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**First consensus document of waiting list prioritization for liver transplantation by the Spanish Society of Liver Transplantation (SETH)**

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**ABSTRACT**

Spain is worldwide leader in deceased donation rates per million habitants and count on a strong network of twenty-five liver transplant institutions. Although the access to liver transplantation is higher than in other countries, approximately 10% of patients qualifying for liver transplantation in Spain will die in the waiting list or would be excluded due to clinical deterioration. A robust waiting list prioritization system is paramount to grant the sickest patients with the first positions in the waiting list for an earlier access to transplant. In addition, the allocation policy may not create or perpetuate inequities, particularly in a public and universal healthcare system. Hitherto, Spain lacks a unique national allocation system for elective liver transplantation. Most institutions establish their own rules for liver allocation and only two autonomous regions, namely Andalucía and Cataluña, share part of their waiting list within their territory to provide regional priority to patients requiring more urgent transplantation. This heterogeneity is further aggravated by the recently described sex-based disparities for accessing liver transplantation in Spain, and by the expansion of liver transplant indications, mainly for oncological indications, in absence of clear guidance on the optimal prioritization policy. The present document contains the recommendations from the first consensus of waiting list prioritization for liver transplantation issued by the Spanish Society of Liver Transplantation (SETH). The document was supported by all liver transplant institutions in Spain and by the Organización Nacional de Trasplantes (ONT). Its implementation will allow to homogenize practices and to improve equity and outcomes among patients with end-stage liver disease.

**KEYWORDS:** Liver transplantation. Waiting list. Gender. Equity. Mortality.

**STATEMENT REGARDING THE USE OF AI:** The authors declare that no Artificial Intelligence technology was used to elaborate the present manuscript.

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**Introduction.**

Liver transplantation (LT) is a precious therapeutic option due to the perpetual shortage of donors. Waiting list prioritization should aim to preserve the ethical principle of need, which implies that the sickest patients should be granted the first positions in the list for an earlier access to LT. There are simple, objective, and accurate scores to predict mortality in the waiting list among patients with end-stage liver disease (1-4) but these should be periodically monitored to avoid inequities by age, gender, ethnicity, or aetiology of the liver disease (5).

In the early days of LT, waiting list prioritization followed the "first come, first served" principle (6) until the United Network for Organ Sharing (UNOS) in the United States established the need of a severity score based in a few number of objective and readily available parameters to determine the individual risk of short-term mortality (7). As a result, the Model For End Stage Liver Disease (MELD) was created, validated, and formally implemented in the United States in 2002 (1). The MELD score spread to other countries and organ transplant allocation systems where it confirmed its ability to decrease waiting list mortality rates (8). However, the implementation of MELD resulted in the creation of gender disparities for accessing LT (8, 9). Women show 30% higher risk of mortality or delisting for sickness tan men (10) and this gap has remained unchanged despite relevant MELD updates, including the incorporation of serum sodium in 2008 (2). If sex-based disparities for accessing LT were amended, a total of 800 women's deaths would have been avoided in the United States in the last decade (11). The main cause of gender disparities for accessing LT is serum creatinine as part of the MELD and MELD-Na scores (12-14). Indeed, with identical renal function, women show lower serum creatinine than men, and therefore lower MELD and MELD-Na scores (15). Gender disparities could be also influenced by other factors such as sarcopenia (16) or lower height, which may hamper finding a suitable donor. However, even among the tallest women (ie. height >170 cm), the probability of receiving a LT is 10% lower than in men of the same height (10).

Spain has been worldwide leader in terms of number of deceased donors per million habitants for the last three decades (17, 18). Despite this, between 2015 and 2021, the probability of mortality or delisting for sickness in patients waiting for LT was 11.4% (19). The length in the waiting list varies widely among different transplant institutions (20) and organ allocation is heterogeneous. Only two regions, namely Andalusia (4 centres) y Catalonia (3 centres), share part of their elective liver transplant waiting lists within their territory to provide regional priority to patients requiring more urgent transplantation, while the remaining 18 centres organize their own waiting list according to local criteria, including different prioritization scores. The expansion of indications for LT could translate in longer waiting times in the next few years (figure 1) and therefore the above referred heterogeneity could become more evident (20). In addition, the higher waiting list mortality rates observed in women compared to men in Spain in recent years make it necessary to consider the adoption of newly created scores able to amend such inequity (19). Finally, the proportion of patients with tumoral indications for LT ranges between 30% and 40%, which require to implement arbitrary exceptions for organ allocation.

The present consensus of the Spanish Society of Liver Transplantation (SETH) aimed to issue a list of recommendations for waiting list prioritization in order to provide clinical guidance regarding organ allocation. Their implementation would contribute to a more homogeneous management of the waiting list in our country.

**Methods.**

The SETH consensus group was composed by hepatologists, and transplant surgeons as follows: three coordinators, twenty-five delegates, each representing a LT institution in Spain, and a delegate from the Organización Nacional the Trasplantes. A Delphi-like methodology was used to build consensus as shown in figure 2 (21). The coordinators performed a literature search to gather the available evidence from MEDLINE, Google Scholar, Pubmed, The Cochrane library, and reports from other scientific societies and organ sharing entities. A dedicated questionnaire to understand the baseline situation of organ allocation in Spain was given to each participating delegate and the results

were summarized by the coordinators. The Organización Nacional de Trasplantes provided data regarding trends on access to LT and waiting list outcomes in recent years. All this information was compiled in a kick-off conceptual document which was sent to the delegates ahead of the consensus meeting.

The coordinators drafted a list of questions following a PICO format as follows:

- Patient: Which indication of LT was the question aimed to. In all, eleven indications (or group of indications) with specific needs regarding waiting list prioritization were identified.
- Intervention: Which prioritization rules should be preferred for each indication.
- Comparison: Which alternate model or rules could be considered, if available.
- Outcome: mortality in the waiting list or exclusion from the waiting list due to clinical deterioration, including not only patients who become clinically unfit for transplant, but also those experiencing a progression of the underlying liver disease beyond transplant criteria.

The consensus meeting was held in Madrid, on the 26th of April 2024. Each PICO question was answered by one or more recommendations from the consensus group. Each recommendation was rated according to the GRADE system ("Grading of Recommendations Assessment, Development and Evaluation") (22), which evaluates two dimensions: a) Strength of the recommendation, rated as "1" if strong (eg. "it should" or "it is recommended"), or as "2" if weak (eg. "it could" or "it may be considered"; and b) Quality of the scientific evidence, rated as "A" (high quality evidence coming from randomized clinical trials or overwhelming data from other sources), "B" (moderate evidence from non-randomized studies with a robust design), or "C" (low quality evidence from observational studies with relevant methodological flaws or expert opinion).

All recommendations were voted during the consensus meeting. A recommendation was considered strong if it was supported by at least 80% of the delegates. If a certain recommendation did not reach 80% of the votes, the consensus panel had a discussion and the voting process was repeated afterwards, maximum in two occasions. After this process, if the recommendation obtained support by 50% to 80% of delegates, the

recommendation was classified as weak. If a minimum of 50% agreement was not reached, the group did not issue that particular recommendation. A certain recommendation could be rated as weak if the consensus group meant to irrespective of the number of supporting votes. After the meeting, the preliminary list of recommendation was circulated among the consensus delegates for a second Delphi round in which minor changes could be implemented upon revision of the coordinators. Any major modification proposals were voted online by the whole consensus group and implemented only if unanimity was reached. The final version of the document was revised and approved by the consensus delegates, the coordinators, and the representative of the Organización Nacional de Trasplantes.

**Hepatic insufficiency.**

Patients included in the waiting list due to hepatic insufficiency are the paradigm of prioritization according to the principle of need. In Spain, this indication accounts for 30.2% of new inclusions in the waiting list for elective LT (19). Prioritization models combine several objective analytical parameters and those including serum sodium have consistently shown more accurate outcome predictions compared with those neglecting this information (2-4, 19). A recent study in Spain revealed that women have 57% higher risk of mortality or delisting for sickness than men after controlling for potential confounders (RR=1.57; IC95% 1.08-2.58; p=0.017) (19), which makes it necessary to implement new models able to correct this disparity. There are two scores specifically aimed to address gender disparities. MELD 3.0 has been created and recently implemented for clinical use in the United States (3). MELD 3.0 incorporated sex and serum albumin to the MELD-Na formula and capped creatinine values at 3 mg/dL. Hitherto, MELD 3.0 has not been externally validated. Failed attempts have been made in South Korea (23), United Kingdom (4), Australia (4), and Italy (24). On the other hand, the Gender-Equity Model for liver Allocation corrected by serum sodium (GEMA-Na) replaced serum creatinine by the Royal Free Hospital Glomerular Filtration Rate formula, which has been specifically designed to estimate renal function in patients with cirrhosis, and combines age, sex, sodium, international normalized

ratio, urea, creatinine, and ascites (if moderate-severe) (25). GEMA-Na was developed in the United Kingdom and has been externally validated in Australia (4), and Italy (24), where it has shown more accurate outcome predictions than MELD 3.0. In a nationwide cohort study including 6,071 adult patients included in the waiting list for elective LT in Spain, GEMA-Na performed significantly better than MELD 3.0 and simulation analyses confirmed that its implementation would save one in 18 deaths in the waiting list (19). The recommendations issued by the consensus group are shown in table 1.

**Acute-on-chronic liver failure.**

Acute-on-chronic liver failure (ACLF) was considered a contraindication for LT until several studies confirmed a pronounced survival benefit for selected patients with ACLF grade 2-3 (26), which motivated its acceptance in Spain as a LT indication in 2021 (27). ACLF is an infrequent indication for LT, but it shows the highest rates of mortality in the waiting list among all elective indications (28). Although patients with ACLF are usually placed within the first positions in the waiting list, the MELD family scores underestimate the true severity and mortality risk of these patients (29-31). Studies regarding the performance of GEMA-Na specifically in patients with ACLF are lacking. The recommendations issued by the consensus group are shown in table 1.

**Refractory ascites.**

Patients with refractory ascites have been historically penalized by the MELD system as they show persistently low MELD scores (32). Some LT institutions in Spain empirically assign extra-MELD points to patients with refractory ascites according to the time spent in the waiting list while others use MELD-Na. Despite that patients with refractory ascites wait longer to receive a LT than patients with hepatic insufficiency in average, their risk of mortality or delisting for sickness at 90 days is slightly lower (5.5% vs. 6.4%) (19). Available studies suggest that GEMA-Na could could grant an earlier access to LT to patients with refractory ascites (4, 19). The recommendations issued by

the consensus group are shown in table 1.

**Elective re-transplantation.**

Patients with severe and irreversible graft dysfunction, either because of recurrence of the pre-existing liver disease or due to complications, could be considered for re-transplantation. Early allograft failure or acute hepatic artery thrombosis within the first week after LT may be eligible for urgent re-transplantation and they would receive nationwide priority "cero", similar to that assigned to patients with acute liver failure. Otherwise, prioritization of candidates for elective re-transplantation mirrors that for hepatic insufficiency in most LT institutions. A particular entity named ischemic cholangiopathy, which is motivated by hepatic artery stenosis or delayed thrombosis, is characterized by a progressive and severe damage of the biliary tree resulting in multiple non-anastomotic strictures, biliary dilations, and ultimately recurrent cholangitis and graft dysfunction (33). The true severity of these patients is not captured by the available scores, which underestimate the risk of short-term mortality. None of the prioritization models have been tested in candidates for elective re-transplantation, neither in patients with ischemic cholangiopathy. The recommendations issued by the consensus group are shown in table 1.

**Non-tumoral special indications.**

Special indications, also known as MELD exceptions, are a heterogeneous group of situations in those the need for LT is not related with the risk of short-term mortality (34). The most frequent special indications are refractory ascites and tumours, which are addressed in specific sections. Here, we discuss indications related to complications of portal hypertension, situations resulting in a deranged quality of life, or aetiologies of liver disease which may motivate LT *per se* (table 2). Some special indications could potentially result in death, while others could motivate severe complications in the future without transplant. The prioritization system may not be

identical for all special indications but should be adapted to their inherent peculiarities. An excessive prioritization of special indications over patients with increased risk of mortality or delisting due to clinical deterioration, including progression of the underlying liver disease beyond transplant criteria, should be avoided. The recommendations issued by the consensus group are shown in table 1.

**Hepatocellular carcinoma without hepatic insufficiency.**

Tumoral indications for LT accounted for 40.6% of new inclusions in the waiting list in Spain from 2016 to 2021, being hepatocellular carcinoma largely the most prevalent (39.1%) (19). The need for waiting list prioritization may not be related to the risk of short-term mortality but to the risk of tumour progression beyond transplant criteria. In Spain, this risk is 3.4% at 90 days, which is much lower than the risk of mortality or delisting for sickness in patients with hepatic insufficiency (6.4%) (19).

According to the survey made for the present consensus, 67% of LT institutions in Spain use the same prioritization score in patients with hepatocellular carcinoma as in patients with hepatic insufficiency, by adding extra prioritization points to patients with hepatocellular carcinoma according to the time spent in the waiting list. Most centres (79%) also condition the assignment of extra points to the tumour burden (ie. diameter of the largest nodule and number of nodules). In other countries, the prioritization system for patients with hepatocellular carcinoma varies widely. The French system combines MELD-derived prioritization points with points obtained according to the tumour burden, serum alpha-fetoprotein, and radiological response to bridging therapies, in a continuous score (35). The Transplant Benefit Score (TBS), which combines more than twenty variables from the donor and the recipient to balance the need (waiting list mortality risk) and the utility (benefit in terms of post-LT survival), is being used in the United Kingdom. The TBS is a complex model which may difficult the access for LT to patients with cancer, including hepatocellular carcinoma (36, 37). However, those prioritization systems that grant very early access to LT to patients with hepatocellular carcinoma may increase the risk of tumour recurrence afterwards, probably owing to the impossibility to identify patients with biologically

aggressive tumours who should be rather selected for other therapeutic options different from LT (38). The risk of delisting due to tumour progression should be balanced with the need of a minimum observation period in the waiting list to identify patients with biologically aggressive tumours (39). The recommendations issued by the consensus group are shown in table 1.

**Cholangiocarcinoma (hilar o intrahepatic).**

Hilar cholangiocarcinoma was initially considered a potential indication for LT as part of the complex neoadjuvant protocol designed in the Mayo Clinic. This protocol has been lately simplified by waiving the need of brachytherapy and by implementing non-invasive re-staging using positron emission tomography (40). Regarding intrahepatic cholangiocarcinoma in patients with chronic liver disease, the available evidence comes from retrospective studies in which these tumours were misdiagnosed as hepatocellular carcinomas in the pre-LT radiological techniques and were incidentally found in the pathological analysis of the explanted liver. In this situation, mainly restricted to patients with primary sclerosing cholangitis, a single nodule less than 2 cm diameter was associated with acceptably low recurrence rates after LT (41). In Spain, both indications are accepted as part of ongoing clinical trials (27). Most centres prioritize these patients by adding extra MELD points empirically as for patients with hepatocellular carcinoma, although the risk of tumour progression beyond transplant criteria is much higher for patients with cholangiocarcinoma. The recommendations issued by the consensus group are shown in table 1.

**Colo-rectal cancer liver metastases.**

This indication for LT was recently described in the SECA 1 and SECA 2 studies, which were performed in Nordic population (42, 43). LT was restricted to patients with a resected primary colo-rectal cancer, with metastatic disease confined into the liver which is not amenable for liver resection (44). Patients may not be eligible for LT if they show BRAF gene mutation, if carcinoembryonic antigen levels are >80 ng/mL, or if

the tumour progresses after a 6-months period without chemotherapy. These are very strict criteria which are seldomly met and in Spain this indication is only accepted as part of well-designed clinical trials (27). There is no evidence on how to prioritize patients with unresectable colo-rectal liver metastases for LT. The available guidelines recommend early access to LT for these patients since there is a mandatory period of 6 months of stable disease before entering the waiting list (44). The recommendations issued by the consensus group are shown in table 1.

**Neuroendocrine liver metastases.**

More than half of patients with neuroendocrine tumours might develop liver metastases. The first therapeutic option is liver resection given the slow progression of the disease (45). However, LT could be considered in patients with unresectable liver metastases. Although the selection of candidates is a matter of controversy, the most widely accepted criteria are the so-called MILAN-TNE (46).

Neuroendocrine liver metastases are a very rare indication for LT (<1%). The need for prioritizing these patients is not related with short-term mortality, which is negligible, but with the risk of extrahepatic disease which could contraindicate LT. The prioritization score assigned to these patients at listing and during their stay in the waiting list is heterogeneous (47). As described for patients with hepatocellular carcinoma, an early access to LT of these patients may not be adequate since an observation period before LT may help to better assess the biological behaviour of the tumour. The recommendations issued by the consensus group are shown in table 1.

**Epithelioid haemangioendothelioma.**

This is a rare vascular tumour with an intermediate biological aggressive behaviour between the haemangioma and the haemangiosarcoma, which also associates frequent extrahepatic spread (48). Its evolution is unpredictable. Neither mitotic activity, nor tumour burden or cellular atypia inform about the aggressiveness of epithelioid haemangioendothelioma (49). Approximately 10%-15% of patients with

epithelioid haemangioendothelioma will receive a LT (50), which in practical terms makes this indication very infrequent (<1%). The largest series published hitherto found 75% overall survival rates at 5 years after LT (51). Noteworthy, extrahepatic involvement of the tumour may not contraindicate LT unless a vital organ is affected. The progression of the extrahepatic disease after LT is slow and radiological stabilization is often observed over years, even in presence of immunosuppressive agents. Waiting list prioritization is based in the assignment of arbitrary points to ensure a chance for accessing liver transplantation but avoiding an excessive prioritization since waiting times <120 days have been associated with worse oncological outcomes after LT (51). In the United States, where the median MELD score for patients with hepatic insufficiency is 24, patients with epithelioid haemangioendothelioma receive additional points according to the time spent in the waiting list to arrive at LT with a median score of 22 points (52). The recommendations issued by the consensus group are shown in table 1.

**The candidate for combined liver-kidney transplantation.**

Prioritization of candidates for combined liver-kidney transplantation involve specific considerations from both organs, including the human leukocyte antigen (HLA) compatibility. In 2016, the 6th SETH consensus meeting addressed this topic (53). There are two main situations to consider liver-kidney transplantation: when a LT candidate shows chronic kidney disease requiring renal replacement therapy; and the candidate for renal transplantation who shows cirrhosis with portal hypertension. The waiting list management of the first situation should mirror the recommendations made for patients with hepatic insufficiency, taking into account that GEMA-Na establish a minimum value or 20 ml/min for the Royal Free Glomerular filtration rate (4), so that patients receiving haemodialysis should be assigned this value automatically by the calculator. In the second scenario, the current prioritization models for LT assign low priority which difficult their access to LT. In Spain, candidates for combined liver-kidney transplantation wait longer to receive a liver graft compared to candidates for LT alone, and this situation worsens in cases with high sensitization.

Some authors do not agree to assign extra prioritization to these patients arguing that it would be in detriment of candidates for kidney transplant alone (54), while others are in favor given the mortality risk associated with prolonged waiting list times (55). Although the present document was elaborated by hepatologists and transplant surgeons, without the expertise of nephrologists, the current prioritization system in these patients is a generalized concern which has been discussed in the consensus meeting to arrive at the recommendations issued in table 1.

**Final remarks.**

The present consensus document comprises a list of practical recommendations to homogenize waiting list prioritization strategies within the Spanish national transplant network, which have been issued according to the best available evidence. These recommendations should be adapted to the geographic peculiarities of each region and to local healthcare policies, as well as to different context of waiting list length and composition. Liver transplant teams in each centre may need to discuss those aspects in which the consensus group was unable reach agreement. Finally, the resolution of ties in the waiting list for two patients with identical prioritization score should motivate individualized decisions according to the premises contained in table 1.

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**Table 1.** List of recommendations issued by the Spanish Society of Liver Transplantation (SETH). Recommendations were classified according to the GRADE system ("Grading of Recommendations Assessment, Development and Evaluation"), which rates the strength of the recommendation (1= strong; 2= weak) and the quality of the supporting scientific evidence (A, B, or C in detrimental quality order).

| RECOMMENDATION | GRADE |
|---|---|
| **Hepatic insufficiency** | |
| In patients with hepatic insufficiency, waiting list prioritization should follow the principle of need by using objective and reproducible scores which inform about the risk of short-term mortality. | 1A |
| Urgency-based prioritization scores incorporating serum sodium (ie. MELD-Na, MELD 3.0, or GEMA-Na) should be preferred over those neglecting this information. | 1A |
| Among prioritization scores incorporating serum sodium, the use of GEMA-Na should be preferred over MELD-Na and MELD 3.0 owing to its improved discrimination capacity and its ability to amend gender disparities for accessing liver transplantation. | 1A |
| The variable "moderate-severe ascites", which may be required for calculating GEMA-Na, should be objectively assessed according to at least one of the following criteria:<br>- Large volume paracentesis (ie. >6 litres) within the 6 weeks prior to the score calculation.<br>- Clinically evident ascites in the physical examination further confirmed by abdominal imaging techniques. | 2B |
| The prioritization score calculation should be updated at least every 90 days while the patient remains on the waiting list, or earlier than that upon a clinically meaningful change in the patient's physical condition. | 1A |
| The sickest patients placed within the first positions of the waiting list should undergo close clinical monitoring and therefore the prioritization score should be updated more frequently. | 1A |
| Wherever several liver transplant institutions share part of their waiting list, the consensus group recommends establishing a threshold of the prioritization score | 1C |

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| beyond which patients would qualify to access the shared waiting list. In absence of comparative studies, this threshold should be agreed by the liver transplant centers which belong to that region. | |
| **Acute-on-chronic liver failure (ACLF)** | |
| In patients with grade 3 ACLF, prioritization scores underestimate the risk of mortality. The same prioritization strategy as for patients with hepatic insufficiency may be used but a geographic priority should be established to ensure an earlier access to liver transplantation. | 1B |
| In patients with grade 2 ALCF, prioritization should follow the same recommendations as for patients with hepatic insufficiency. A geographic priority could be considered to facilitate an earlier access to liver transplantation. | 2B |
| The prioritization score calculation should be updated at least every 7 days while the patient remains on the waiting list, or earlier than that upon a clinically meaningful change in the patient's physical condition. | 1C |
| A futility threshold of the prioritization score to exclude patients with ACLF from the waiting list could not be identified. However, the consensus group recommend establishing futility in patients with unresponsive cardio-respiratory failure. The decision to exclude the patient from the waiting list should be taken within the multidisciplinary transplant team in a case-by-case basis. | 1C |
| **Refractory ascites** | |
| Prioritization should follow the same recommendations as for patients with hepatic insufficiency. | 1B |
| We do not recommend assigning additional points to the prioritization score systematically in patients with refractory ascites according to the time spent in the waiting list. However, this could be considered in selected patients with persistently low prioritization score after a reasonable length in the waiting list if agreed by the multidisciplinary transplant team. | 2C |
| The consensus group do not consider it necessary to set an upper threshold for the prioritization score in these patients, although the empirical assignment of extra prioritization points, if implemented, should not allow the prioritization of patients with refractory ascites over patients with severe hepatic insufficiency. | 2C |
| **Elective re-transplantation** | |
| Prioritization should follow the same recommendations as for patients with hepatic insufficiency. | 1C |
| We do not recommend assigning additional points to the prioritization score in candidates for elective re-transplantation according to the time spent in the waiting list. | 1C |
| The consensus group do not consider it necessary to set an upper threshold for the prioritization score in these patients. | 2C |
| In patients with ischemic cholangiopathy, we recommend assigning additional points to the prioritization score empirically to ensure an early access to re-transplantation. | 1C |
| **Non-tumoral special indications** | |
| We recommend assigning a fixed and predetermined prioritization score to these patients upon inclusion in the waiting list. | 1C |
| In general, we do not recommend assigning additional points to the prioritization score systematically according to the time spent in the waiting list, although it | 2C |

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| could be considered in those special indications in which there is a meaningful risk of mortality or delisting for sickness such as hepato-pulmonary syndrome, recurrent cholangitis, or polycystic liver-kidney disease. | |
| **Hepatocellular carcinoma with preserved liver function** | |
| We recommend assigning a fixed and predetermined prioritization score to these patients upon inclusion in the waiting list. | 1C |
| We recommend assigning additional points to the prioritization score systematically according to the time spent in the waiting list only in the following situations (priority criteria):<br>- Multinodular disease (ie. two or more nodules categorized as LIRADS 5).<br>- Single nodule > 3 cm.<br>- Serum alpha-fetoprotein >200 ng/mL.<br>- Objective ineligibility for locoregional bridging therapies. | 1B |
| The consensus group do not consider it necessary to set an upper threshold for the prioritization score in these patients, although the empirical assignment of extra prioritization points, if implemented, should not allow the prioritization of patients with hepatocellular carcinoma over patients with severe hepatic insufficiency. | 2C |
| **Hilar or intrahepatic cholangiocarcinoma** | |
| We recommend assigning a fixed and predetermined prioritization score to these patients upon inclusion in the waiting list to ensure an early access to liver transplantation. This score should be equivalent as or higher than that assigned to patients with hepatocellular carcinoma meeting priority criteria. | 1C |
| The consensus group do not consider it necessary to set an upper threshold for the prioritization score in these patients, although the empirical assignment of extra prioritization points, if implemented, should not allow the prioritization of patients with cholangiocarcinoma over patients with severe hepatic insufficiency. | 2C |
| **Unresectable colo-rectal cancer liver metastases** | |
| We recommend assigning a fixed and predetermined prioritization score to these patients upon inclusion in the waiting list to ensure an early access to liver transplantation. This score should be equivalent as or higher than that assigned to patients with hepatocellular carcinoma meeting priority criteria. | 1C |
| The consensus group do not consider it necessary to set an upper threshold for the prioritization score in these patients, although the empirical assignment of extra prioritization points, if implemented, should not allow the prioritization of patients with colo-rectal cancer metastases over patients with severe hepatic insufficiency. | 2C |
| **Neuroendocrine liver metastases** | |
| We recommend assigning a fixed and predetermined prioritization score to these patients upon inclusion in the waiting list to ensure an early access to liver transplantation. This score should be equivalent as that assigned to patients with hepatocellular carcinoma meeting priority criteria. | 1C |
| The consensus group do not consider it necessary to set an upper threshold for the prioritization score in these patients, although the empirical assignment of extra prioritization points, if implemented, should not allow the prioritization of patients with neuroendocrine liver metastases over patients with severe hepatic insufficiency. | 2C |
| **Epithelioid haemangioendothelioma** | |
| We recommend assigning a fixed and predetermined prioritization score to these | 1C |

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| patients upon inclusion in the waiting list to ensure an early access to liver transplantation. This score should be equivalent as or lower than that assigned to patients with hepatocellular carcinoma meeting priority criteria. | |
| The consensus group do not consider it necessary to set an upper threshold for the prioritization score in these patients, although the empirical assignment of extra prioritization points, if implemented, should not allow the prioritization of patients with epithelioid haemangioendothelioma over patients with severe hepatic insufficiency. | 2C |
| **Liver-kidney combined organ transplantation** | |
| In patients with preserved liver function, the current waiting time for combined transplantation is too prolonged so it seems necessary to assign extra prioritization points to these patients. | 2C |
| **General recommendations to solve ties in the waiting list** | |
| The multidisciplinary transplant team at each center should discuss each tie in the waiting list in a case-by-case basis. If a donation occurs with two or more suitable recipients in the waiting list showing identical prioritization score, the on-call team may reach an agreement regarding the optimal donor-recipient matching. | 1C |
| As a rule of thumb, a tie in the waiting list could be solved by prioritizing patients with hepatic insufficiency over special indications. | 2C |
| The time spent in the waiting list could be another criterion to be considered when the tie occurs between two patients with special indications in whom the risk of short-term mortality is negligible. | 2C |
| The multidisciplinary transplant team and, in the last instance, the on-call transplant team will be responsible for the final decision to assign an organ according to the principles or urgency, utility, and equity. | 1C |

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**Table 2.** List of accepted special indications for liver transplantation.

| TUMORS | COMPLICATIONS OF PORTAL HYPERTENSION | COMPLICATIONS UNRELATED WITH PORTAL HYPERTENSION | DISEASES |
|---|---|---|---|
| Hepatocellular carcinoma<br>Multiple adenomas<br>Epithelioid haemangioendothelioma<br>Intrahepatic cholangiocarcinoma<br>Hilar cholangiocarcinoma<br>Neuroendocrine liver mets.<br>CRC liver mets. | Refractory ascites<br>Recurrent hydrothorax<br>Chronic/recurrent encephalopathy<br>Recurrent VB<br>Hepatopulmonary syndrome<br>Porto pulmonary hypertension | Refractory pruritus<br>Recurrent cholangitis | Polycystic liver disease<br>Primary hyperoxaluria<br>OTC deficiency<br>Familial hypercholesterolemia<br>Familial amyloid polyneuropathy<br>Cystic fibrosis<br>Hereditary haemorrhagic telangiectasia |

CRC; colo-rectal cancer; VB: variceal bleeding; Mets.: Metastases; OTC: ornithine transcarbamylase.

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## FIGURE LEGENDS

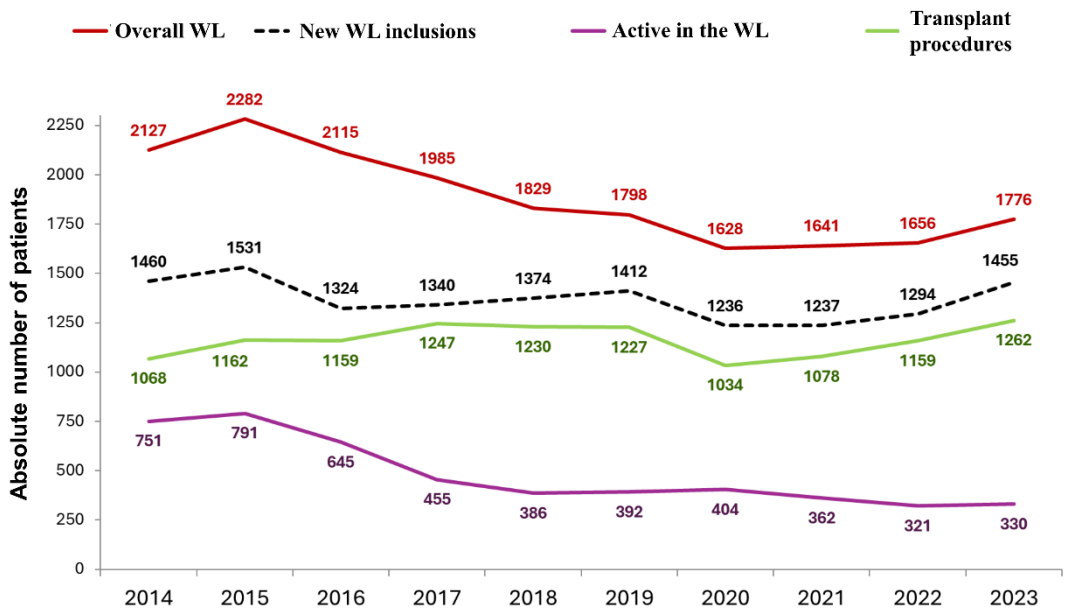


**Figure 1.** Donation and liver transplant activity in Spain from 2014 to 2023. The figure depicts annual activity in terms of overall number of patients in the waiting list (red line), number of new patients included in the waiting list (black dotted line), number of liver transplant procedures (green line), and number of patients active in the waiting list at the end of each year (purple line). The data was obtained from the annual report of the Organización Nacional de Trasplantes (ONT) published in 2023. Available at: https://www.ont.es/. WL: waiting list.

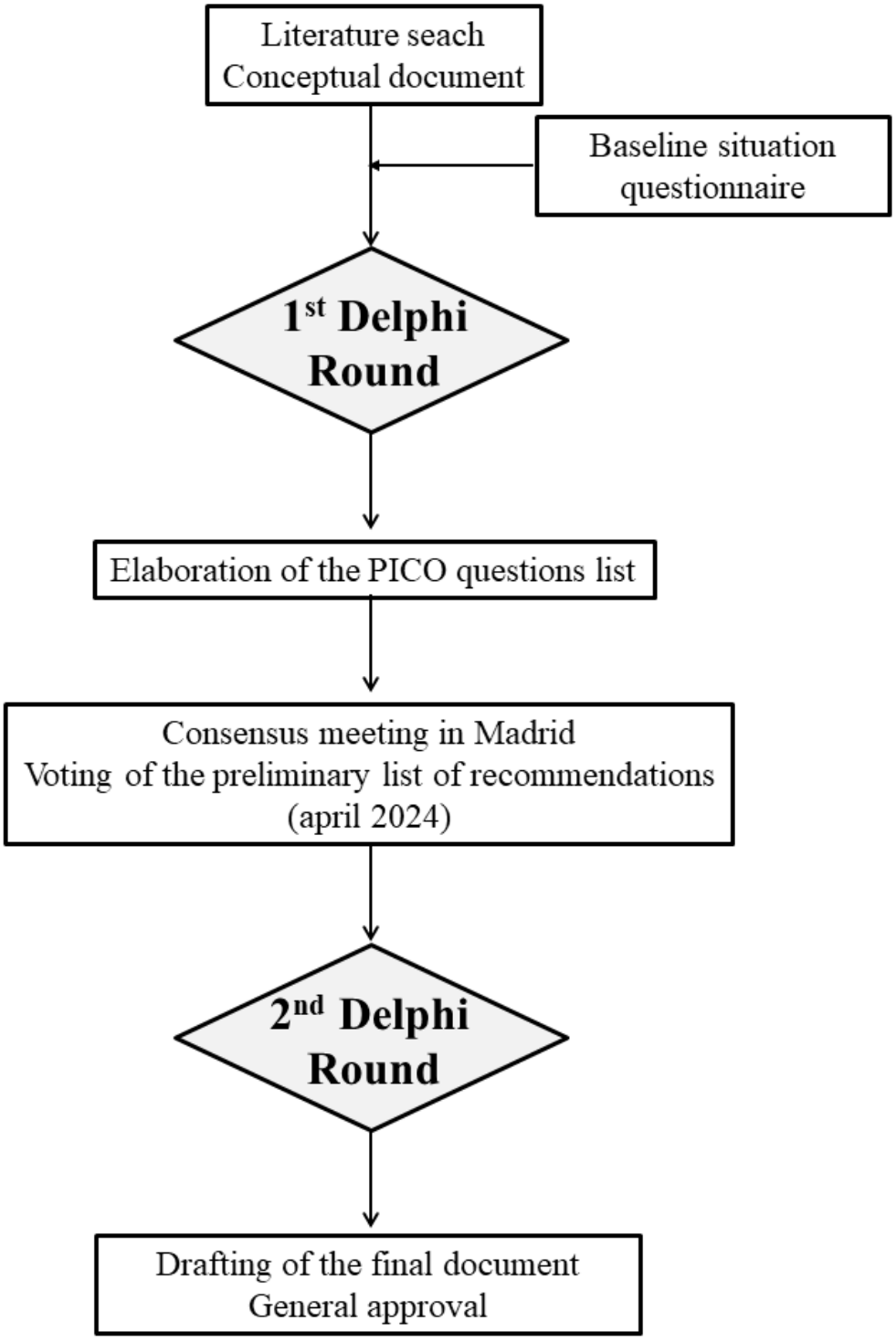


**Figura 2.** Delphi-like methodology used to build consensus in the Spanish Society of Liver Transplantation (SETH).

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