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Combined heart and liver transplantation: State of knowledge and outlooks

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Summary Various types of liver impairment have been described in patients with end-stage heart failure who are awaiting heart transplantation. The liver impairment may be severe, characterized by a high model for end-stage liver disease (MELD) Score and/or the presence of ascites, both of which are associated with a high risk of failure after single heart transplantation. A liver function assessment is therefore necessary before registration on the heart transplant list, moreover in case of long-developing heart failure, such as with congenital heart disease or in the presence of risk factors for chronic liver disease including excessive alcohol consumption, metabolic syndrome or chronic viral hepatitis B or C. In these instances, screening for cirrhosis with liver biopsy and for hepatocellular carcinoma through imaging must be systematic and when present, the indication for combined heart-liver transplantation must be considered. Its benefits, however, in case of liver failure with a high MELD score or multi-organ failure remains to be demonstrated. An exception in which the liver shows no morphological or functional alteration is with familial amyloid neuropathy, during which moderate to severe heart failure implies surgical treatment consisting of a liver or even heart-liver transplantation. These must be done early and are mainly contraindicated according to the level of neurological damage.

Introduction

Three models of interaction between the heart and liver have been described in patients with end-stage heart failure:

- heart disease chronically affects the liver, thereby progressing to chronic hepatic congestion, primarily in congenital heart disease;
- common risk factors of liver disease and heart disease are present, including excessive alcohol consumption and metabolic syndrome, which may progress to simultaneous liver and heart failure; and;
- the liver negatively affects the heart, such as in familial amyloid neuropathy.

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The first two models may advance to severe liver damage, such as cirrhosis or hepatocellular carcinoma. The three models presents specific indications of combined heart-liver transplantation (CHLT) with varying results.

Congenital heart diseases

The incidence of children reaching the age of adulthood despite congenital heart disease is on the rise. As a result, 3% of the indications for heart transplant concern adults with congenital heart disease. The results of HT for congenital heart disease are derived from small American series with excellent short and medium-term results, and even appear superior in the long-term to other indications [1,2]. These are subject to the expertise of the cardiothoracic surgeon in this type of pediatric surgery and in a context of iterative sternotomies. Results must be interpreted cautiously due to the absence of formal criteria used in the series for the diagnosis of cirrhosis and the absence of long-term survival data. According to Lewis et al. [3], a subgroup of patients who underwent the Fontan surgical procedure had much higher early morbidity-mortality after heart transplantation alone, with 44% mortality at one month. This abnormally high death rate appears to be related to the occurrence of hemorrhagic accidents and a higher frequency of primary graft dysfunction. The involvement of perioperative liver failure in this type of complication is suspected [3]. For reference, the Fontan surgical procedure is proposed in case of tricuspid atresia, restricted right ventricle (Tetralogy of Fallot) or a single ventricle. The intervention involves diverting the venous blood from the right atrium to the pulmonary arteries through various techniques (venotomy, shunt, tubes), which leads to central venous hypertension and a decrease in cardiac output, followed by late ventricular dysfunction. These post-operative hemodynamic disturbances associated with a long period of hypoxia prior to the intervention are risk factors of chronic hepatic lesions specific to chronic hepatic congestion. Microscopically, non-inflammatory necrotic lesions and sinusoidal distension lesions of centrilobular topography will promote the inhomogeneous appearance of atrophic and compensatory areas that gradually progress to regenerative nodular hypertrophy. This occurs by means of microthrombi from the hepatic venous network. Fibrosis may appear secondarily and in case of extensive fibrosis, the histological involvement is improperly referred to as ''cardiac cirrhosis''. The presence of hepatic lesions before the actual stage of cirrhosis upon liver biopsy (LB) is not associated with an abnormally high rate of post-operative mortality, including after heart transplant alone, and is therefore insufficient for applying the indication for double transplant [4]. In the recent series by K. Pundi et al. [5], 40 of the 195 patients (21%) had cirrhosis an average of 23 years after the Fontan procedure. Hepatocellular carcinoma (HCC) was diagnosed in five of these patients. Once the diagnosis of cirrhosis was made, spontaneous survival at 1 and 5 years decreased to 57% and 35%, respectively.

Finally, after heart transplantation for Fontan's failure, 8 pre-operative factors would promote the occurrence of early death: anatomic risk factors, elevated pre-operative pulmonary artery pressure, atrio-pulmonary Fontan, heart failure symptoms, arrhythmia, moderate/severe ventricular dysfunction or atrioventricular valve regurgitation, protein losing enteropathy, and end organ disease (cirrhosis or renal insufficiency) including a model for end-stage liver disease (MELD) Score higher than 19, and the need for ECMO or for hemodialysis [6,7].

CHLT must therefore be considered in the presence of true cirrhosis with liver failure or HCC only in young patients mainly in the event of failure of the Fontan procedure, in accordance with transplantability criteria. This indication accounts for close to 20% of CHLT indications in the United States.

Cirrhosis and end-stage heart failure

We know that in other cardiac surgery besides transplantation or after placement of a ventricular assist device, the presence of decompensated cirrhosis is associated with an abnormally high level of mortality. As a result, the diagnosis of cirrhosis is a contraindication for heart transplant for most teams. Early mortality also increases to 50% after heart transplantation according to a Taiwanese retrospective study that analyzed the surgical risk in only 12 patients, just seven of whom had histologically-proven cirrhosis [8]. A major limitation in all of the studies was that the diagnosis of cirrhosis was not systematically confirmed with LB but was nearly always made using indirect criteria, including the Child-Pugh or MELD Scores with values suggestive of advanced liver damage (Child C and MELD > 14, respectively). Although limited by its small number and the absence of histological proof, this data shows that screening for cirrhosis and knowing the extent of hepatic decompensation are crucial before heart transplantation.

In the cohort of patients enrolled on the waiting list for a heart transplant at Pitié-Salpêtrière Hospital between 2004 and 2010 ($n = 398$), at least 2% of them had advanced fibrosing liver disease (METAVIR Score F3) or cirrhosis (F4). This proportion of severe fibrosis diagnosed by LB increased to 15% when ascites was present; one out of six patients on the list had ascites [9]. In addition, the prevalence of patients with advanced fibrosis is undoubtedly underestimated in our series, since only patients with one or more risk factors of chronic liver disease and/or a presentation of hepatic decompensation received biopsies, on the condition that they were hemodynamically controlled.

Shared risk factors of fibrosing steatopathy

In current practice when a hepatological opinion is sought during a pre-heart transplant assessment, patients are primarily male and over 50 years old, with 50% to 60% of cases having either ischemic (ICM) or dilated (DCM) cardiomyopathy. Both of these heart diseases are associated with a risk of chronic steatohepatitis. Over one-third of cases of ICM are associated with metabolic syndrome, and half the cases of DCM are associated with abusive alcohol consumption (typically > 90 g/day) [10]. As a result, there is a potential risk of advanced hepatic fibrosis in these patients. It is therefore necessary to know how to systematically screen for advanced liver disease in patients with ICM or DCM. It is also necessary to keep in mind the possibility of chronic viral hepatitis C in patients with cardiomyopathy with previous

multiple operations. More generally, chronic viral hepatitis B or C still accounts for 1% to 2% of patients on the transplant list. Finally, hemochromatosis should be tracked in case of restrictive cardiomyopathy.

Familial amyloid neuropathy

Familial amyloid neuropathy (FAN) is a genetic disease that is autosomal dominant, although with variable penetrance, in adults over 30 years old. It is characterized by progressive ascending sensorimotor neuropathy and autonomic nervous system involvement with digestive, urinary and blood pressure dysautonomia. It gradually progresses to bed confinement, with a life expectancy of only 5 to 15 years after the diagnosis. The diagnosis is confirmed on electromyogram (EMG) and biopsy (e.g., rectal) in which the presence of extracellular amyloid deposits can be seen using Congo red stain. In 93% of cases there is a specific mutation (*Val30Met*) on the transthyretin (*TTR*) gene, which is synthesized almost exclusively in the liver. There is no other treatment besides liver transplantation for limiting the progression of the neuropathy. An ongoing evaluation is underway on the efficacy of oral treatments, such as tafamidis, which inhibits the tetramerization of TTR, thereby limiting its accumulation. To date more than 2000 liver transplants have been done worldwide, resulting in a 10-year survival of over 80% (http://www.fapwtr.org). This indication enables livers from patients with FAN to be used for another transplant in a second receiver (the so-called ''domino technique''). The main factors associated with successful liver transplantation in FAN are age (< 50 years), the level of peripheral neurological involvement, the absence of orthostatic hypotension and the absence of undernutrition (body mass index [BMI] × serum albumin < 600 kg/m/g/L) [11]. In 7% of cases, other mutations of the *TTR* gene are predominantly associated with myocardial damage with conduction disorders and/or end-stage restrictive cardiomyopathy (RCM). The neurological involvement is then of secondary priority, with the first symptoms occurring later (> 40 years). In this context, survival after liver transplant is then only 52% at 10 years, with persistence of long-term cardiac risk. The indication of double heart-liver transplantation will therefore be discussed in the presence of moderate to severe RCM, which may be associated with conduction disorders that cannot be managed with a device. 99mTechnetium bone scintigraphy and amyloid binding targeted PET imaging for transthyretin cardiac amyloidosis are emerging as highly accurate methods the risk of concomitant heart problems [12]. As with the *Val30Met* mutation, this combined transplantation can only be carried out in the absence of severe neurological involvement, i.e. the patient is not bedridden, and there is no orthostatic hypotension or undernutrition (Fig.1).

Over 70 combined transplantations have been done to date, with the USA accounting for close to 25 to 30% of the CHLT indications. The largest published retrospective series comes from the Mayo Clinic, with 21 out of 27 patients with FAN who had a CHLT [13]. As expected, these patients did not have an increased surgical risk from a hepatic perspective. Heart transplantation on extracorporeal membrane oxygenation (ECMO) was followed by liver transplantation using standard operating procedures; this provided excellent peri- and early post-operative results with low morbidity (mean duration on mechanical ventilation, length of stay in intensive care and length of hospitalization were 1.5, 8.5 and 25 days, respectively) and a 3-month survival greater than 95%. Twelve domino transplants could be done at the same time. An analysis of the 26 CHLT in the global FAN registry (www.fapwtr.org) showed a 10-year survival of 61%. The experience at Pitié-Salpêtrière Hospital with combined transplant for FAN concerned only five patients, three of whom died the first year. This highlights the importance of a strict selection of these patients, including the absence of advanced neurological or autonomic nervous system damage, which is more common in patients over the age of 50 years.

Diagnostic methods for severe chronic liver disease in patients with heart failure

Non-invasive diagnostic methods

The high frequency of disturbances in laboratory liver tests (transaminases, GGT, ALP, serum bilirubin, serum albumin, INR) found in over 60% of cases and the use of vitamin K antagonists (VKA) in one-third of patients limits the use of the most common biological markers for the screening of extensive fibrosis. Composite scores including these same markers, such as the Child-Pugh score or the MELD Score, would have these same limitations. The performance of non-invasive tests such as FibroTest® is non-contributory in 53% of cases. This is due to the frequently increased GGT and bilirubin and the reduction in serum apolipoprotein A1, all of which render FibroTest uninterpretable. With regard to elastometry techniques (FibroScan, Aixplorer®, etc.), their performance is limited by ascites, and the values are overestimated by hepatic congestion. The predictive value of these non-invasive tests seems to be lower than that of LB when the complete analysis of liver explants from patients that had a combined heart-liver transplantation is used as a reference (personal data).

The benefits of morphological tests such as ultrasound or CT scan are limited by the low predictive value of the classic sign of cirrhosis in cases of chronic heart failure. Indeed, the presence of ascites via supra-hepatic block, of congestive hepatomegaly or the possibility of a dysmorphic liver suggestive of cirrhosis in relation to regenerative nodular hyperplasia limit the diagnostic value. They are, however, still beneficial in the screening of HCC, which justifies their performance in cases of advanced hepatic fibrosis.

Role of liver biopsy

Despite its invasive quality, the performance of LB, usually performed via the transjugular route, remains the only useful test for screening chronic liver disease in patients with severe heart failure. The examination conditions are limited by hemodynamic instability and hemorrhagic risk despite the systematic performance via the transjugular route. The benefits of investigating intrahepatic block via the transjugular route remain to be demonstrated since the

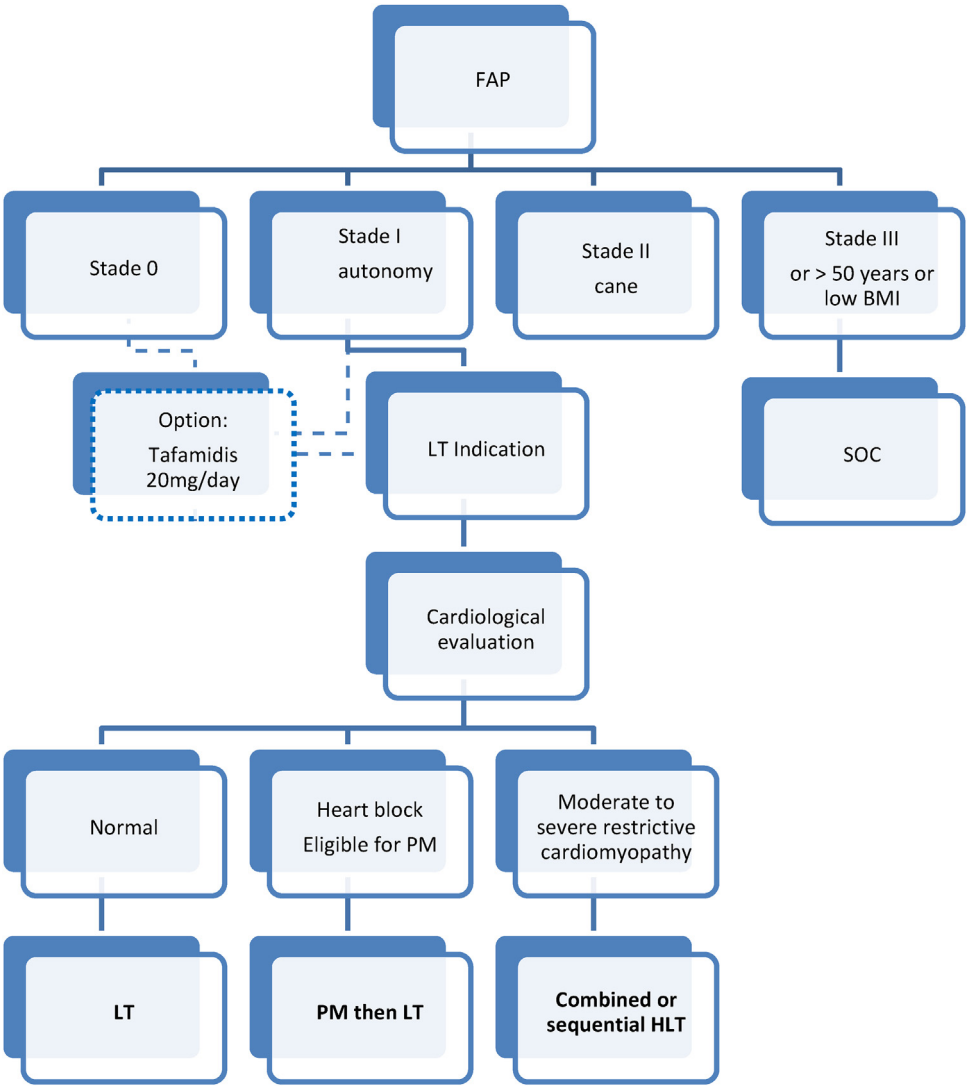

Figure 1 Therapeutic management of familial amyloid neuropathy. N.B: BMI: body mass index; RCM: restrictive cardiomyopathy; FAN: familial amyloid neuropathy; PM: pacemaker; SOC: standard of care; HT: heart transplantation; CD: conduction disorder; LT: liver transplantation.

steady increase in the free hepatic venous pressure related to excess pressure in the right cavities underestimates the intrahepatic pressure gradient (personal data). LB detects common histological abnormalities in cases of heart failure, such as the presence in the centrilobular area of sinusoidal dilatation, fibrosis (70%), hepatocytic atrophy (60%) or hemorrhage (50%) [14]. Centrilobular necrosis can be related to ischemic involvement. Fibrosis that is predominantly centrilobular is suggestive of cardiac origin and seems to be correlated with right cardiac dysfunction, irrespective of the etiology. Its association with periportal fibrosis might suggest more severe cardiac involvement [15,16].

Periportal fibrosis however, must also prompt an investigation for the presence of another cause of liver disease (steatohepatitis and viral hepatitis mainly). Perisinusoidal fibrosis suggests rather alcohol-induced liver disease.

To date there is no known recognized staging for liver fibrosis of cardiac origin. Based on the reading of autopsy studies, a 5-stage staging process, the Congestive Hepatic Fibrosis Score, was recently proposed [16]. Its inter-observer reproducibility, however, seems poor [14].

Although the clinical, biological and morphological data appear inefficient for the diagnosis of cirrhosis, the question remains regarding their ability to predict the success of heart transplant.

Prognostic factors of hepatic dysfunction

Before a heart transplant, several parameters are used to predict the severity of the cardiopathy and to justify priority access.

Although several donor parameters limit the success of the transplant (age, sex match, duration of cold ischemia), they are sufficiently considered during the choice of the graft so as to not put some or all of the receivers at a disadvantage. However, the increase in the early death rate in France until 2015 (25% mortality at 1 year) could be partially related to the increase in the age of the donors.

According to recipient criteria, the requirement of permanent intravenous catecholamines or the placement of a temporary ventricular assist device enables patient prioritization in most countries. Several classifications have thus been established, such as in France (''super emergency'' SU1, 2 and 3) and the United States (UNOS I, II status scores). These prioritization rules have improved the pre- and post-operative mortality rates (efficiency policy) while also equalizing the chances for transplant access (fairness policy).

In a context of multi-organ failure, the implementation of univentricular mechanical assistance (for left dysfunction) or of a total artificial heart (for biventricular dysfunction) is considered a temporary solution or a last recourse in several countries including the USA (bridge to transplantation or bridge to decision therapy). The most severe patients no longer have priority access to transplants, which enabled satisfactory survival rates to be maintained, although to the detriment of the principle of fairness. Moreover, some categories of patients, remain disadvantaged with limited access to transplants. This is true of right heart failure without possibility of assistance and congenital heart disease.

Contrary to an overly strict selection of patients with the risk of excessive exclusion of some of them, a refined assessment of the extra-cardiac comorbidities could improve the results after transplantation. As an example, when renal failure is present the risk of post-operative failure is high, and in France a GFR < 40 mL/min is an exclusion criterion. Undoubtedly, however, the level of severity or the type of renal failure onset (acute, chronic, acute-on-chronic) do not present the same level of risk. The combination of several types of failure would also increase the risk of failure, as highlighted in studies analyzing the influence of MELD. This score, which combines three parameters in its initial version (INR, total serum bilirubin and serum creatinine) appears to be associated with the severity of cardiac involvement according to two recent articles drawn from the UNOS database that includes 36,000 patients [17,18] (Fig.2). Due to a modification of the INR in patients on VKA, it is a simplified score known as MELD XI (MELD eXcluding INR), which was studied the most frequently. A MELD XI Score > 14, as measured before the transplant, is an independent factor of mortality in these studies from the first month, as well as during the first month post-transplant. When the subgroup of patients with a serum creatinine below 1 mg/L was analyzed, the influence of the MELD XI Score persisted, which attests to the importance of liver involvement on the post-transplant prognosis. It should be noted, however, that the MELD XI Score only estimates the level of hepatic damage based on hyperbilirubinemia.

In our series of 321 patients who received transplants between 2004 and 2010 and were followed-up for 5 years, we analyzed the MELD Score on the day of the transplant as well as from the time of enrolment on the waiting list [9]. In patients receiving VKA therapy, the INR was approximated using Factor V and not the prothrombin level, thereby allowing the evaluation of hepatic damage according to two distinct markers. It should be noted that in contrast to studies from American registries, the patients from our cohort were more severe, since at the enrolment they had more multi-organ failure and the indication for prioritization. They also received transplants from donors that were older by an average of 10 years.

Similar to the American cohort, however, the MELD Score remained a major and independent factor of mortality at 3 months, including MELD at listing. In addition, the presence of clinical ascites was also a strong independent factor. Finally, the need for mechanical ventilation was also associated with early mortality, although only in univariate analysis. The existence of one of these parameters at the enrolment was also associated with the need for early post-operative ECMO, which was the most important prognostic factor of post-operative survival in the study. A prognostic score combining both the significant parameters at listing as MELD and ascites (i.e. Score MA) appeared superior to the MELD Score or each of above parameters for predicting the success of the transplant.

In this same study, the analysis of causes of early death showed that there was an association between extra-cardiac parameters, early complications and post-operative ECMO. The occurrence of primary non-function seems to be related to the presence of ascites, with septic complications related to an increase in serum creatinine and to the need for mechanical ventilation. Finally, hyperbilirubinemia was related to a third group of fatal complications including all other causes, hemorrhagic in particular.

In order to improve the selection of HT candidates, theses scores, as well as the combination of the MELD Score with the Metavir Score [19], warrant confirmation.

The policy of selection and prioritization of the most serious patients in France until 2018 is nevertheless the primary reason for an abnormally high death rate. In other systems of allocation, the first-line implementation of permanent ventricular assist in the most serious patients or their exclusion has allowed the maintenance of a satisfactory early survival rate (10—15% mortality at 1 year). To improve the survival rate following heart transplantation at a national level, the French cardiac transplant community is developing a new graft allocation model based on two specific risk scores of mortality on the waitlist or following heart transplantation. The final score includes objective parameters at listing, reflecting liver impairment in particular (i.e. short-term MCS, bilirubin, GFR and natriuretic peptide), and has now been applied since January 2018.

Combined heart-liver transplantation

In patients with liver failure, the indication of double transplantation should be discussed case by case, similar to the double heart-kidney transplant, which is proposed after optimization of the hemodynamic parameters with a GFR < 30 mL/min. An overview of the results and indications for the combined heart-liver transplant are presented below.

Indications

Up until 2015, 190 and 45 CHLTs, respectively, were performed in the USA and France. The data was derived either from small single-center series or from the retrospective analysis of American databases [20,21]. To date there are no cohorts that can be analyzed in France or in Europe. A com-

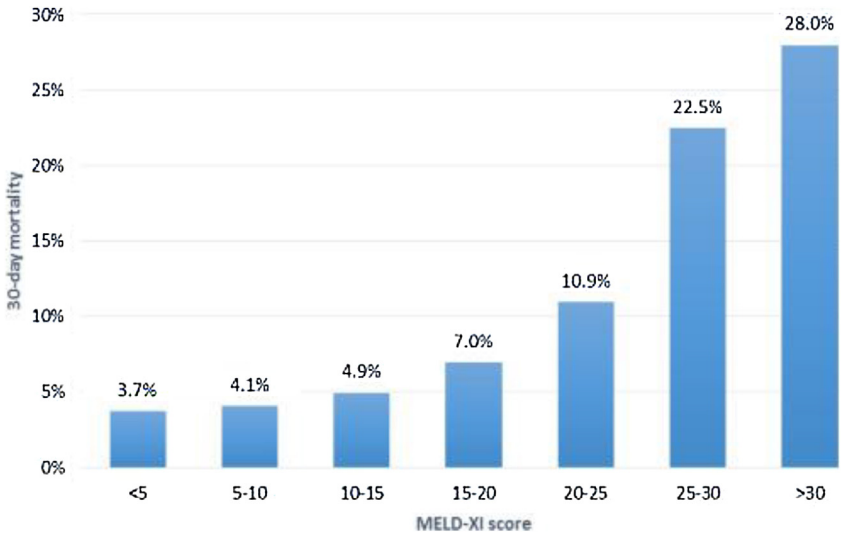

Figure 2 Influence of the MELD Score excluding INR (MELD-XI) on early mortality after heart transplantation alone [UNOS data ($n = 36,000$)]. N.B: MELD: model for end-stage liver disease.

parative analysis of the heart-liver transplant indications in patients receiving transplants in the United States via the UNOS database ($n = 98$) and in our center (Pitié-Salpétrière Hospital, Paris, France, $n = 18$) shows these findings:

- a rate of transplant access in the United States that is below that of France (50% versus 78%) [20];
- the predominance of combined transplantations for restrictive (39%) and congenital (21.5%) heart disease in the United States, and the predominance at Pitié of dilated and ischemic cardiomyopathies (28% each), with alcohol, metabolic syndrome and chronic viral hepatitis as the main risk factors of liver disease;
- the near systematic presence of F3-4 fibrosis on the explants of patients from Pitié; and;
- as a corollary, HCC as a possible indication for transplant.

Surgical technique

There is no major difference in the surgical techniques with regard to the methods of transplantation for each organ [21]. CHLT is generally performed during the same operative time. It begins with the heart transplantation, thus limiting the cold ischemia time of the cardiac graft and avoiding any risk of heart failure during reperfusion of the hepatic graft. The heart transplant procedures are standardized, except for the indications of congenital heart disease. It is done using extra-corporeal circulation and is followed by open-chest liver transplantation. There are two main techniques of liver transplantation: en-bloc resection, including the retrohepatic segment of the inferior vena cava under venovenous extracorporeal circulation, and the piggyback technique using a temporary portocaval shunt in which end-to-side or side-to-side anastamosis unites both vena cavas. Some centers transplant the heart and the liver en-bloc, arguing that the procedure minimizes hepatic cold ischemia time. Others choose to maintain ECMO during the liver intervention [22,23]. Finally, some centers have practiced transplantations in two stages with different donors (sequential transplantations).

The perioperative results could only be analyzed for the cohort from the Mayo Clinic, which was mainly comprised of patients with FAN. The results were excellent, with very low cold ischemia times, transfusion needs, and lengths of stays in intensive care [13]. Other than the quality of the operators, these results are due to the absence of pre-operative liver damage (normal hemostasis, low MELD Score, no portal hypertension) and to moderate cardiac disease.

Survival after combined transplantation

An analysis of the American cohort shows survival results that replicate those obtained in single-organ heart transplantation, with a 3-year survival of 79 versus 75% ($n = 98$; $P = NS$) [15]. In the subgroup of patients receiving transplants for congenital heart disease, the 10-year survival seems even superior compared with that of single heart transplants (83% vs. 39%, $P = 0.03$) [23].

As mentioned previously, the limitations of the preoperative assessment of liver fibrosis levels, the differences in indications or techniques, and, according to the countries, transplant access rates, necessitate a critical analysis of the results of the combined transplant. These results need to be compared with those obtained in single-organ transplantation over a similar period and according to the allocation policies and the indications.

Within the cohort at Pitié, the 3-year survival is only 55%, with a post-heart transplantation survival of 70%. Several factors contribute to this difference. First, it should be emphasized that the policy for prioritization in France from 2005 to 2015 favored transplantation of the most serious patients. As a result, survival after single-organ heart transplant during this period was lower than in other countries. This policy was also applied to patients who received a CHLT, in which an overall rate of access to transplant (81%) and in emergency (20% via SU1) were greater than those of the American cohort (50%, with 4% via UNOS I). Second, it

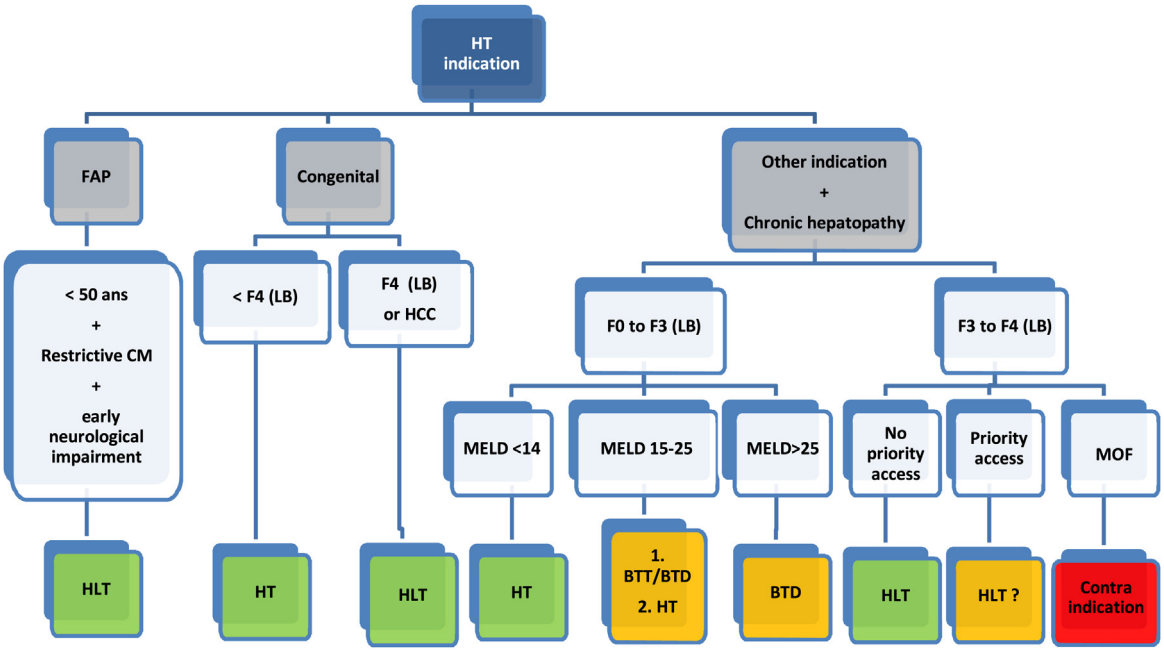

Figure 3 Indications of the combined heart-liver transplantation according to the level and type of liver damage. Decisional tree proposal. N.B: BTD: bridge to decision; BTT: bridge to transplantation; CMR: restrictive cardiomyopathy; F: stage of liver fibrosis according to METAVIR histological classification; FAP: familial amyloid polyneuropathy; MELD: model for end-stage liver disease; LB: liver biopsy; HLT: combined heart and liver transplantation; HT: heart transplantation; LT: liver transplantation; MOF: multi-organ failure.

should be noted that the mean age in France was 10 years higher in the donors (43 versus 28 years) and in the receivers (53 versus 43 years). Third, although the mean MELD Scores seemed to be similar at the transplant (13.8 at Pitié vs. 14.9; *P* = NS), the proportion of patients with F3—F4 fibrosing liver disease was much greater at Pitié (88% versus 25%) and was explained by a predominance of steato- or viral hepatitis in our cohort. And finally, a preliminary analysis suggests that the addition of risk factors, namely the extent of cardiac emergency and the presence of one or more extra-cardiac failures before transplant, increase the risk of early failure.

At present, the French Biomedicine Agency (ABM) has readjust the rules for transplant allocation by taking into account not only the level of cardiac severity but also the presence of one or more extra-cardiac failures. This change will also apply to patients with an indication for CHLT, which risks limiting access to transplants for patients with less failure (e.g., with HCC or without standby therapeutic ressource).

In practice

Subject to validation, a proposal for a decision algorithm is presented in Fig. 3. The treatment decision (contraindication, CHLT) depends on four criteria:

- the model of liver damage;
- the level of liver fibrosis;
- the degree of liver impairment; and;
- the number of organ failures.

The indication for CHLT in patients with FAN is formalized when there is moderate to severe heart damage that cannot be improved with placement of a pacemaker. It is only useful, however, when there is no debilitating neurological involvement or advanced undernutrition.

When there is pure congestive hepatopathy or associated liver disease, the absence of severe fibrosis (i.e. Metavir score F0 to F2) or HCC would argue for heart transplantation alone. In the presence of (pre) cirrhosis (i.e. Metavir Score F3 to F4) or HCC, and in accordance with transplantability criteria, CHLT must be discussed collegially. Nevertheless, a MELD Score > 14 must raise consideration of first-line ventricular assist in order to improve the hepatic or renal dysfunction related to heart failure. An indication for heart transplant alone or CHLT may only be considered according to the improvement of the multi-organ failure under mechanical assistance. Persistence of multi-organ failure, however, contraindicates the organ transplant.

Conclusion

We have seen that there are three distinct forms of combined cardiac and hepatic impairment. Familial amyloid neuropathy with cardiac involvement presents clear indications for CHLT. In other patients with end-stage heart disease, liver damage characterized by a high MELD score or the presence of ascites is frequent and non-specific but is associated with a high risk of failure after heart transplantation alone. In the event of prolonged cardiac progression, as in congenital cardiopathy or when risk factors of chronic liver disease are present, screening for cirrhosis through liver biopsy or for HCC through imaging must be system-

atic at the patient's pre-transplant assessment. When there is proven cirrhosis or HCC that meet the transplantability criteria, the indication for CHLT must be made.

Disclosure of interest

The authors declare that they have no competing interest.

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