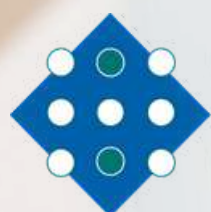


VII Jornades IdISBa

PÒSTERS DE L'ÀREA:

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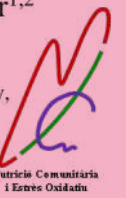
INTRAHEPATIC FAT CONTENT IS ASSOCIATED WITH OXIDATIVE STRESS AND PRO-INFLAMMATORY STATUS IN NON-ALCOHOLIC FATTY LIVER DISEASE PATIENTS



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INTRODUCTION

Non-alcoholic fatty liver disease (NAFLD) is defined by excessive fat accumulation, especially triglycerides, in hepatocytes. It can progress to non-alcoholic steatohepatitis (NASH) and continue to fibrosis, cirrhosis or hepatocarcinoma, if the pathology is not properly treated. Up to now, therapeutic approaches to fight against this disease are basically dietary and lifestyle modifications because there are no effective pharmacological therapies against NAFLD. The aim was to identify plasma biomarkers of liver damage, oxidative stress and inflammation that facilitate the early diagnosis of the disease and control its progression.

EXPERIMENTAL PROCEDURE

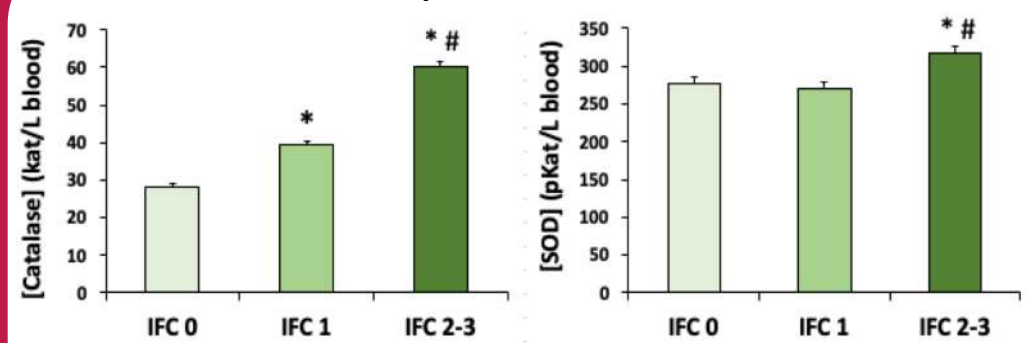
Antioxidant and inflammatory biomarkers were determined in plasma of patients diagnosed with NAFLD (n=100 adults; 40-60 years old) living in the Balearic Islands, Spain. Patients were classified attending to the amount of intrahepatic fat content (IFC) measured by Magnetic Resonance Imaging (MRI). Statistical Package for Social Sciences (SPSS v.25 for Windows) was used to carry out the statistical analysis. Results were expressed as the mean ± standard error of the mean (SEM).

Characteristics of participants with NAFLD according to the amount of intrahepatic fat content (IFC)

	Reference values	IFC=0 (n=30)	IFC=1 (n=35)	IFC≥2 (n=35)	P-value
Age (years)		52.5 ± 1.1	53.5 ± 1.2	51.7 ± 1.1	0.510
Female [n (%)]		16 (54.5)	17 (48.6)	14 (40.7)	0.136
Male [n (%)]		14 (45.5)	18 (50.0)	21 (59.3)	
Weight (kg)		88.0 ± 2.5	94.2 ± 2.5	95.1 ± 1.9	0.073
Height (cm)		164.5 ± 1.5	168.8 ± 1.7	166.2 ± 1.6	0.165
BMI (kg/m ²)		32.4 ± 0.7	33.0 ± 0.7	34.3 ± 0.6	0.109
Glucose (mg/dL)	70-110	99.9 ± 3.4	109.3 ± 3.6	121.7 ± 6.2*	0.005
Hb1Ac (%)	3.8 - 6.2	5.68 ± 0.09	5.80 ± 0.15	7.14 ± 0.65*#	0.015
Triglycerides (mg/dL)	<149	132.1 ± 8.6	207.6 ± 19.5	254.5 ± 42.4*	0.010
HDL-chol. (mg/dL)	≥60	51.0 ± 1.3	42.8 ± 1.1*	41.3 ± 0.9*	<0.001
LDL-chol. (mg/dL)	<100	142.5 ± 3.5	126.2 ± 3.6*	133.5 ± 3.9	0.007
Cholesterol total (mg/dL)	<200	219.7 ± 4.2	209.7 ± 5.1	221.4 ± 6.7	0.254
AST (U/L)	5 - 34	22.6 ± 1.8	25.0 ± 1.7	28.9 ± 1.8*	0.045
ALT (U/L)	0 - 55	27.8 ± 2.2	33.2 ± 4.4	45.2 ± 3.1*#	0.002
GGT (U/L)	12 - 64	48.5 ± 5.9	48.2 ± 5.4	49.5 ± 5.2	0.983

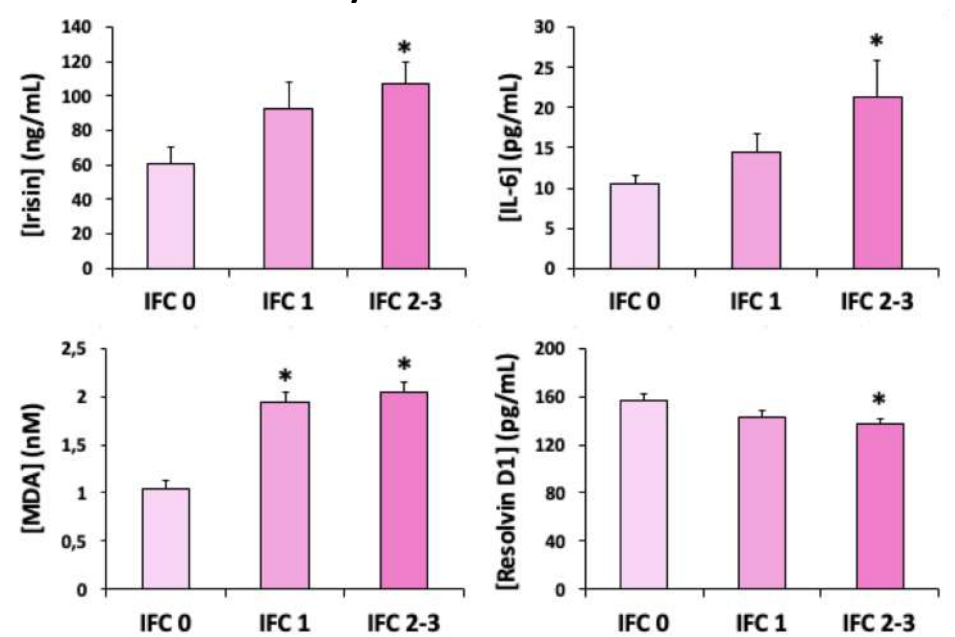
One-way ANOVA (p<0.05): *respect to IFC=0; # respect to IFC=1.

Catalase and superoxide dismutase activities



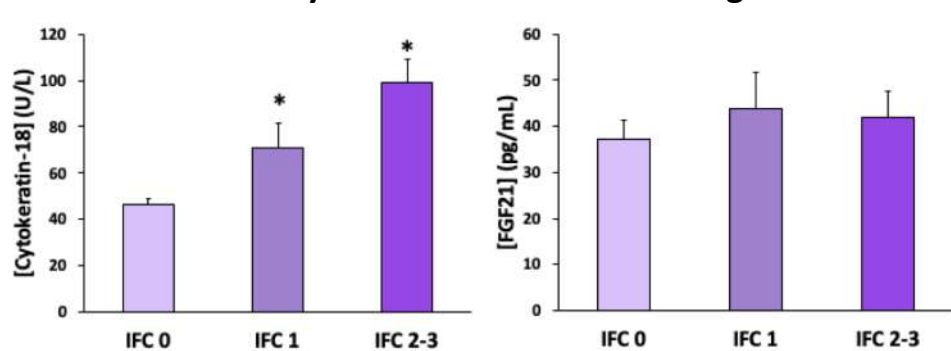
One-way ANOVA (p<0.05): *respect to IFC=0; # respect to IFC=1.

Inflammatory and oxidative stress markers



One-way ANOVA (p<0.05): *respect to IFC=0.

Plasma levels of cytokeratin 18 and fibroblast growth factor 21



One-way ANOVA (p<0.05): *respect to IFC=0.

RESULTS

Circulating glucose, triglycerides, low-density lipoprotein-cholesterol, glycosylated haemoglobin, aspartate aminotransferase and alanine aminotransferase were higher in patients with IFC ≥2 of NAFLD with respect to patients with IFC 0 and 1. Plasma activity of catalase and superoxide dismutase and the levels of irisin, interleukin-6, malondialdehyde, and cytokeatin 18 were higher in stage ≥2 subjects, whereas resolvin D1 levels were lower. No differences were observed in xanthine oxidase, myeloperoxidase, protein carbonyl and fibroblast growth factor 21 depending on liver status.

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CONCLUSION

The severity of NAFLD is associated with an increase in oxidative stress and pro-inflammatory status.

Because diagnostic tests such as MRI are not routinely performed in clinical practice to diagnose or monitor fatty liver, combining various non-invasive markers would allow the monitoring and evolution of NAFLD.

Acknowledgments: This study was supported by the Spanish Government, Institute of Health Carlos III (Projects 17/01827 and CIBEROBN CB12/03/30038) co-funded by the European Regional Development Fund, Fundació La Marató TV3 (201630.10), and EU-COST Action CA16112.

The first penetrance estimate in Val30Met hereditary transthyretin amyloidosis (ATTRv) from Mallorca

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INTRODUCTION

- ATTRv is a rare, progressive, life-threatening illness caused by mutations in the TTR gene that result in amyloid fibril accumulation in peripheral nerves and vital organs.
- Mallorca is the third most important focus of ATTRv Val30Met (pVal50Met) in Europe.
- Previous epidemiological studies estimated the disease prevalence at 5/100.000 inhabitants including patients with early (< 50 years) and late age of onset (AO) (≥ 50 years) (1).
- The phenotypic presentation is a progressive axonal sensorimotor polyneuropathy, although some late onset patients present an associated cardiomyopathy (2).
- The reason for such phenotypic variation between patients, eventually within the same family, remains unelucidated.
- Acknowledge the risk of being affected (penetrance) for gene carriers is important to guide their management across time, allowing early diagnosis and on-time therapeutic initiation.

OBJECTIVE

- Estimate Penetrance in a large sample of Val30Met ATTRv families from Mallorca.

MATERIAL / METHODS

- Genealogical data were collected, between 2002 and 2018, from Val30Met ATTRv families monitored at the referral center for ATTRv in Mallorca (Hospital Universitario Son Llàtzer).
- Relevant data included: year of birth, date of last news (or death) for all individuals, and phenotypic and genotypic status when available. In asymptomatic individuals, the date of last news is defined by the last visit or hear say. In patients, the AO was set at the time of the first clinical manifestation related to the disease with certainty.
- Analysis were performed with NPSE method based on a survival approach as described previously (3).
- Risk estimates were analysed overall and according to gender and to the parent of origin (POO) with a Cox model.

RESULT I

- Among, 51 unrelated Val30Met ATTRv families initially investigated, 48 (928 subjects) were retained for the analysis, including 147 patients (86 men), 123 asymptomatic carriers (53 men) and 20 obligate carriers (10 men). In total, the rate of genotyped individuals in the families was 42%.

Figure 1: Distribution of age of onset in the Mallorca families

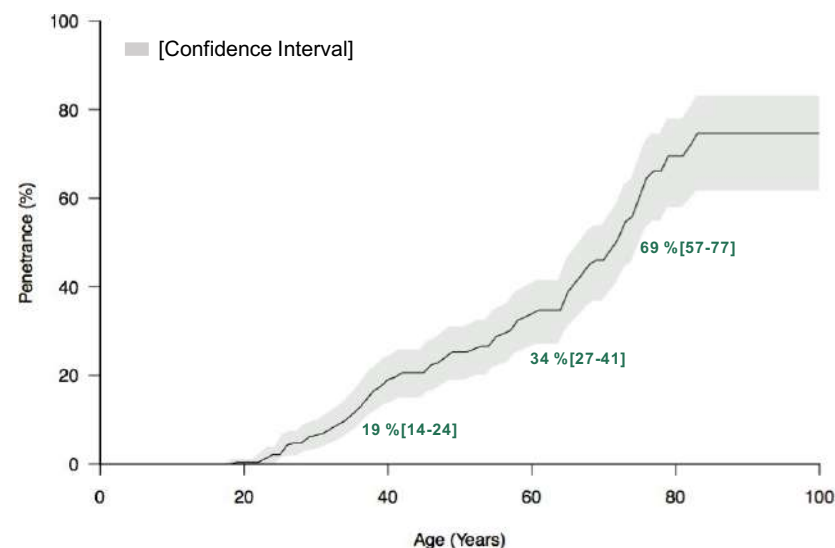


- Overall, mean AO (± Standard Deviation) was 49 (±17) years, with a wide range from 22 to 82 years and no difference of AO according gender.
- We observed a heterogeneity of AO with one peak at 20-40 y-o (early).
- Early and late onset patients were observed simultaneously within 40% of families.

RESULT II

Overall, penetrance estimate

Figure 2: Penetrance curve from 48 Mallorcan families



- Penetrance is incomplete up to 75% [61-83] at age 90 years-old.
- The disease risk increased progressively from 20 y-o. At the age of 30, 50 and 70 years, the penetrance was 7% [3-10], 25% [19-31] and 25% [19-31], respectively.

Penetrance estimates according to gender and POO.

- We found no difference of penetrance between men and women or according the POO (Figure 3).

Figure 3: Penetrance values (%) with adjustment on the POO

Ages (Years)	30	50	80
Paternal transmission	6 [3-10]	24 [17-31]	68 [52-79]
Maternal transmission	7 [3-10]	25 [17-32]	69 [55-79]

DISCUSSION / CONCLUSION

- Here, we provide the first study on penetrance estimates in Mallorca, area of high disease prevalence of Val30Met ATTRv.
- We observed a wide range of AO between and within 40% of the families.
- Overall, we showed an intermediate disease risks compared to the Val30Met Portuguese (high penetrance) and Swedish (low penetrance) families (4,5). The penetrance increased from the age of 20 years until the age of 85 years, reflecting the heterogeneity of AO.
- There was no difference of penetrance according to gender or the POO. These results differ from the POO effect previously identified in the Portuguese and Swedish Val30Met families. The mechanism of the POO effect remains unclear. One hypothesis put forwards was a link between the mitochondrial DNA copy number and the AO (6).
- The wide range of AO found within 40% of the Malloccan families living in a restricted geographic area might suggest an interaction of modifier genes on phenotype rather than an epigenetic factor.
- Our results are helpful to adjust genetic counseling and the management of gene carriers in families.

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RESULTADOS INICIALES DE LA CIRUGÍA RENAL ASISTIDA POR ROBOT EN NUESTRO CENTRO

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OBJECTIVO

La cirugía asistida por robot supone una evolución tecnológica hacia nuevas técnicas quirúrgicas mínimamente invasivas, aportando un mayor control y precisión que las técnicas convencionales. Nuestro objetivo es describir la experiencia inicial en cirugía renal asistida por robot en nuestro centro.

MATERIAL Y MÉTODOS

Se realizó una evaluación de los resultados obtenidos a nivel quirúrgico, oncológico y funcional de 42 intervenciones quirúrgicas realizadas en nuestro centro entre Febrero 2012 y Setiembre 2020. Se recopilaron los datos retrospectivamente para realizar un análisis descriptivo.

RESULTADOS

Se analizaron retrospectivamente 27 nefrectomías parciales, 7 nefrectomías radicales, 7 pieloplastias y 1 quistectomía renal.

NEFRECTOMÍAS RADICALES	
Género masculino	100% (7)
Mediana edad	62 (24-76)
Mediana índice masa corporal	25 (20-35)
Mediana índice Charlson	4 (0-7)
Mediana RENAL	10 (9-11)
Mediana PADUA	10 (9-12)
Mediana tiempo quirúrgico (min)	226 (90-310)
Mediana tiempo hospitalización (d)	4 (2-7)
Mediana filtrado glomerular	
Preoperatorio	78 (8-101)
Postoperatorio precoz (24h)	55 (8-79)
Postoperatorio tardío (6m)	62 (8-95)
Mediana tamaño tumoral (cm)	6,7 (4-8)
Lateralidad	
Derecha	43% (3)
Izquierda	57% (4)
Tipo histológico	
Células claras	14% (1)
Papilar tipo I	14% (1)
Papilar tipo II	29% (2)
Oncocitoma	14% (1)
Carcinoma asociado a enf renal multiquística	14% (1)
Márgenes	
Libre	83,3% (6)
Afecto	16,7% (1)
Complicaciones (Clavien-Dindo)	
I	28,6% (2) íleo paralítico
Tiempo seguimiento (meses)	2,2 (1-8)

NEFRECTOMÍAS PARCIALES	ROBÓTICA	LAPAROSCÓPICA
Mediana edad	62 (42-76)	59 (18-82)
Mediana índice masa corporal	29 (22-46)	28 (20-46)
Mediana índice Charlson	5 (2-9)	4 (0-11)
Mediana RENAL	7 (4-10)	7 (4-11)
Mediana PADUA	8 (6-12)	8 (6-14)
Mediana tiempo quirúrgico (min)	230 (145-360)	180 (60-360)
Mediana tiempo isquemia caliente (min)	18 (0-30)	17 (0-55)
Mediana tiempo hospitalización (días)	3 (1-30)	4 (2-50)
Mediana filtrado glomerular		
Preoperatorio	86 (32-110)	91,5 (31-133)
Postoperatorio precoz (24 horas)	70 (27-109)	90 (18-139)
Postoperatorio tardío (6 meses)	82 (57-108)	93 (32-139)
Mediana tamaño tumoral (cm)	3 (1,5-8)	2,8 (0,8-7,5)
Márgenes Libres	75% (15)	78,3% (90)
Afectos	10% (2)	21,7% (25)
Focalmente afectos	15% (3)	
Complicaciones intraoperatorias		
0	78,3% (18)	97,4% (113)
Apertura de cápsula tm	17% (4)	
Laceración esplénica	4% (1)	
Conversión vía abierta	4% (1)	
Sangrado		1,7% (2)
Lesión víscera hueca		0,9% (1)
Complicaciones post (CD)		
0	82,6% (19)	79,3% (92)
I	9% (2) pancreatitis	4,3% (5)
II	0	8,6% (10)
III	4% (1) fuga urinaria	6,9% (8)
IV	4% (1) s. hemorrágico	0
V	0	0,9% (1) exitus
Trifecta Sí	68% (15)	50,4% (58)
No	32% (7)	49,6% (57)

CONCLUSIONES

La cirugía renal asistida por robot es una técnica factible en nuestro centro, segura y eficaz. Será necesario ampliar el número de pacientes tratados para valorar los resultados de esta técnica a largo plazo.

IMPACTO DE LOS TIEMPOS DE ISQUEMIA Y CARACTERÍSTICAS DEL DONANTE Y RECEPTOR EN EL TRASPLANTE RENAL MAASTRICHT III

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1.- INTRODUCCIÓN Y OBJETIVOS

La donación en asistolia (DA) ha permitido la expansión del pool de donantes en el trasplante renal. Sin embargo, existe la preocupación de que los resultados del injerto sean inferiores en comparación con los donantes en muerte encefálica. El objetivo de este estudio es describir los resultados en nuestro programa de trasplante renal de DA y analizar qué factores pueden predecir los resultados de los implantes.

2.- MATERIAL Y MÉTODOS

Se ha realizado un estudio unicéntrico retrospectivo de todos los pacientes que han recibido un trasplante renal de DA controlada (categoría Maastricht III) en nuestro centro entre junio de 2016 y noviembre de 2019. Realizamos un análisis descriptivo de las características de los donantes y receptores y estudiamos la asociación entre estos factores con la función retardada del injerto (FRI) y la creatinina sérica (Cr) al alta hospitalaria, a los tres y doce meses. También se ha considerado la relación entre los tiempos de isquemia y los resultados del trasplante.

3.- RESULTADOS

Durante el periodo estudiado se han realizado 86 trasplantes renales en DA controlada. Las características de los donantes y receptores se describen en la Tabla 1. Además, se ha realizado una comparación entre los grupos con FRI y sin FRI (Tabla 2). Observamos una asociación significativa entre la edad del donante ($p = 0,014$) y estar en hemodiálisis ($p = 0,001$) con la FRI. Los resultados no revelaron diferencias significativas entre los diferentes tiempos de isquemia y la FRI. Por otro lado, el análisis de regresión logística muestra que el tiempo de isquemia fría (TIF) superior a 540 min y el tiempo desde la limitación del esfuerzo terapéutico (LET) hasta la parada cardiorrespiratoria (PCR) superior a 15 min son factores de riesgo no estadísticamente significativos para presentar FRI. Por otro lado, una diuresis residual mayor de 500 ml y los receptores en diálisis peritoneal son factores protectores estadísticamente significativos para FRI (Tabla 3). Finalmente, el análisis de correlación ilustra una correlación positiva significativa entre la edad del donante y la Cr al alta y a los 3 meses, pero no a los 12 meses. Además, el TIF se correlaciona con una mayor Cr al alta y el IMC con la Cr a los 12 meses (Tabla 4).

4.- CONCLUSIONES

En nuestro centro la incidencia de FRI es inferior (37,5% vs 53%) respecto a los datos nacionales (ONT). El análisis realizado no muestra una asociación significativa entre los diferentes tiempos de isquemia y la FRI. Sin embargo, parece que el TIF superior a 540 min y el tiempo desde la LET hasta la PCR superior a 15 min son factores de riesgo para la FRI. La edad del donante y estar en hemodiálisis son factores de riesgo de la FRI, pero la edad del donante no se asocia con una peor función renal a los 12 meses de seguimiento. Estos resultados apoyan el uso de donantes de mayor edad dado que no afectan a la función renal a largo plazo.

DONANTES (n 50)		TIEMPOS ISQUEMIA (minutos)	
Edad (IQR)	63 (56-68)	LET - PCR (IQR)	15 (11-18)
Varones (%)	65 (75,6%)	TIC funcional (IQR)	19 (14-22)
Mujeres (%)	21 (24,4%)	PCR - PERFUSION (IQR)	9 (8,3-10,8)
Criterios expandidos (%)	34 (68%)	TIF (IQR)	140 (375-1125)
RECEPTORES (n 68)		RESULTADOS	
Edad (media)	61 (52-66,3)	FRI (%)	30 (37,5%)
Varones (%)	67 (77,9%)	Supervivencia del injerto (%)	78 (90,7%)
Mujeres (%)	19 (22,1%)	Trasplantectomias (%)	1 (1,3%)
Diabetes Mellitus	32 (37,2%)	Cr 3 meses (IQR)(mg/dL)	1,49
IMC (media +/- DE)	27,1 +/- 4,5	Cr 1 año (IQR) (mg/dL)	1,44
Dialisis peritoneal (%)	24 (27,9%)	Cr en 2020 (IQR)(mg/dL)	1,53
Hemodialisis (%)	50 (58,1%)		
Anticipado (%)	12 (14%)		
Trasplante previo (%)	12 (14%)		
Diuresis Residual:			
<500ml	34 (39,5%)		
500-1000mL	17 (19,8%)		
>1000mL	35 (40,7%)		

LET: Limitación Esfuerzo Terapéutico; PCR: Parada Cardiorrespiratoria; TIC: Tiempo Isquemia Caliente; TIF: Tiempo Isquemia Fría; Cr: Creatinina; IMC: índice de Masa Corporal

	No-FRI	FRI	p <0,05
DONANTE			
Edad	60 (51-65)	65(57,5-70)	0,014
Varones	39 (78%)	22 (73,3%)	0,635
Mujeres	11 (22%)	8 (26,7%)	
Criterios Expandidos	27 (56,3%)	20 (66,7%)	0,36
RECEPTOR			
Edad	59 (50,5 - 66)	62(53,8 - 67,5)	0,171
Varones	37 (74%)	24 (80%)	0,542
Mujeres	13 (26%)	6 (20%)	
Diabetes Mellitus	16 (32%)	11 (36,7%)	0,669
IMC	26,9 ± 4,5	26,8 ± 4,6	0,949
Dialisis Peritoneal	16 (32,0%)	5 (16,7%)	0,131
Hemodialisis	22 (44,0%)	25 (83,3%)	0,001
Anticipado	12 (24,0%)		
Trasplante Previo	6 (12,0%)	5 (16,7%)	0,739
Diuresis Residual:			
<500ml	14(28%)	18(60%)	0,013
500-1000mL	10(20%)	5(16,7%)	
>1000mL	26(52%)	7 (23,3%)	
TIEMPOS DE ISQUEMIA			
LET - PCR	14(11- 18)	15(11 - 18)	0,897
TIC funcional	19 (15- 28)	18 (13 - 20)	0,13
PCR - PERFUSION	9 (7 - 10)	9(7 - 12)	0,635
TIF	520,5(358,8-1038,8)	915(380,8-1161,3)	0,303

	Cr al alta		Cr 3 meses		Cr a 12 meses	
	Rho	P	Rho	P	Rho	P
Edad receptor	0,113	0,317	-0,012	0,918	0,012	0,929
Edad donante	0,362	0,001**	0,219	0,056*	0,171	0,213
LET - PCR	0,166	0,158	0,064	0,599	-0,064	0,661
TIC funcional	-0,035	0,770	-0,044	0,718	-0,149	0,307
PCR - PERFUSION	-0,084	0,475	-0,148	0,218	-0,158	0,279
TIF	0,255	0,022**	0,132	0,253	-0,040	0,773
IMC	0,129	0,255	0,137	0,235	0,265	0,050*

(**) 95% CI; (*) 90% CI

	OR	IC 95% OR	
		Inferior	Superior
Edad donante	1,064	1,008	1,122
Edad donante ≥ 63	2,739	1,05	7,144
TIF >540'	1,308	0,526	3,25
LET - PCR >15'	2,087	0,781	5,58
DP	0,275	0,087	0,874
Hemodiálisis	3,636	1,144	11,555
DR >500mL	0,259	0,1	0,675

Low Albumin Levels Are Associated with Poorer Outcomes in a Case Series of COVID-19 Patients in Spain: A Retrospective Cohort Study

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BACKGROUND

The SARS-CoV-2 outbreak first identified in Wuhan in December 2019 has rapidly spread worldwide [1]. COVID-19 has a rather heterogenous presentation. While many patients remain asymptomatic carriers, others can show a wide array of symptoms, from mild flu-like manifestations such as dry cough, phlegm, myalgia or diarrhea, to severe pneumonia or even acute respiratory distress syndrome (ARDS) [1,2]. The exact pathobiology responsible for severe and critically ill cases is still not clear. It has been proposed that a hyperinflammatory syndrome may play a central role in the progression from mild to severe or critical COVID-19 [3].

OBJECTIVES

The objective of this study was to describe the epidemiological and clinical characteristics of 48 hospitalized patients with COVID-19 and to compare patients who were admitted to the intensive care unit (ICU) care with those who did not receive ICU care, staying at a ward.

MATERIAL AND METHODS

This is a retrospective study conducted at Son Llatzer University Hospital, a public tertiary care center in Mallorca, Spain; *Study population*: hospitalized COVID-19 positive patients by RT-PCR; *Variables*: Clinical and laboratory data collected at triage

RESULTS

Table 1. Baseline characteristics of 48 patients with COVID-19 at triage, prior to hospitalization.

Clinical Characteristics	All (n = 48)	Non-ICU (n = 27)	ICU (n = 21)	p Value
At triage				
Age, yrs.	65.98 (13.91) [33–88]	66.30 (14.90) [33–88]	65.57 (12.87) [44–82]	0.856
Males, n%	32 (67%)	18 (67%)	14 (67%)	1
Fever, °C	37.03 (0.94) [36–39]	36.84 (0.88) [36–39]	37.28 (0.98) [36–39]	0.147
Systolic Pressure, mmHg	129.6 (18.9) [90–180]	130.7 (16.6) [90–180]	128.1 (21.9) [90–180]	0.642
Diastolic Pressure, mmHg	73.3 (11.7) [50–111]	75.9 (12.1) [50–110]	70.03 (10.44) [52–92]	0.058
Heart Rate, bpm	85.6 (14.59) [58–120]	86.9 (17.4) [58–120]	83.8 (11.2) [58–106]	0.712
SpO ₂ , %	89.31 (10.64) [38–99]	93.44 (6.63) [66–99]	84 (12.51) [38–99]	<0.001 *
Symptoms Reported n%				
Asthenia	10/46 (21%)	6/25 (22%)	4/21 (19.1%)	1
Dyspnea	35/46 (76%)	16/26 (61%)	19/20 (95)	0.022 *
Vomiting	6/47 (13%)	4/25 (16%)	2/21 (9%)	0.870
Diarrhea	16/38 (42%)	12/25 (44%)	4/13 (31%)	0.070
Coughing	39/46 (85%)	20/27 (74%)	19/20 (95%)	0.225
Fever	48/48 (100%)	27/27 (100%)	21/21 (100%)	1
ARDS	20/46 (44%)	0/27 (0%)	21/21 (100%)	<0.001 *
Pneumonia	44/47 (94%)	24/27 (89%)	20/20 (100%)	0.078
Bilateral pneumonia	44/47 (94%)	21/27 (77%)	20/20 (100%)	NA
Comorbidities n%				
Hypertension	33/47 (70%)	22/27 (82%)	11/20 (55%)	0.101
Dyslipidemia	29/47 (62%)	16/27 (60%)	13/20 (65%)	1
Type 2 Diabetes	11/45 (24%)	9/27 (33%)	5/20 (25%)	0.286
Cardiovascular disease	14/47 (30%)	7/27 (26%)	7/20 (35%)	0.726
Ictus	3/46 (6%)	2/27 (7%)	1/20 (5%)	0.662
Cancer or another malignancy	10/47 (21%)	4/27 (15%)	6/20 (30%)	0.640
COPD	5/47 (11%)	4/27 (15%)	1/20 (5%)	0.544
VII	1/46 (2%)	0/26 (0)	1/20 (5%)	0.894
Renal chronic disease	8/46 (17%)	4/27 (15%)	4/19 (21%)	0.877
Other, n%	26/47 (55%)	13/27 (52%)	12/20 (60%)	0.921
Smoking	10/47 (21%)	6/26 (22%)	4/20 (19%)	0.934

Data are mean (SD), range [] or %. * statistically significant. Not all the patients had complete information in all the comorbidities, or symptoms. In those cases, the total number of patients are indicated for every outcome.

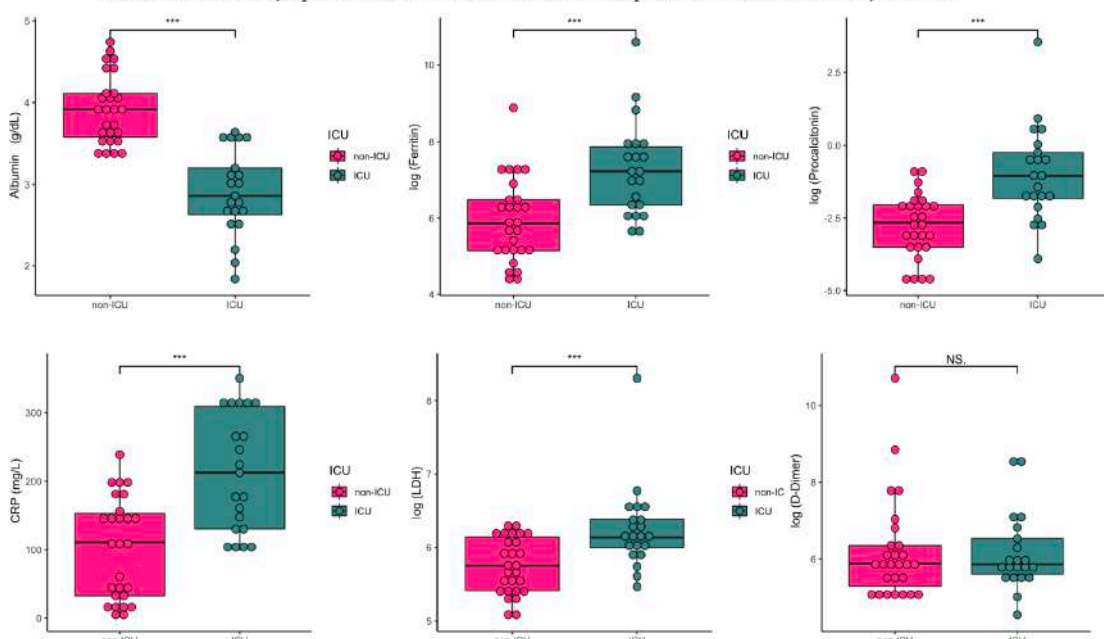


Figure 1. Representative scatterplots of inflammatory markers in the 48 patients with COVID-19. ***statistically significant; CRP (C-reactive protein); LDH (lactate dehydrogenase)

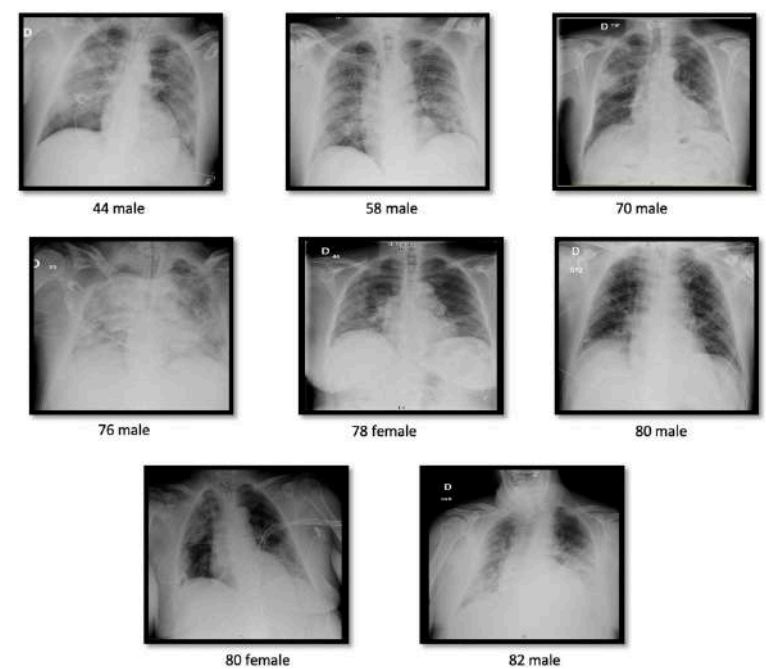


Figure 2. Chest X-ray images from all the deceased intensive care unit (ICU) patients. Most of the patients presented bilateral pneumonia at triage.

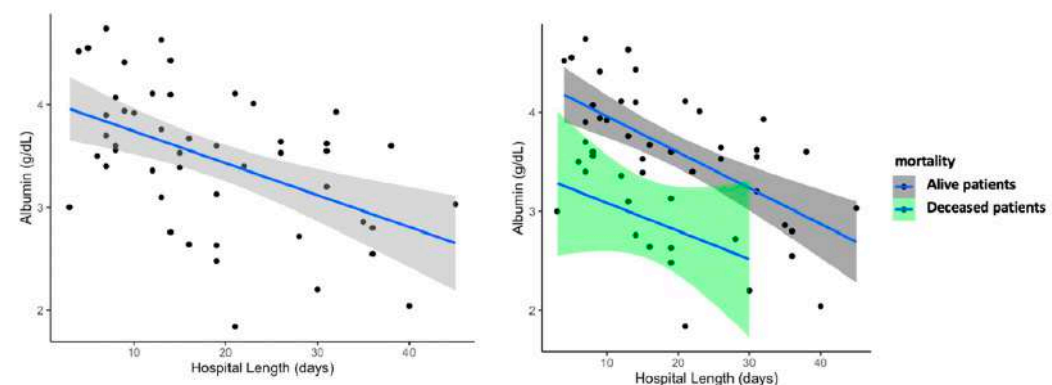


Figure 3. Association of serum albumin levels with hospital length in COVID-19.

CONCLUSIONS

ICU-patients had lymphopenia as well as hypoalbuminemia. LDH, PCR and procalcitonin were significantly higher in ICU patients compared to non-ICU ($p < 0.001$). In multivariable linear regression models, lower albumin levels were associated with poor prognosis measured as longer hospital length ($r = -0.472$, $p < 0.001$) and mortality ($r = -0.424$, $p = 0.003$). Critically ill patients with COVID-19 present lymphopenia, hypoalbuminemia and high levels of inflammation.

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[1] Huang C et al., 2019; [2] Wang D et al., 2020; [3] de la Rica et al., 2020

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INFLUÈNCIA DEL TEIXIT ADIPÓS BLANC INFLAMAT SOBRE LA RESPOSTA VASCULAR ALS ESTROGENS

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INTRODUCCIÓ

El teixit adipós juga un paper crucial com a regulador de la salut cardiovascular mitjançant la secreció d'adipoquines i productes bioactius implicats en un ampli ventall d'efectes paracrins i endocrins sobre el sistema vascular. En l'obesitat, la resistència a la insulina i la inflamació sistèmica associada provoquen una alteració de la funció del teixit adipós (Trayhurn et al., 2008; Chait et al., 2020). D'aquesta manera, el secretoma del teixit adipós experimenta un canvi de perfil caracteritzat per un increment de l'alliberació d'adipoquines proinflamàtores i proaterogèniques que donen lloc a alteracions a nivell cardiovascular (Hajer et al., 2008).

Diversos estudis epidemiològics suggereixen que la prevalença de síndrome metabòlica en dones premenopàusiques obeses i diabètiques és similar a la de les dones postmenopàusiques (Nakhjavani et al., 2014). A més, l'estat diabètic podria atenuar els efectes protectors dels estrògens sobre l'aparició de malalties cardiovasculars (MCV) en dones premenopàusiques (Di Carli et al., 2002; Masding et al., 2003; Regitz-Zagrosek et al., 2007).



OBJECTIU

Estudiar els efectes de l'ovariectomia i el tractament amb 17β-estradiol (E2) sobre el secretoma del teixit adipós gonadal (TABg) i la seva influència sobre la funció endotelial, en un context d'obesitat i diabetis.



MATERIALS I MÈTODES

Es van combinar estudis *in vivo*, *ex vivo* i *in vitro*. Rates femella ZDF (Zucker Diabetic Fatty rats) de 15 setmanes d'edat, es van dividir en 3 grups: SHAM (*sham-operated*), OVA (ovariectomitzades) i OVA+E2 (ovariectomitzades i tractades amb E2 durant 5 setmanes - 3 µg/dia). Es van cultivar explants de TABg per a l'obtenció de medis condicionats, que es van utilitzar, en combinació amb TNFα (10ng/ml), pel tractament *in vitro* de les cèl·lules endotelials HUVEC. Es va mesurar l'expressió d'adipoquines proinflamàtores i quimiocines al teixit adipós i els nivells d'adiponectina als medis condicionats. A les cèl·lules HUVEC, es va analitzar la viabilitat cel·lular, la diferenciació mitocondrial (*Mitotracker™ Green FM*) i l'expressió de gens marcadors de disfunció endotelial i d'inflamació.



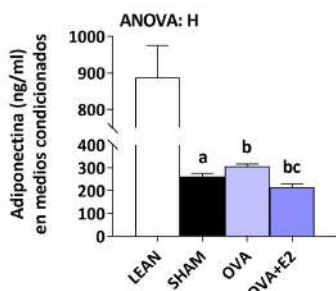
RESULTATS

A les rates diabètiques i obesas, l'ovariectomia millorà el secretoma del TABg atenuant l'expressió d'adipoquines proinflamàtores i quimiocines i estímulant l'alliberació d'adiponectina al medi condicionat, mentre que l'E2 augmentà el grau d'inflamació. A més, el tractament de les HUVEC amb el medi condicionat provinent de les rates OVA, estimulà la funció mitocondrial i reduí l'expressió de marcadors de disfunció endotelial i d'inflamació, efecte que no s'observà quan foren tractades amb el medi condicionat provinent de les rates OVA+E2.

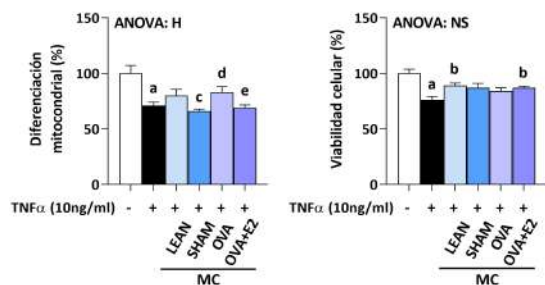
L'expressió de citoquines proinflamàtores s'activà en el TABg de les rates SHAM. L'ovariectomia atenuà l'expressió de les citoquines mentre que el tractament amb E2 estimulà l'expressió de TNFα, PAI-1, MIP-1α i CD68, l'expressió de la IL-6 i IL-1β es mantení sense canvis.

	LEAN	SHAM	OVA	OVA+E2	ANOVA
IL-6	1,00 ± 0,24	6,44 ± 0,40 ^a	4,56 ± 0,54 ^b	4,40 ± 0,59 ^b	H
TNFα	1,00 ± 0,15	3,56 ± 0,21 ^a	2,73 ± 0,25 ^b	3,98 ± 0,36 ^c	H
IL-1β	1,00 ± 0,20	1,70 ± 0,30 ^a	1,14 ± 0,14 ^b	0,95 ± 0,24 ^b	NS
PAI-1	1,00 ± 0,10	6,01 ± 0,83 ^a	2,65 ± 0,26 ^b	6,35 ± 0,62 ^c	H
MIP-1α	1,00 ± 0,22	9,49 ± 0,70 ^a	7,13 ± 0,81 ^b	10,5 ± 0,68 ^c	H
CD68	1,00 ± 0,17	14,1 ± 1,10 ^a	11,89 ± 1,00 ^b	17,8 ± 1,99 ^c	H
Adipoq	1,00 ± 0,20	0,42 ± 0,05 ^a	0,54 ± 0,06	0,34 ± 0,04 ^c	H

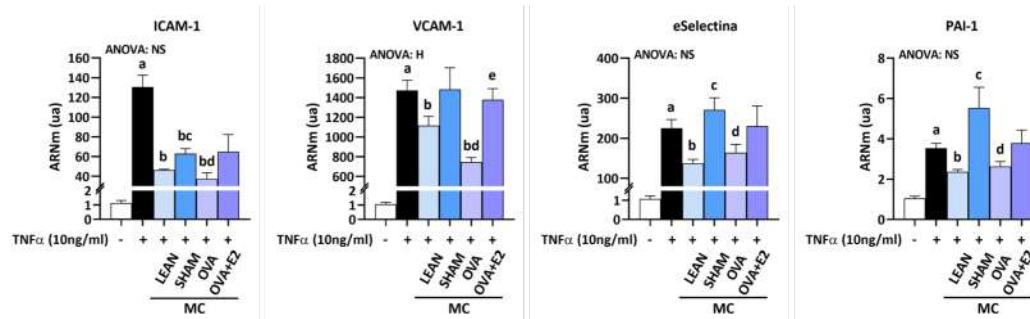
L'ovariectomia augmentà de forma significativa la concentració d'adiponectina alliberada al medi.



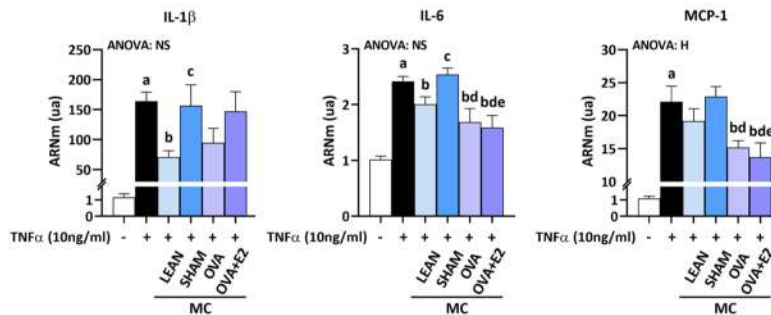
El tractament amb TNFα disminuí la viabilitat de cel·lular i la diferenciació mitocondrial de les HUVEC. L'ovariectomia estimulà la diferenciació mitocondrial mentre que l'E2 revertí els efectes.



El tractament amb TNFα activà l'expressió de marcadors de disfunció endotelial a les HUVEC. L'ovariectomia atenuà els efectes induïts per TNFα, l'E2 incrementà únicament l'expressió de VCAM-1.



De la mateixa manera, el tractament amb TNFα activà l'expressió de marcadors d'inflamació a les HUVEC. El medi obtingut de les rates OVA atenuà els efectes induïts per TNFα, efecte que no s'observà que les HUVEC foren tractades amb el medi de les rates OVA+E2.



CONCLUSIONS



En un model d'obesitat i diabetis, el tractament amb E2 induiria, en el TABg un secretoma proaterogènic, la qual cosa suposaria la pèrdua de part dels efectes protectors de l'hormona sobre la inflamació i la funció endotelial.



Els nostres resultats recolzen la importància de les hormones sexuals femenines com a factors a tenir en compte en les estratègies de prevenció i tractament de les MCV en el context de la síndrome metabòlica.

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