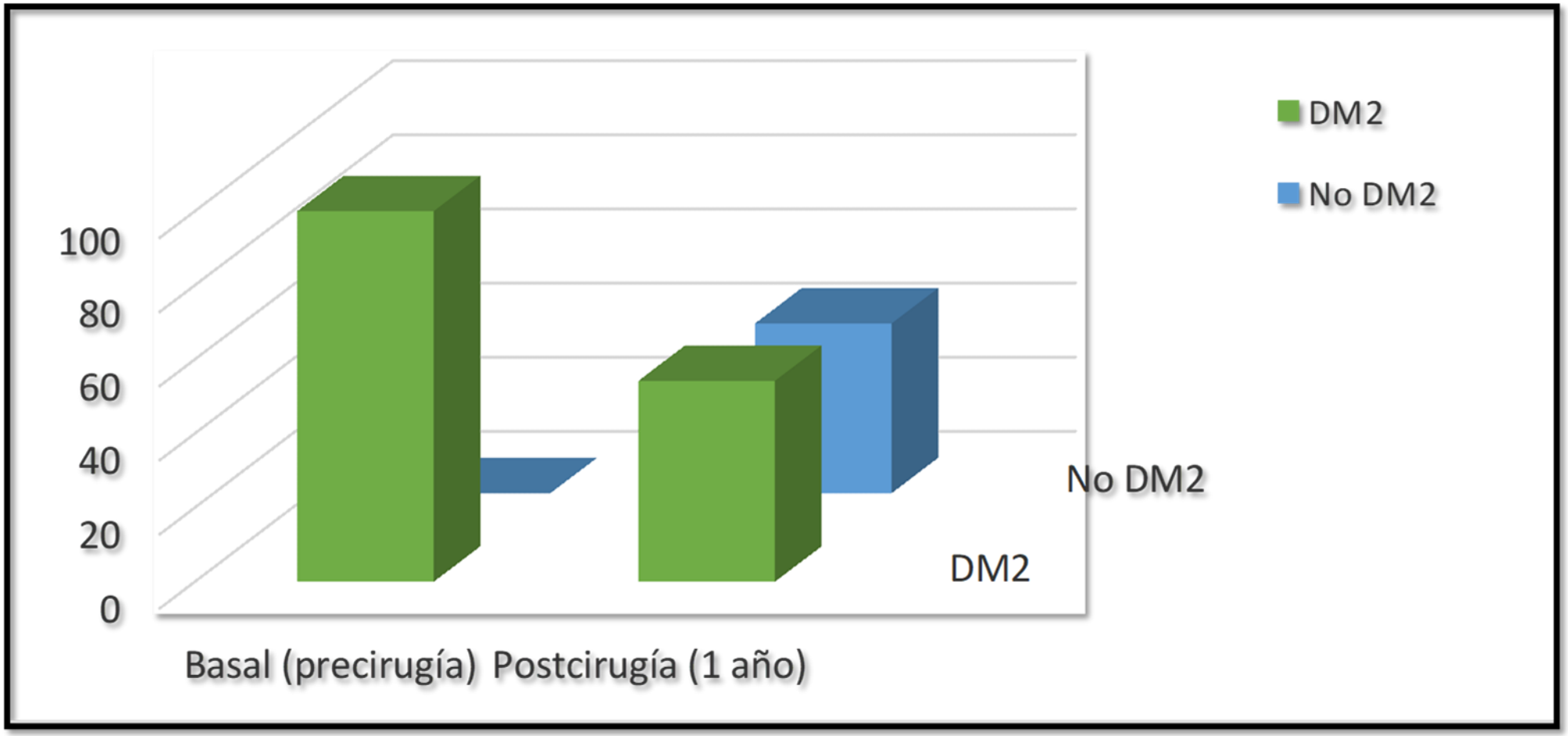
.- Based on the classification of patients according to whether there was remission of DM2 at one year after surgery, a regression analysis was performed in which a statistically significant association was found only with bilirubin (p=0.019).

Características antropométricas y bioquímicas de los pacientes incluidos en el estudio previo a la cirugía (pre-cirugía) y en el seguimiento a 1 año tras cirugía (post-cirugía).

VARIABLES	*PRE-CIRUGÍA*	*POSTCIRUGÍA*	*SIGNIFICANCIA (p)*
Sexo (H/M)	12/12		
Edad (años)	49,5 ± 8,1		
Peso (kg)	128,9 ± 18,4	95,6 ± 18,5	<0,001
IMC (kg/m²)	45,6 ± 6,3	34,1 ± 6,5	<0,001
Cintura (cm)	134,6 ± 13,8	110,5 ± 15,7	<0,001
Cadera (cm)	138,7 ± 12,7	117,5 ± 15,5	<0,001
Plaquetas (10^9/L)	269,3 ± 70,2	259,0 ± 92,8	0.145
HbA1c (%)	6,2 ± 0,972	5,4 ± 0,6	<0,001
Glucosa (mg/dL)	114,9 ± 25,7	90,6 ± 15,2	<0,001
Colesterol (mg/dL)	185,4 ± 45,4	178,3 ± 38	0,430
Triglicéridos (mg/dL)	168,7 ± 45,4	102,6 ± 48,3	<0,001
HDL-colesterol (mg/dL)	41,2 ± 7,8	51,1 ± 11,1	0,002
LDL-colesterol (mg/dL)	112,5 ± 38,8	106,5 ± 33,9	0,580
Bilirrubina total (mg/dl)	0,558 ± 0,211	0,774 ± 0,301	<0,001
AST (U/L)	28,5 ± 10,2	29,4 ± 30,4	0,014
ALT (U/L)	39,2 ± 18,8	36,1 ± 52,8	0,006
GGT (U/L)	32 ± 16,9	25,8 ± 27,2	0,007
Fostatasa Alcalina (U/L)	77,1 ± 22,2	71,4 ± 14,4	0,070
Insulina (µUI/mL)	20,9 ± 8,1	10,9 ± 5,6	<0,001
HOMA-IR	5,9 ± 2,6	2,5 ± 0,4	<0,001
Tratamiento con metformina	9 (37,5%)	4 (16,7%)	
Tratamiento con GLP-1	8 (33,3%)	6 (25%)	
Tratamiento con metformina y GLP-1	7 (29,2%)	3 (12,5%)	

Scores de hígado graso de los pacientes con obesidad mórbida pre- cirugía y post-cirugía.

VARIABLES	*PRE-CIRUGÍA*	*POST-CIRUGÍA*	*SIGNIFICANCIA (P)*
Fibroscan (Kpascales)	9,9 ± 5,7	5,8 ± 2,3	0,002
	SCORES		
HSI	59,6 ± 8,3	45,1 ± 6,4	0,003
LAP	143,8 ± 90,7	61 ± 32,7	0,007
FLI	98,4±1,5	69,5 ± 22,7	<0,001
NAFLD-FS	1,3 ± 1,1	0,115 ± 1,3	<0,001
HEPAMET	0,142 ± 0,087	0,118 ± 0,156	0,125
FIB4	0,957 ± 0,432	1 ± 0,630	0,377
APRI	0,332 ± 0,156	0,338 ± 0,5,9	0,048



Porcentajes de DM2 basalmente (pre-cirugía) y al año de seguimiento (post-cirugía), **A:** Frecuencia de DM2 al inicio del estudio**, B:** Frecuencia de DM2 un año después de la intervención

Análisis se regresión según hubiera o no remisión de la DM2 al año tras la cirugía

VARIABLES	NIVELES PRE-CIRUGÍA		
	No DM	Sí DM	Significancia (*p*)
N	11	13	-
Sexo (H/M)	5/6	7/6	-
Edad (años)	48,9 ± 8,5	50,1 ± 8,1	0,392
Peso (kg)	128 ± 15,6	129,7 ± 15,6	0,531
IMC (kg/m^2)	46,4 ± 6,2	45,5 ± 6,6	0,608
Cintura (cm)	133,4 ± 15,4	135,6 ± 12,7	0,608
Cadera (cm)	140,6 ± 15,1	137,1 ± 10,7	0,569
TAS (mmHg)	130,1 ± 11,2	135,7 ± 29,2	0,865
TAD (mmHg)	81 ± 9,8	83,4 ± 14,5	0,865
Urea	33,1 ± 83,6	36,5 ± 80,2	0,494
Ácido úrico	10,5 ± 13.4	6,5 ± 1,6	0,134
Proteínas totales	13,2 ± 191,6	7 ± 0,9	0,146
Glucosa (mg/dl)	108,5 ± 18,5	120,3 ± 30,1	0,417
HbA1c (%)	5,98 ± 0,68	6,4 ± 1,1	0,424
Triglicéridos (mg/dl)	141,7 ± 68,8	191,4 ± 109,1	0,384
Colesterol (mg/dl)	167,4 ± 31,5	200,5 ± 50,8	0,063
HDL-colesterol (mg/dl)	40,1 ± 7,6	42,1 ± 8,1	0,331
LDL-colesterol (mg/dl)	99 ± 30,3	124 ± 42,6	0,186

VARIABLES	NIVELES PRE-CIRUGÍA		
	No DM	Sí DM	Significancia (*p*)
N	11	13	-
VLDL-colesterol (mg/dl)	283,4 ± 1377,1	382,9 ± 2181,6	0,392
Insulina (µUI/ml)	20,8 ± 9,9	21 ± 6,6	0,776
Péptido C (ng/ml)	27,4 ± 0,798	30,13 ± 0,751	0,908
HOMA-IR	5,7 ± 3,2	6,1 ± 2,1	0,392
Bilirrubina	0,686 ± 0,229	0,45 ± 0,117	0,005
AST	29 ± 10,7	28,1 ± 10,2	0,976
ALT	41,1 ± 21,1	37,5 ± 17,4	0,691
GGT	24,8 ± 7,4	38,1 ± 20,3	0,082
Fosfatasa alcalina	74,6 ± 20	79,1 ± 24,5	0,649
Albúmina	4,06 ± 0,329	4,03 ± 0,332	0,776
SCORES HEPÁTICOS			
HSI	60,3 ± 7,8	59 ± 8,8	0,75684
LAP	105,3 ± 36,9	206,5 ± 146,7	0,141
NAFLD-FS	1,43 ± 1	1,3 ± 1,1	0,852
HEPAMET	0,125 ± 0,112	0,156 ± 0,064	0,151
FLI	98,4 ± 1,4	98,4 ± 1,7	0,749
FIB4	0,911 ± 0,345	0,993 ± 0,499	0,535
APRI	0,329 ± 0,136	0,335 ± 0,175	0,951
Fibroscan	10,1 ± 6,9	9,71 ± 4,5	0,622

CONCLUSIONS:

.- In our study, CB is an effective treatment for DM2, which also improves numerous anthropometric and biochemical variables, as well as other entities such as MAFLD.

.- The relationship of bilirubin with DM2 and fibrosis is widely investigated, although further studies are still needed to confirm previous hypotheses.

.- The results obtained in our study are in line with the growing scientific evidence that bilirubin has an indirect relationship with diabetes and MAFLD.

.- It is expected that this study will contribute to a deeper understanding of the relationship between blood bilirubin levels, liver fibrosis and diabetes remission in patients with obesity undergoing bariatric surgery.

.- If the hypothesis is confirmed, these findings could have important implications for clinical practice, including risk identification, outcome prediction, and the development of personalized treatment approaches to address obesity, T2DM, and MAFLD.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