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The Relentless Progression of Metabolic Dysfunction–associated Steatotic Liver Disease in Liver Transplantation in Spain

Laura Martínez-Arenas, MSc,[1] Ângela Carvalho-Gomes, PhD,[2] Enrique Vidal, PhD,[3] Danielle Brandman, MD, PhD,[4] Saleh Elwir, MD, PhD,[5] Mohammad S. Siddiqui, MD, PhD,[6] Sanjaya K. Satapathy, MD, PhD,[7] Coleman Smith, MD, PhD,[8] Mary E. Rinella, MD, PhD,[9] Fernando Díaz-Fontenla, MD, PhD,[10] Sara Lorente, MD, PhD,[11] Marta Guerrero-Misas, MD, PhD,[12] Ignacio Herrero, MD, PhD,[13] Nazia Selzner, MD, PhD,[14] Kymberly D. Watt, MD, PhD,[15] and Marina Berenguer, MD, PhD[16]

Background. Metabolic dysfunction–associated steatotic liver disease (MASLD) is increasingly recognized as a significant indication for liver transplantation (LT) in North America. Yet data on its impact in other countries, such as Spain, remain limited. This study aimed to evaluate the prevalence and trajectory of MASLD-related LT in Spain and compare these findings with broader national data and international data sets. **Methods.** Multicenter retrospective cohort study including adults (18 y and older) undergoing LT for MASLD between 2010 and 2023 in 5 large Spanish centers. Additional data were obtained from the Spanish Transplant Registry (Organización Nacional de Trasplantes) and high-prevalence LT centers in the United States (n = 7) and Canada (n = 1). **Results.** Among 3448 LTs performed in the 5 Spanish centers, 3.4% (n = 117) were MASLD-related. An increasing trajectory of MASLD-related LT was observed, with predictions suggesting a rise to 5.4%–10.8% of LTs for MASLD by 2028. These trends were consistent with Organización Nacional de Trasplantes data. Compared with North American data, the growth trajectory in Spain showed a less steep increase. Hepatocellular carcinoma rates were higher in the Spanish MASLD-LT recipients, yet metabolic comorbidities were frequent in all populations. **Conclusions.** The burden of MASLD-related LT in Spain is growing, yet at a less pronounced rate than in the United States/Canada. Whether this slower increase will persist or decline in the future as newer antiobesity and MASLD-related drugs are increasingly used is still unknown. In the meantime, our results highlight the need for tailored approaches to management and prevention in the Spanish population and underscore the importance of continued monitoring and research into the evolving impact of MASLD on LT in Spain and beyond.

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[1] *Hepatology, Hepatobiliopancreatic Surgery and Transplant Laboratory, IIS La Fe Health Research Institute, Universitat Politècnica de València, CIBEREHD, ISCIII, Valencia, Spain.*

[2] *Hepatology, Hepatobiliopancreatic Surgery and Transplant Laboratory, IIS La Fe Health Research Institute, CIBEREHD, ISCIII, Valencia, Spain.*

[3] *Clinical and Translational Oncology Laboratory, IIS La Fe Health Research Institute, Valencia, Spain.*

[4] *Division of Gastroenterology and Hepatology, University of California at San Francisco, San Francisco, CA.*

[5] *Department of Internal Medicine, Baylor University Medical Center, Dallas, TX.*

[6] *Divisions of Gastroenterology and Hepatology, Virginia Commonwealth University, Richmond, VA.*

[7] *Division of Surgery, Methodist University Hospital Transplant Institute, Memphis, TN.*

[8] *MedStar Georgetown Transplant Institute, MedStar Georgetown University Hospital, Washington, DC.*

[9] *Division of Gastroenterology and Hepatology, Northwestern University, Chicago, IL.*

[10] *Liver Unit, Digestive Department, Gregorio Marañón University General Hospital, Madrid, Spain.*

[11] *Hepatology and Liver Transplantation Unit, Lozano Blesa University Clinic Hospital, Aragón Health Research Institute (IIS Aragón), University of Zaragoza, Zaragoza, Spain.*

[12] *Department of Hepatology and Liver Transplantation, Reina Sofía University Hospital, Maimonides Institute of Biomedical Research of Cordoba, CIBEREHD, ISCIII, Córdoba, Spain.*

[13] *Department of Internal Medicine, University Clinic of Navarra, Navarra Health Research Institute, CIBEREHD, ISCIII, Pamplona, Spain.*

[14] *Department of Medicine, Ajmera Transplant Center, University of Toronto, Toronto, ON, Canada.*

[15] *Division of Gastroenterology and Hepatology, Department of Medicine, Mayo Clinic, Rochester, MN.*

[16] *Hepatology and Liver Transplantation Unit, La Fe University and Polytechnic Hospital, IIS La Fe Health Research Institute, University of Valencia, CIBEREHD, ISCIII, Valencia, Spain.*

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INTRODUCTION

Metabolic dysfunction–associated steatotic liver disease (MASLD) is known to be the most common chronic liver disease globally, with adult population prevalence rates of 31.2% and 25.1% in North America and Europe, respectively.[1] In United States, >80 million individuals were estimated to have MASLD in 2016.[2] In Spain, although MASLD is also a widespread cause of liver disease, particularly in individuals with features of metabolic syndrome (MS), its exact prevalence and incidence are not completely known.

Poor metabolic health drives this increasing MASLD prevalence, with 80%–90% and 50%–70% of individuals living with obesity and diabetes having coexisting MASLD, respectively.[3] Furthermore, MASLD can evolve over time to advanced disease stages. MASLD complications, such as metabolic dysfunction–associated steatohepatitis (MASH), MASLD-related fibrosis and cirrhosis, or hepatocellular carcinoma (HCC), are associated with an increased risk of liver-related morbidity and mortality, and the need for liver transplantation (LT).[4] Indeed, MASLD is the second most common indication for LT in United States and is expected to achieve the top indication in the coming years.[5-7] In Europe, although MASLD is emerging as a leading cause of chronic liver disease, the impact on LT waiting lists has been negligible, until recently.[8-10]

Given the relative low frequency of this indication in Spain and the fact that most studies on trends in LT for MASLD have been performed in large North American data sets, the aims of this study were (1) to establish the prevalence of MASLD-LT and the estimated trajectory for the future burden of MASLD-related LT in Spain based on a data set from selected Spanish LT centers; (2) to compare and validate findings from the initial data set against broader national data, identifying potential regional or institutional disparities; and (3) to compare the prevalence, phenotype, and survival of patients transplanted for MASLD across Spain versus multiple high-prevalence international centers.

MATERIALS AND METHODS

Sampling Population

We conducted a multicenter retrospective cohort study in which adult patients transplanted for MASLD-related cirrhosis from 2010 to 2023 in 5 LT reference centers in Spain were included. The selection of centers and period of inclusion were based on data availability and the cooperation of national experts. The 5 Spanish centers represent the largest LT centers in Spain, distributed throughout the Regions.

Prespecified criteria for diagnosing pure MASLD were applied in all centers to select the sampling population: pre-LT presence of overweight/obesity and/or type 2 diabetes mellitus (T2DM) as well as dyslipidemia, hypertension (HTN), or steatosis in >5% of hepatocytes on a previous liver biopsy or the explant, in the absence of risky alcohol intake (women: ≥20 g/d or men: ≥30 g/d) and other well-known causes of liver fat accumulation, such as drugs with a steatogenic potential, Wilson's disease, and hepatitis C virus genotype 3.[8,9,11,12] After an exhaustive review of the clinical charts, patients who met these criteria were included. Participants transplanted for MASLD-associated HCC and cryptogenic cirrhosis with MS were also included in the study. Milan criteria were the standard of care to select candidates with HCC for LT.[13] We excluded patients under the age of 18 y, those positive for HIV infection, and those with previous or combined LT, except simultaneous liver-kidney transplantation. Although patients with overlap MASLD (defined by meeting the criteria for both MASLD diagnosis and any coexisting etiology of chronic liver disease) were not included in the primary analysis, a secondary analysis was done, including this subgroup of patients, to further compile data on those with metabolic dysfunction and alcohol associated steatotic liver disease.[14,15]

In addition, to further assess the future potential impact of MASLD in all Spanish transplant centers, we also performed a similar analysis using the national database of the Organización Nacional de Trasplantes (ONT), with the understanding of the potential limitations associated with the "MASLD code" in this National Transplant Registry, since MASLD diagnosis (or previous nonalcoholic steatohepatitis [NASH]) has only been recently incorporated and there has been a lack of consistent criteria to define MASLD-related LT indication.[14] On this point, we included all adult patients transplanted in all Spanish LT centers between 2010 and 2023 for "cryptogenic cirrhosis," "other causes of cirrhosis," or "HCC" and "MASLD" or "NASH" based on the ONT database.

Finally, to evaluate the impact of MASLD in high-prevalence international centers compared with the Spanish centers, we performed an analysis that included data from multiple reference LT centers in the United States and Canada. Collaboration with the established working group on MASLD and LT (NailNASH consortium[16]), including adult patients transplanted for MASLD-related cirrhosis from 2010 to June 2017 in 7 US centers, represented US data. In Canada, adult patients transplanted for MASLD-related cirrhosis from 2010 to 2020 in the center with the greatest transplant activity were included. All participating centers followed the same study protocol.

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Correspondence: Marina Berenguer, MD, PhD, Hepatology and Liver Transplantation Unit, Hospital Universitario y Politécnico La Fe, 106 Fernando Abril Martorell Avenue, F Tower, 5th Floor, 46026 Valencia, Spain. (marina.berenguer@uv.es); Laura Martínez-Arenas, MSc, Hepatology, Hepatobiliopancreatic Surgery and Transplant Laboratory, La Fe Health Research Institute, 106 Fernando Abril Martorell Ave, A Tower, 5th Floor, lab 5.28, 46026 Valencia, Spain. (laura_munera15@hotmail.com).

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Data Collection

Data were retrospectively gathered from medical records, which contained clinical and demographic information, and compiled into a unified database for analysis. Variables recorded at LT were sex, age, native model for end-stage liver disease (MELD) score (no exception points), body mass index (BMI), presence of HCC, T2DM, obesity, HTN, dyslipidemia, prior cardiovascular disease (CVD), portal vein thrombosis, and chronic kidney disease. Furthermore, survival rates up to 5 y post-LT were recorded.

Definitions of Metabolic Risk Factors

1. Overweight/obesity: overweight was defined as a BMI ≥25 and <30 kg/m^2, and obesity as a BMI ≥30 kg/m^2.[17]
2. T2DM: defined as abnormal blood glucose level—fasting glucose ≥126 mg/dL or 2-h post-load glucose ≥200 mg/dL in at least 3 consecutive determinations—or the need for antidiabetic drug treatment.[18]
3. MS: defined as at least 3 of the following criteria: waist circumference >102 cm (men) or >88 cm (women), plasma triglycerides levels ≥150 mg/dL, HDL cholesterol levels <40 mg/dL (men) or <50 mg/dL (women), blood pressure ≥130/85 mm Hg, and impaired fasting plasma glucose levels ≥110 mg/dL.[19]
4. HTN: using the hypertension diagnostic criteria from this era of transplant recipients, this is defined as a systolic blood pressure ≥140 mm Hg and/or a diastolic blood pressure ≥90 mm Hg in at least 3 consecutive determinations or the need for antihypertensive drug treatment.[20]
5. Dyslipidemia: fasting total cholesterol levels ≥240 mg/dL and/or fasting triglyceride levels ≥150 mg/dL in at least 3 consecutive determinations or the need for antilipidemic drug treatment.[21]
6. CVD: defined as any of the following events: arrhythmia, transient ischemic attack, stroke, heart failure, peripheral arterial disease, unstable angina, or myocardial infarction.[22]

Statistical Analysis

The annual number of LT and the number of transplants due to MASLD were used to calculate the annual proportion of LT performed for MASLD indication per year; subsequently, the observed trajectory of LT for MASLD over time was developed. Based on these numbers, future predictions up to 5 y were generated. The MASLD observed trajectories and the MASLD predictions were addressed following a similar modeling strategy as previously described.[23] It assumed that transplant numbers followed a Poisson distribution and used general additive models to estimate smooth time trajectories. Differences between data sets were compared by fitting 2 model types: one common model for all data sets, and another that allowed for different trajectories per data set. In essence, if the common model was found to better describe the data, there was low evidence for differences among data sets. In contrast, data sets differed if the model allowing for different trajectories better described the data. The models were compared using the coefficient of determination (R^2) and the Akaike information criterion. Predicted trajectories for MASLD rates contained 50% and 95% prediction intervals.

Categorical variables were reported as percentage relative frequency (absolute frequency). Continuous variables were reported as mean ± SD. Categorical variables were compared using the chi-square test. Continuous variables were assumed to follow a normal distribution and have equal variances, according to the central limit theorem,[24] and were compared using the independent-sample T test computed from summary data. Survival was plotted with Kaplan-Meier curves and compared using the log-rank test. A P value of <0.05 was considered as statistical significance. Statistical analysis was performed using R version 4.0.2 (R Foundation for Statistical Computing).

Ethics Approval

All research was conducted following both the Declaration of Helsinki and the Declaration of Istanbul. The study protocol was approved by La Fe University and Polytechnic Hospital's local ethics committee (Comité de Ética de la Investigación con Medicamentos [CEIm] del Hospital Universitario y Politécnico La Fe, February 26, 2020, registration number: 2019/0124) and by the Spanish Agency of Medicine and Sanitary Products (Agencia Española de Medicamentos y Productos Sanitarios [AEMPS], January 20, 2020, reference: 54823DD7BB). A protocol agreement was signed by principal investigators of the other centers (La Fe University and Polytechnic Hospital is the coordinator center in charge of data storage and analysis).

RESULTS

Study Population

Of 3448 LTs performed between 2010 and 2023 in the 5 Spanish LT centers, 3.4% (n = 117) had underlying MASLD-related disease. The main characteristics of the Spanish data set are described in Table 1. The mean age was 62.0 ± 6.5 y, and 35.9% were women. The mean MELD score was 14.4 ± 6.8, and the mean BMI was 30.0 ± 4.8 kg/m^2. Almost half of the patients had an HCC at the time of LT. Comorbid conditions, such as T2DM, obesity, HTN, dyslipidemia, and CVD, were found in the majority of patients. Portal vein thrombosis and chronic kidney disease rates were 23.1% (n = 27) and 28.2% (n = 33), respectively. Comorbid conditions among overlap (excluded) versus pure (included) MASLD did not differ (**Table S1, SDC,** https://links.lww.com/TP/D317). T2DM and HTN rates were higher in the MASLD cohort with HCC (P < 0.05; **Table S2, SDC,** https://links.lww.com/TP/D317). Regarding the HCC features, most patients were within Milan criteria (80.0%, n = 40), a high proportion of patients were treated with locoregional therapies (86.0%, n = 43), intravascular invasion was present in 16.0% (n = 8), and 86.0% of HCC were moderately or poorly differentiated (72.0%, n = 36, and 14.0%, n = 7, respectively; **Table S3, SDC,** https://links.lww.com/TP/D317).

Table S4 (**SDC,** https://links.lww.com/TP/D317) summarizes the main features of MASLD-LT patients in the US and Canadian data sets. A lower proportion of patients in these North American centers had HCC (P < 0.001), and the MELD score was accordingly higher (P < 0.001). US and Canadian cohorts were younger (P = 0.010 and P = 0.176, respectively) and had higher rates of men (P = 0.008). A longer intensive care unit stay (P < 0.001) and hospital stay (P = not significant) were observed in

TABLE 1.

Characteristics and phenotype of the Spanish MASLD data set

	N = 117
Years	2010–2023
Centers	5
Age at LT, y, mean ± SD	62.0 ± 6.5
Sex, female, n (%)	42 (35.9)
MELD score, mean ± SD	14.4 ± 6.8
BMI, mean ± SD	30.0 ± 4.8
HCC, n (%)	50 (42.7)
T2DM, n (%)	79 (67.5)
Obesity, n (%)	70 (59.8)
HTN, n (%)	75 (64.1)
Dyslipidemia, n (%)	50 (42.7)
Prior CVD, n (%)	23 (19.7)
PVT, n (%)	27 (23.17)
CKD, n (%)	33 (28.2)

BMI, body mass index; CKD, chronic kidney disease; CVD, cardiovascular disease; HCC, hepatocellular carcinoma; HTN, hypertension; LT, liver transplantation; MASLD, metabolic dysfunction-associated steatotic liver disease; MELD, model for end-stage liver disease; PVT, portal vein thrombosis; T2DM, type 2 diabetes mellitus.

the Spanish data set compared with the Canadian data set (**Table S5, SDC,** https://links.lww.com/TP/D317).

Actuarial survival at 1, 3, and 5 y post-LT was, respectively, 0.95, 0.88, and 0.83 in the Spanish data set, similar to that observed in the US and Canadian patients (P = not significant; **Figure S1, SDC,** https://links.lww.com/TP/D317).

MASLD Trajectory

Of the 3448 LTs performed in the 5 Spanish LT centers (Figure 1A, orange trajectory), 117 (3.4%) had underlying MASLD-related disease. Analyzing MASLD-related LT over time, an increasing trajectory in the number of LT for MASLD was observed (Figure 1B, orange trajectory), as well as in the proportion of MASLD among total LT over time (Figure 1C, orange trajectory). Based on our model, we estimated an increase in the transplants for MASLD for the coming years (Figure 2). Based on our predictions, by 2028, between 5.4% and 10.8% of LT in the Spanish centers will be due to MASLD (Table 2). When considering overlap MASLD individuals, the proportion of LT due to overlap MASLD is also estimated to increase in the following years in the Spanish centers (**Figure S2, SDC,** https://links.lww.com/TP/D317), reaching figures between 15.3% and 38.2% in 2028 (**Table S6, SDC,** https://links.lww.com/TP/D317).

The evolution of LT for MASLD, considering data from the Spanish Transplant Registry (ONT), is described in Figure 1 (pink trajectory). Of 15911 LTs performed between 2010 and 2023 in all Spanish LT centers (Figure 1A, pink trajectory), 3.0% (n = 473) had underlying MASLD-related disease (Figure 1B, pink trajectory). Results using the Spanish Transplant Registry followed similar trends in the proportion of MASLD among total LTs over time compared with those depicted using detailed data from the 5 largest LT centers (Figure 1C; Akaike information criterion decreased from 158.2032 to 156.8233 for the common model for the 2 data sets).

Figure 3 illustrates the progression of LT for MASLD based on data from US and Canadian centers, compared with the 5 Spanish centers. Of 5906 LTs performed in the 7 US centers between 2010 and June 2017 (Figure 3A), 12.0% (n = 709) were performed for MASLD-related liver disease, and of 1899 LTs performed in the Canadian center from 2010 to 2020 (Figure 3A), 11.8% (n = 224) described MASLD as the primary cause. Analyzing MASLD-related LT over time, the Spanish, Canadian, and US data sets presented an increasing trajectory in the number of LT for MASLD over time (Figure 3B), as well as in the proportion of MASLD on total LT over time (observed from 2013 onward in the US data), yet with differences in the "slope" (Akaike information criterion decreased from 199.2587 to 194.9240 for the model allowing different temporal trajectories per data set), with the Spanish data set having reached the lowest numbers (Figure 3C).

DISCUSSION

This multicenter retrospective cohort study shows an increase in LT for MASLD over time in Spain, with overlapping and comparable trajectories between 5 large LT centers with detailed, reviewed data and the Spanish Transplant Registry (ONT). It predicts a growing burden of disease for the Spanish transplant community in the years to come.

A progressive increase in patients with MASLD cirrhosis has been observed worldwide, concurrent with the epidemic of obesity and diabetes, with a rise of 170% of new waitlist registrants with MASLD from 2004 to 2013 in the United States.[25] To date, the data on this indication elsewhere is relatively small.[10] In particular, in Spain, there has been no data on the incidence and prevalence of MASLD-LT. Although there is a general conviction that MASLD is a disease responsible for LT infrequently relative to other nations, we are observing in daily clinical practice an increasing number of patients with advanced decompensated liver disease from MASLD. Preliminary data from La Fe University Hospital (the largest LT center in Spain) pointed to a prevalence of MASLD cirrhosis of around 5%.[8]

Our study reveals a prevalence of 3.4% for MASLD cirrhosis as an LT indication in Spain, and based on a prediction model, expectations are that by 2028, between 5.4% and 10.8% of LT in the Spanish centers will be due to MASLD. The observed increase in MASLD-related LT in the initial data set of 5 Spanish transplant centers aligns closely with the trends noted in the broader Spanish Transplant Registry (ONT). This consistency validates the representativeness of the selected centers and highlights the growing burden of MASLD across Spain. These 5 centers allowed for more granular data analysis on MASLD-associated cardiometabolic risk factors, as well as other possible non-MASLD causes. This allowed for the generation of predictions for "pure MASLD" and "combined MASLD (particularly with alcohol)".[15] Indeed, it is still unclear whether the bulk of MASLD cases are pure MASLD versus mixed (+ alcohol ± evidence of prior hepatotropic infections) indications and whether there are differences in terms of cardiometabolic profile among these indications. Of the 93 individuals (56%) excluded from the Spanish centers because they had a diagnosis of

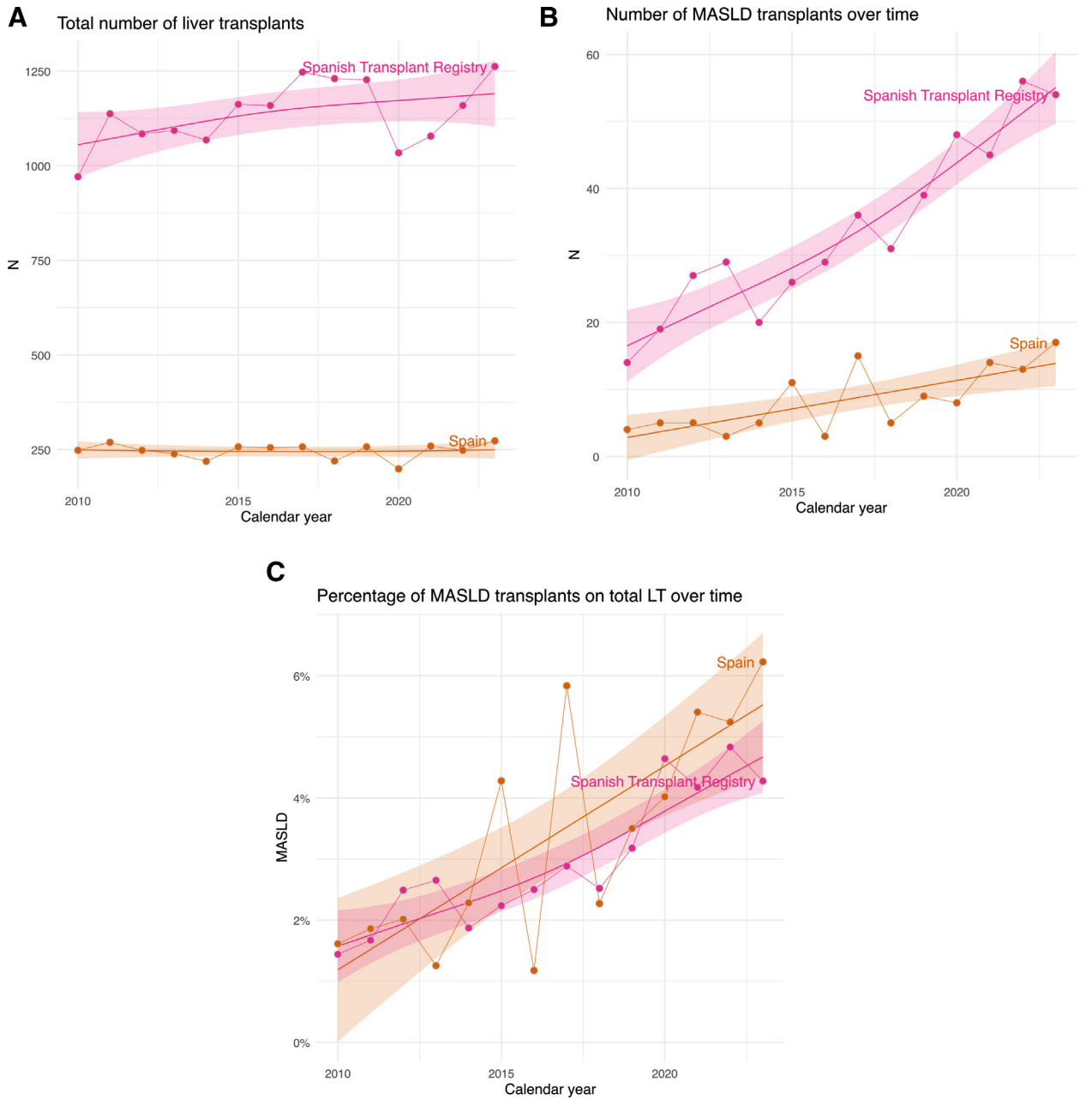

FIGURE 1. Evolution of transplants for MASLD between 2010 and 2023 in the 5 Spanish LT centers (orange) and in the Spanish Transplant Registry (pink). A, Total number of LT over time. B, Number of transplants for MASLD over time. C, Proportion of MASLD on total LT over time. R^2 = 75% and AIC = 156.8233 for the common model for 2 data sets; R^2 = 75% and AIC = 158.2032 for the model allowing different temporal trajectories per data set. A, Five Spanish centers (n = 3448): n = 248 in 2010, n = 255 (1.0×) in 2016 and n = 273 (1.1×) in 2023; Spanish Transplant Registry (n = 15911): n = 971 in 2010, n = 1159 (1.2×) in 2016 and n = 1262 (1.3×) in 2023. B, Five Spanish centers (n = 117): n = 4 in 2010, n = 3 (0.8×) in 2016, and n = 17 (4.3×) in 2023; Spanish Transplant Registry (n = 473): n = 14 in 2010, n = 29 (2.1×) in 2016, and n = 54 (3.9×) in 2023. C, Five Spanish centers: 1.6% in 2010, 1.2% (0.8×) in 2016, and 6.2 (3.9×) in 2023; Spanish Transplant Registry: 1.4% in 2010, 2.5 (1.8×) in 2016, and 4.3% (3.1×) in 2023. AIC, Akaike information criterion; LT, liver transplantation; MASLD, metabolic dysfunction–associated steatotic liver disease.

overlap MASLD, the cardiometabolic risk did not differ from the pure MASLD data set, and predictions showed similar trends. More data are needed in this overlap patient population.

When comparing our findings to those from North America, distinct differences emerge. Although the trajectory of MASLD-related LT in Spain exhibits a relatively linear increase over time, the slopes in North American data sets are significantly steeper, reflecting a more rapid growth in MASLD prevalence and its impact on LT waiting lists. In fact, MASLD was the second most common indication for LT in the United States in 2019 and the fastest increasing indication.[5] Although comparisons with national registry data from the United States and Canada could provide a broader epidemiological context, our study focused on data from selected centers using a harmonized protocol. This approach allowed for a more consistent and detailed analysis across sites. Future studies could expand this comparison using national registry data to complement our findings.

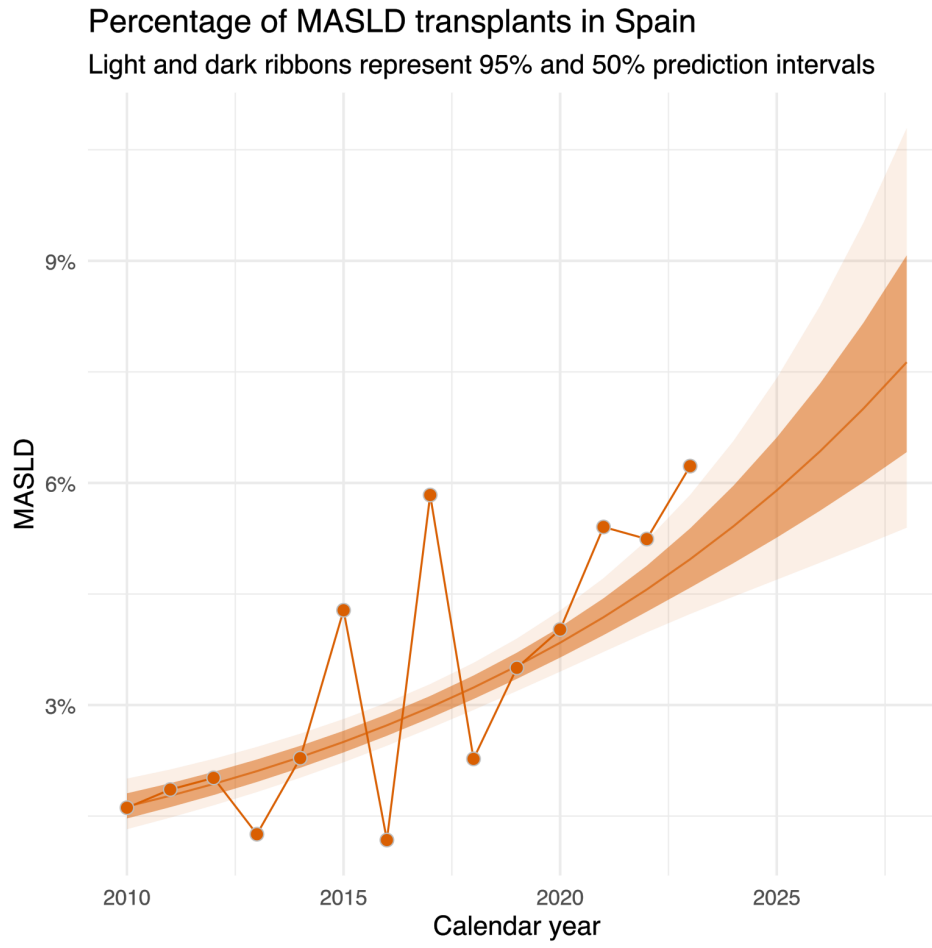

FIGURE 2. Predicted trajectory of transplant proportion for MASLD from 2024 to 2028, considering the observed MASLD data in the 5 Spanish LT centers from 2010 to 2023. Light and dark ribbons represent 95% and 50% prediction intervals, respectively. An estimated 7.6% (95% PI, 5.4%-10.8%; n = 22.4) of transplants for MASLD in 2028, for example, 4.8× compared with 2010, 6.3× compared with 2016, and 1.2× compared with 2023. LT, liver transplantation; MASLD, metabolic dysfunction–associated steatotic liver disease; PI, prediction interval.

Comparing data from higher MASLD prevalence international LT centers to characterize the trajectory of MASLD as an indication for LT, we were able to establish that our Spanish community is experiencing a slower growth of MASLD-related LT recipients compared with that observed in the 2 North American data sets. These contrasting patterns may be attributed to earlier and more widespread obesity and diabetes epidemics in North America, which have accelerated the progression of MASLD-related liver disease compared with Spain.[1,26-28] Protective dietary patterns, such as adherence to the Mediterranean diet and calorie restriction, may be linked to a lower risk of obesity, diabetes, and MS in the Spanish population, and consequently lower figures of MASLD-related LT.[29,30] Additionally, despite its high global prevalence, MASLD is often underrecognized because of the lack of reliable noninvasive biomarkers for diagnosis and staging. It is estimated that about 16% of patients with MASLD have MASH, resulting in a global MASH prevalence of 5% in the general population.[1] Our study reveals a prevalence of 3.4% for MASLD cirrhosis as an LT indication in Spain. This figure indicates that the proportion

TABLE 2.

Five-year predictions of the total number of LT and the number of transplants for MASLD between 2024 and 2028 in the 5 Spanish centers

Year	Total LT, n	MASLD-LT, % (n)	95% PI	50% PI
2024	264.9	5.4 (14.3)	4.5-6.6	4.9-6.0
2025	271.8	5.9 (16.0)	4.7-7.4	5.3-6.6
2026	278.9	6.4 (18.0)	4.9-8.4	5.6-7.3
2027	286.1	7.0 (20.0)	5.2-9.5	6.0-8.2
2028	293.6	7.6 (22.4)	5.4-10.8	6.4-9.1

LT, liver transplantation; MASLD, metabolic dysfunction–associated steatotic liver disease; PI, prediction interval.

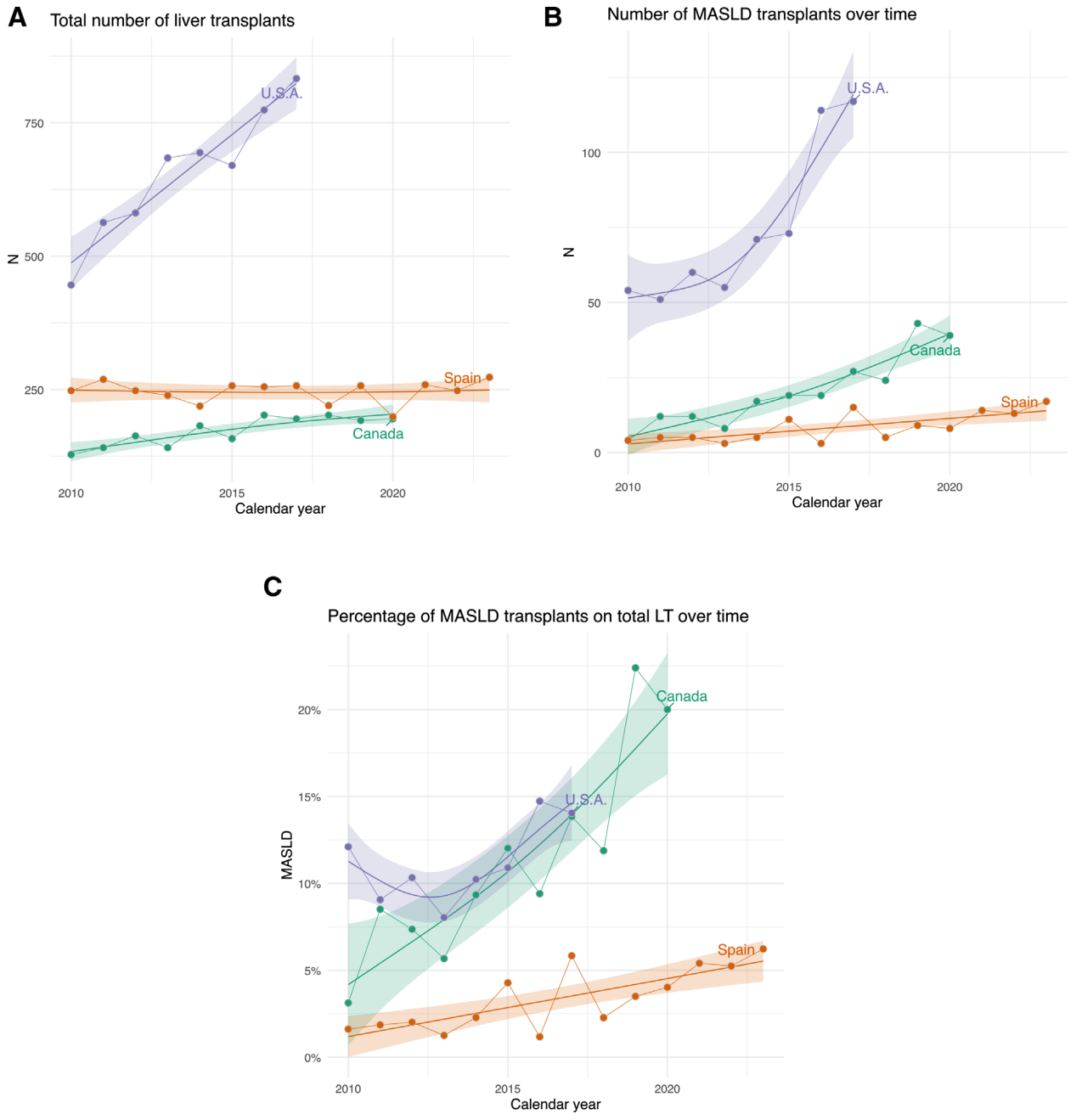

FIGURE 3. Evolution of transplants for MASLD between 2010 and 2023 in the Spanish data set (orange), between 2010 and 2020 in the Canadian data set (green), and between 2010 and June 2017 in the US data set (purple). A, Total number of LT over time in the Spanish, Canadian, and US data sets. B, Number of transplants for MASLD over time in the Spanish, Canadian, and US data sets. C, Proportion of MASLD on total LT over time in the Spanish, Canadian, and US data sets. R^2 = 89% and AIC = 199.2587 for the common model for all data sets; R^2 = 89% and AIC = 194.9240 for the model allowing different temporal trajectories per data set. A, Canadian data set (n = 1899, 1 center): n = 128 in 2010, n = 202 (1.6×) in 2016 and n = 195 (1.5×) in 2020; US data set (n = 5245, 7 centers): n = 446 in 2010, n = 774 (1.7×) in 2016 and n = 833 (1.9×) in 2017; Spanish data set (n = 3448, 5 centers): n = 248 in 2010, n = 255 (1.0×) in 2016 and n = 273 (1.1×) in 2023. B, Canadian data set (n = 224, 1 center): n = 4 in 2010, n = 19 (4.8×) in 2016 and n = 39 (9.8×) in 2020; US data set (n = 709, 7 centers): n = 54 in 2010, n = 114 (2.1×) in 2016 and n = 117 (2.2×) in 2017; Spanish data set (n = 117, 5 centers): n = 4 in 2010, n = 3 (0.8×) in 2016 and n = 17 (4.3×) in 2023. C, Canadian data set (1 center): 3.1% in 2010, 9.4% (3.0×) in 2016 and 20.0% (6.5×) in 2020; US cohort (7 centers): 12.1% in 2010, 14.7% (1.2×) in 2016 and 14.0% (1.2×) in 2017; Spanish data set (5 centers): 1.6% in 2010, 1.2% (0.8×) in 2016 and 6.2 (3.9×) in 2023. AIC, Akaike information criterion; LT, liver transplantation; MASLD, metabolic dysfunction–associated steatotic liver disease.

of transplants for MASLD lags behind the prevalence of MASLD in the greater community, highlighting a need to evaluate and refer more of these patients.

Many studies have reported data on poor metabolic health in the Spanish population, whereas Lecube et al[31] demonstrated the low self-perception of obesity among Spaniards. A representative sample of Spanish adults showed that more than half had excess weight (BMI >25 kg/m^2) and cardiometabolic risk (35.8% and 19.9% of overweight and obesity rates, respectively).[32] Rodríguez-Rodríguez et al[33] reported an overweight prevalence of 34.2% and an obesity prevalence of 13.6% in a smaller

cohort. In a Spanish primary care setting, a random population-based sample of 10 579 adults showed an age-adjusted prevalence of T2DM of 11.5%.[34] Overweight (38.6%) and obesity (18.4%) were also common in the Spanish working population and were related to a significant increase in the prevalence of cardiovascular risk factors.[35] In addition, the prevalence of excess body weight in childhood has substantially increased in the past decade, reaching figures of 39.9% and 35.3% in Spanish children aged 2–6 y and 7–13 y, respectively, during 2011–2021.[36] Furthermore, Herreras López et al[37] reported that MS was present in 20% of LT candidates.

Although the epidemiology of obesity and diabetes (and consequently MASLD) is more time honored in America than in Europe, this study provides a realistic concern that Spain, a country that is expected to have a low MASLD prevalence, is also at risk of catching up on those figures in the long-term future. Alternatively, the irruption of new antiobesity and anti-MASLD drugs may have a profound impact on the natural history of this disease bending a curve that is already less pronounced than that observed in North America.

The strength of this study lies in the multicentered cohort of 117 individuals from the largest LT centers in Spain and represents the Spanish population with MASLD. MASLD data from the Spanish Transplant Registry (data from all Spanish LT centers) showed that the time trajectory was similar to that from the 5 representative Spanish LT centers. These 5 centers provided detailed data for analyzing MASLD-associated cardiometabolic risk factors and exploring other potential non-MASLD causes.

In summary, MASLD-related cirrhosis is also increasing as an indication for LT in Spain, akin to Western regions, yet at a lower rate. The increasing time trajectory of MASLD over time, the future predictions expected, and the high prevalence of metabolic comorbidities in these patients support the notion that this indication has no regard for geographical boundaries.

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