We are IntechOpen, the world’s leading publisher of Open Access books
Built by scientists, for scientists

6,600
Open access books available

177,000
International authors and editors

195M
Downloads

154
Countries delivered to

TOP 1%
Our authors are among the most cited scientists

12.2%
Contributors from top 500 universities

WEB OF SCIENCE™
Selection of our books indexed in the Book Citation Index in Web of Science™ Core Collection (BKCI)

Interested in publishing with us?
Contact book.department@intechopen.com

Numbers displayed above are based on latest data collected.
For more information visit www.intechopen.com
Chapter

Economic Evaluations of Liver Transplantation as Tools for Decision-Making and Implications in Clinical Practice

Santiago Rodríguez Villafuerte, Adilson Renato Veríssimo, Luis Geovanny Mochas, Fabian Andrés Zurita and Julio Patricio Salazar

Abstract

The economic theory of liver transplant (LT) and issues specifically related to the waiting list are still in their early days, not being fully explored from the theoretical, empirical point of view and their implications for the formulation of evidence-based public policies. The success of each LT stage (pre-LT, LT, and post-LT) is based on the success of the previous one, hence the need for a detailed study of each of them. Previous economic analyses have focused only on the cost of LT. However, comprehensive economic assessments that allow the integrated and detailed study of each of the steps will allow investment in the most critical points of the processes. In this way, there will be effective management with the elaboration and implementation of public policies that make processes more cost-effective, maximizing the benefit of LT. Our chapter will focus on the pharmacoeconomic study of the different stages that make up LT in chronic liver diseases. It will also allow reflection and analysis of the policies established in transplant centers; in this way to make better use of resources and seek a greater benefit from the transplant.

Keywords: liver transplant, economic evaluation, public policies, cirrhosis, portal hypertension

1. Introduction

In recent decades, epidemiological changes and technological advances warned in the health sector have improved the quality of life of patients and reduced the morbidity and mortality rates of a significant number of diseases [1–3].

The wide range of health technologies—medicines, materials, equipment, procedures, organizational, educational, information, and support systems that allow
health care and care—have made it necessary to analyze evidence-based analysis, taking into account aspects such as efficacy, accuracy, effectiveness, and costs in the decision-making process, so that they can be made available in health systems; consequently, there is a constant concern with the sustainability of health systems and the ability to maintain long-term benefits, thus in order to evaluate the relationship between the health sector budget and the different technologies, economic assessments emerged, since the different interventions compete with each other for finite resources—cumulative technologies, non-substitute [1–4].

Among the technologies (procedures) that have improved in the last six decades is solid organ transplantation, which evolved from experimental procedures to standard procedures that save lives [5].

Regarding the area of hepatology and liver transplantation (LT), the first economic evaluations date back to the 1990s and described only the cost of LT [6–8]. Further analyses focused on the economic impact of different liver diseases [9–13] and on cost-effectiveness and cost-utility studies of treatments and screening tools for both liver diseases and their decompensation [14–19].

However, data on costs related to the management of patients on the waiting list and the economic impact of complications of chronic liver disease in this clinical scenario as well as in the follow-up of patients in the post-LT are scarce and should be considered in the global evaluation [20–23]; in this sense, this chapter seeks to contribute to: (a) debate, (b) decision-making process, and (c) development of evidence-based public policies that allow maximizing the benefit of LT in chronic liver diseases and minimizing the cost of opportunity in a scenario with limited resources.

We will also carry out a short review of pharmacoeconomic studies in the scenario of LT in acute liver failure.

2. General concepts

LT is the therapeutic option of choice for patients with acute or chronic end-stage liver failure (Table 1) [24–26]. It should be recommended for patients whose estimated survival after LT exceeds or exceeds life expectancy without the procedure or when it is expected to enable significant improvement in quality of life [27].

The survival benefit is considerable. In Europe, according to the European Liver Transplant Registry (ELTR), survival rates in 1 and 5 years are 83 and 71%, respectively [28].

In the United States, according to the Organ Procurement and Transplantation Network (OPTN)/United Network for Organ Sharing (UNOS), survival rates for recipients who received deceased donor grafts are 91.2% in the first year and 75% in the fifth year [29].

Cirrhosis, by any etiology, is the most frequent indication of LT [30, 31]; however, the diagnosis of cirrhosis per se does not justify the indication of LT. Although cirrhotic patients have lower survival when compared with the general population, the presence of decompensation of the underlying liver disease does not completely justify the indication, even because many of them can be controlled or avoided with effective medical treatments [31, 32].

Patients should be carefully evaluated and prioritized using prognostic models that incorporate clinical and laboratory variables, which helps the indication for LT [24, 31].
Currently, in many countries, the severity and risk of death from chronic liver disease are estimated by the MELD score (Model of End-stage Liver Disease), a robust predictor of survival in 3 months [33–35]. For its calculation, three laboratory tests are used: total bilirubin, creatinine, and international normalized ratio (INR) [36]. In other words, the success of the transplant depends, in part, on timely indications, on careful evaluation, on proper prioritization and allocation, and on enough donors. However, when is the appropriate time to indicate the LT and which people should be included in the list are issues that continue to arouse interest and controversy [24, 26, 30].

3. Waiting list management

3.1 Evaluation of candidates and selection

Early identification of patients considered as candidates for LT is crucial to ensure the greatest possible benefit [25–27]. Although the severity of liver disease is the initial concern, a number of considerations guide the evaluation process. Examinations and consultancies preferably performed in the outpatient setting allow: (a) to confirm the lack of effective therapeutic options for underlying liver disease; (b) identify and optimize the factors that may affect the survival of candidates after inclusion on the waiting list; (c) identify, evaluate, and determine the impact of comorbidities on post-LT results; (d) fully evaluate psychosocial aspects and educate candidates and their families about the LT process, post-surgical care, and long-term care to exclude absolute and relative contraindications [25, 31].

Commonly, multidisciplinary teams are composed of hepatologists, transplant surgeons, anesthesiologists, psychiatrists, physicians from other specialties, specialist nurses in LT, nutritionists, psychologists, etc. [25, 31].

There are assessments common to all candidates and others that adapt to specific clinical conditions (Table 2).

Grafts should be allocated, ideally, to patients with a higher probability of list death and, at the same time, a higher probability of survival after the LT [37, 38]. However, if, on the one hand, the best LT results are achieved when the patient is not...
decompensated and has a good general condition, on the other hand, it is decompensated patients who need urgent LT because they have a worse prognosis [39].

The dissociation between the number of candidates and donors remains one of the greatest limitations for performing transplants. This creates an extremely complex situation in the management of waiting lists [30, 31]. Once the MELD model with good prognostic capacity was defined in terms of short-term survival of cirrhotic patients, we tried to define a cutoff point from which patients should be included in the list. A study [37] conducted in the United States evaluated 12,996 patients included on the waiting list for LT between 2001 and 2003 (patients listed for acute liver failure and hepatocellular carcinoma (HCC) were excluded from the analysis). Patients were followed up until death on a list or 1-year post-LT. At the time of inclusion, more than 50% of the candidates had <15 points and, at the end of the follow-up period, 24% of the LT were performed in patients with MELD <15. Among the patients who were still on the waiting list, 75.9% of those included in the list with a score between 6 and 11
remained with the same score and less than 5% had a higher score. Regarding death rates in 1 year after the LT, patients who transplanted with <15 scores had 3.66 times [confidence interval (CI): 2.23–5.95; \( p < 0.001 \)] were more likely to die than patients with higher scores, suggesting that the risk of LT in patients with meld score <15 is higher than the benefit [37]. Thus, in the United States, grafts should be offered at the local and regional level primarily for patients with a MELD >15 [40].

The model has limitations, not aforementioned to the severity of some of the complications of chronic liver disease, such as refractory ascites, portosystemic encephalopathy, and HCC. Situations in which the score does not reflect the natural history of the disease are known as special situations. For patients with special situations, points are awarded, independent of the calculated MELD score, which would be equivalent to the increase in mortality while on the waiting list. The score attributed to these patients is different between countries and/or transplant centers.

4. Economic assessments

4.1 On the waiting list

In the United States, the waiting list stay time for LT is approximately 11 months and has been decreasing [41]. Longer list times may mean transplanting patients with more advanced disease and, therefore, less cost-effective transplants, due to increased costs of the procedure and/or pre-LT care [42].

Economic analyses have focused on the economic impact of liver disease and the cost of LT, without considering that waiting list patient management is also a costly process [20–23].

The lack of integrated medical records between outpatient services and hospitalizations and specific software for hospital management, in addition to overhead costs not always available in hospital cost appropriation systems, makes it difficult to study the economic impact of waiting list management [20–22].

The inclusion of patients on the waiting list for the LT comprises two subperiods: (a) evaluation, during which the need for the patient to be transplanted and investigated the presence of absolute or relative contraindications; and (b) permanence in the list, from the date of inclusion to the outcome, be it transplantation, death, or exclusion. However, studies evaluating the cost of waiting list management have focused on the length of stay on the list.

A retrospective North American study [20] evaluated costs of 58 patients included in the waiting list between November 1996 and December 1997. The analysis included different moments: permanence on the waiting list (treatments for liver disease, comorbidities, and complications), perioperative, and post-LT. The costs were grouped into five categories: professional and hospital services during hospitalizations, organ uptake, outpatient services, and post-LT medications. Costs related to outpatient consultations or examinations performed outside the transplant center were not included. After 2.5 years of follow-up, there were 19% of deaths on the waiting list, 36% remained on the waiting list, and 45% had undergone transplantation. While waiting lists, patients had 9.7 outpatient visits and 3.1 hospitalizations (52.8 days/patient or 3062 days in total). The cost associated with hospitalizations was US$ 3.37 million (for every dollar spent on professional services during hospitalizations, an additional amount of US$ 2.75 corresponding to hospital expenses was requested to support the services). The subgroup analysis found that the cost to stay on the waiting...
list on an average of 14 months was $1.8 million for the 26 patients who received deceased donor graft ($70,000/patient), $0.3 million for patients who remained on the waiting list ($14,000/patient), and $0.8 million for patients who died on the waiting list ($74,000/patient), statistically significant when compared with that of patients on waiting lists ($p < 0.01). Spending in the waiting list period accounted for 41% of the total expenditure. The sensitivity analysis indicated that the variation of the dollar per diem by ±50% during hospitalizations would modify the cost of staying on a waiting list between 36 and 46%. The authors pointed out some limitations of the study: it was conducted in a single center, and the average cost of treatment could be explained by the inclusion of young patients with less severe liver disease, even though there was no statistically significant difference between the characteristics of the sample. In addition, they stressed the importance of including care costs from other centers to comprehensively assess the impact of the waiting list on the total cost and the need for national studies enabling more accurate subgroup analyses. In other words, they suggest using the social perspective in future studies [20].

A retrospective North American study [21] with OPTN data analyzed the costs of 990 adult patients submitted to LT (94% of deceased donor and 6% living) between March 2002 and August 2007. Patients undergoing double liver and kidney transplantation were included in the analysis. Using the perspective of health plans, the researchers divided expenses into three periods: pre-LT (365 days before LT up to 3 days before admission to LT), LT (2 days before admission to LT up to 90 days post-LT), and post-LT (91–365 days post-LT). Of the 990 patients included in the analysis, 778 had health insurance coverage in the pre-LT, 690 in transplantation, and 678 in the post-LT, and 365 patients had coverage in the three periods. The costs were associated with the MELD score at the time of transplantation. Patients with a MELD score <20 points were more frequently white, presented etiology of HCV liver disease associated with HCV, and received grafts from a living donor ($p < 0.005). Patients with ≥21 points had more frequent double liver and kidney transplantation, had more frequent liver disease decompensation (ascites and portosystemic encephalopathy), and had time on mechanical ventilation and in the ICU after the greater LT ($p < 0.05). Regarding the severity of liver disease, the MELD score at the time of LT was significantly associated with pre-LT and post-LT ($p < 0.0001) costs in the univariate model (MELD 6–14: US$ 77,100 ± 86,800; MELD 15–20: US$ 92,400 ± 110,500; MELD 21–27: $158,300 ± 262,300; MELD 28–40: $237,300 ± 229,800). After adjusting the values for age, diagnosis of HCV, HBV, HCV, ABO group and re-LT, it was observed that patients with MELD score 28–40 points and submitted to double liver and kidney transplantation had statistically higher costs compared with the other groups in the pre-LT and transplantation period (MELD 28–40: US$ 145,500 and US$ 60,700; double transplantation: $178,300 and $90,900, respectively). The authors pointed out that the main driver of the high cost of LT is the pre-LT and LT costs [21].

US researchers [22] using data from OPTN/UNOS and the American Public Health System (Medicare) studied the association between the cost of waiting list stay and the severity of liver disease, assessed by the MELD score. We analyzed 15,710 adult patients of both sexes, included on the waiting list between 2002 and 2008. In both cohorts—OPTN/UNOS and Medicare—the median age was 56.2 and 46.3 years, respectively. The most frequent etiology of liver disease was HCV, and 8% of patients had associated HCC. The most frequent comorbidities were type II diabetes mellitus and hypertension. The monthly cost of patients on the waiting list was $1805. However, medical costs varied according to the MELD score, being higher in those with more severe diseases and, therefore, with higher scores. In patients with a MELD
score 5–10, the average expenditure was US$ 260 ± 2453, while in those with a MELD score of 35–40, it was US$ 33,792 ± 118,952. Age (p = 0.01), female gender (p = 0.03), and diagnosis of HCC (p = 0.03) were associated with higher costs during waiting list stay. The increase in the MELD score during the waiting list was associated with higher costs (US$ 165 for each additional MELD point; p < 0.0001), and expenses with more severe patients (with MELD >30) score were 10 times higher compared with less severe patients (MELD <20 points). As warned by the authors, the study presented some limitations: (a) the cohort studied represented only patients with Medicare health insurance, that is, 27% of the population listed for LT during the study period; (b) higher MELD scores were reported more frequently than lower scores, which could lead to underreporting of these patients. On the other hand, the costs reported by Medicare ensured that the differences in expenditure reflected the actual intensity of resource use. The authors also emphasized that cirrhotic patients with less social support may require more additional care and social services, leading to higher costs [22].

A prospective Brazilian study [23] based on the microcosting methodology evaluated the total cost of patients on the waiting list for LT and the costliest resources. Adult patients enrolled on the waiting list for the LT between January 2012 and December 2013 were prospectively followed up until the date of transplantation, death, exclusion or, at the end of the follow-up, if still on the list. For the analysis, the patients were subdivided into four groups (quartiles) according to the severity of the disease, estimated by the MELD score. The data were obtained through the analysis of medical records and included: number of consultations with health professionals, number and type of procedures performed, and hospitalizations. When the analysis was performed, of the 482 patients included, 27.8% had been transplanted, 21.4% had been removed from the waiting list, 13.9% had died, and 36.9% remained on the list. The mean number of hospitalizations per patient was 1.4. In the inclusion in the list, 27.39% had ≤ MELD score, 17 points, 25.31% had a MELD score of 18–24 points, 23.44% had a MELD score of 25–30 points, and 23.86% had a MELD score ≥ 30 points. The total cost to attend for 24 months the 492 patients was US$ 6,064,986.51. Of this total, US$ 1,965,045.52 (32.4%) were generated by outpatient services and US$ 4,099,940.99 (67.60%) per hospitalization. In the outpatient setting, the costliest sectors were: medications (44.31%), clinical analyses and imaging tests (31.68%), and medical professionals (8.96%). During hospitalizations, the most onerous sectors were: medications (35.2%), daily in hospitalization units (26.38%), and imaging tests and clinical analyses (16.72%). Regarding the MELD score, the highest costs were for patients with MELD 25–30 (US$ 16,686.74 ± 16,105.02), being lower for patients with MELD <17 (US$ 5703.22 ± 9318.68). The cost was directly proportional to the number of hospitalizations and hospitalization time [23].

4.2 In LT

The first economic assessments of liver transplantation began in 1990 [43–50] in developed countries. The vast majority were retrospective studies that evaluated transplantation for both chronic diseases and acute liver failure. One of them evaluated double liver-kidney transplantation and the other with an inter-living donor. These studies used different and variable methodologies, considering different periods and long follow-up, which is why there is no uniformity of data or an idea of certain costs (Table 3).
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Parents</td>
<td>US</td>
<td>France</td>
<td>US</td>
<td>US</td>
<td>Netherlands</td>
<td>Italy</td>
<td>US</td>
</tr>
<tr>
<td>Sample (n)</td>
<td>144</td>
<td>38</td>
<td>109</td>
<td>1148</td>
<td>100</td>
<td>252</td>
<td>67</td>
</tr>
</tbody>
</table>

- **Outline**
  - Retrospective
  - Prospective

- **Cost elements**
  - Direct costs (from pre-LT to hospital discharge excluding professional fees)
  - Direct costs (from LTx to hospital discharge)
  - Direct costs (from pre-TxH to 1 year after Tx)

- **Donor type**
  - Deceased donor
  - Donor deceased

- **Euro costs (€)**
  - 132.930 ± 47.079
  - 154,610
  - 116,866
  - 107,675
  - 75.747 ± 83.846
  - 102.220 ± 123,600

- **Risk factors for high cost**
  - Not reported
  - Donor and recipient age
  - Retransplantation, advanced age (>40 years), Grav of liver disease, Rej sharp
  - Pre-Tx kidney function Insuff—fulminant liver disease (UNOS Status 1)
  - Pre Renal Tx Mechanical ventilation dependent
  - Pre Renal Tx non-alcoholic liver disease insuf hep Fulm, Portal vein thrombosis

| Table 3. | LTx economic assessments. |
Due to the development and improvement of more objective mathematical models, which took into account selected risk factors for chronic liver disease and the subsequent adoption of the MELD score for organ allocation, previous research aimed to evaluate the economic burden of liver transplantation according to MELD-based levels of liver disease severity.

Williams et al. [51] determined that the average value of liver transplantation in Memphis, United States, was $92,866 in 1984 (the value updated by inflation for 1995 is approximately $150,000), ranging from $34,997 to 319,337.

Researchers from Turkey in 2011 [52] evaluated the costs of liver transplantation from the admission of pre-transplant to hospital discharge from 1999 to 2009. The sample consisted of 279 patients, the mean age of the recipients was 35.7 ± 14.1 years, and 70.6% were men. The main etiology of transplantation was HBV (44.8%, n = 125), HCV (12.5%, n = 35), alcoholic liver disease (6.5%, n = 18), cryptogenic cirrhosis (7.9%, n = 22). One-hundred and eighty-four (184) patients (65.9%) had MELD from 11 to 20; seven patients (2.5%) had MELD around 31 points, with a correlation to CTP 53.8% (n = 150), belonged to class B, and 38.8% (n = 108) belonged to class C. The average length of hospital stay was 39.4 days in 1999 and 41.7 days for 2009. There was no significant difference when comparing the length of hospital stay with body mass index, MELD, and CTP scores.

The researchers concluded that the medical items that generated the highest costs during the study period were medications, medical equipment, and the operating room. There was no statistically significant difference between the etiology of transplantation and cost [52].

When compared with the MELD score, there was no significant MELD difference between 1 and 10 (n = 45) US$ 28,539; MELD between 11 and 20 (n = 184) US$ 30,798; MELD between 21 and 30 (n = 43) US$ 32,564; MELD ≥31 (n = 7) $35,478. Regarding CTP, there was a significant difference with \( p < 0.01 \) CTP A (n = 21), spent US$ 34,664; CTP B (n = 150) US$ 27,821; CTP C (n = 108) US$ 34,245.

The researchers also concluded that the transplant, when performed in a living donor, presented higher costs; when compared with deceased donor, $33,454 $27,582, respectively with \( p < 0.05 \) [52].

The group of Boerr et al. [53] evaluated the cost of LT from the perspective of a high complexity hospital and its relationship with the degree of severity of the underlying liver disease using the MELD score, using microcosting analysis.

The economic analysis included the cost of hospitalization in different areas, cost resulting from diagnostic and therapeutic procedures, as well as payroll. Administrative costs were not assessed. Patients diagnosed with HCC were not included in the analysis because they were transplanted earlier by the additional points in the MELD score.

The authors evaluated 77 patients submitted to LT from 2006 to 2010 and divided them into two groups according to MELD score: group 1: MELD score from 6 to 19; group 2: MELD score from 20 to 40. The mean age was 53 ± 14 years, the mean hospitalization was 11.6 ± 8.9 days. The average cost of LT was US$ 33,461 ± 12,896 per patient [53].

The authors concluded that the cost of LT is directly proportional to the MELD score, and the higher the score at the time of transplantation, the higher the cost.

The authors concluded that the cost of LT is directly proportional to the MELD score, and the higher the score at the time of transplantation, the higher the cost. (group 1: US$ 30,493 ± 8825 per patient, group 2: US$ 36,506 ± 15,833 per patient with \( p = 0.04 \)). The cost of intensive care unit admission was also related to the MELD score (group 1: US$ 3094 and group 2: US$ 4255 \( p < 0.01 \) [53].
4.3 In the post-LT

The LT has become one of the main treatments for properly selected patients. Nowadays, the long-term survival has improved, many are being tending outside a post-transplant center, which had led to a general familiarity with the complications that could be presented [54].

Many post-transplant complications are being mentioned in medical literature, listing the most common ones below [55]:

• Acute or chronic rejection.

• Complication of the immunosuppression that includes hypertension, renal failure, malignancy, a variety of dermatological complications, and metabolic diseases such as diabetes mellitus, obesity, hyperlipidemia, and osseous disease.

• Biliary complications.

• Reappearance of primary hepatic disease.

• Thrombosis.

4.3.1 Factors involved in the cost of post-LT

If we consider the economic inversions we make in the pre-transplant and transplant, by itself they generate considerable expenses in the health budget, the post-transplant period, and we are not exclusively talking about the immediate recovery but also about all the treatments and possible complications that could appear in long term; this also ends up influencing the health cost elevations that intervene in this type of processes, not only under the perspective of health systems but also from the people, their families, and/or caregivers.

The post complications of LT are relatively common and expensive. As an example, the acute rejection can be presented with an incidence from 20 to 60%. The infections affect up to 70% of the receptors. The thrombosis of the hepatic artery complicates from 4 to 12% of the liver transplants in adults, and the biliary complications occur with an incidence from 10 to 30%; nevertheless, the incremental costs of them are unknown as well as who will assume the price for the complications (the center or the payer) [56].

Several studies suggest that the post-surgery complications are expensive for both the medic center and the payer. Some data alludes that, from these two, the payers are the ones to endure the highest financial burden associated with the posterior complications, and the average hospital costs can increase more than six times when a complication is presented [57].

The shift of this costs depends of various factors, one of them being the type of complications developed by the patient. In such way, we can observe that the biliary complications and the ones that require a reoperation are associated with an increase of prices [56].

Axelrod et al. [58] mention in their study that in centers found in the highest quartile of complications, the biliary issues significantly associate with more heavy costs compared with the centers in the lowest quartile of complications [58]. It is also known that, in this latter centers, there is a 2.73 times more risk of post-transplant readmission [59].
It has also been observed that even when estimating costs in patients with “ideal” LT, meaning they have no risk of complications, whose post-surgery process results are simple (hospital stay <14 days and home discharge), there still exists a significant variety in the use of resources and the medical attention expenses, so understanding the factors that determine this variability in the costs is vital for diminishing unnecessary outlays [60].

But not only are complications considered a factor in the rise of the post-transplant costs, it is also important to mention that these complications depend on risk factors that existed previously in the transplant, in such way that is mentioned in several studies that diabetes and the dialysis dependency could be considered factors that condition the appearance of subsequent complications; therefore, the increase of the costs [59].

Another factor involved in the variation of the costs is the MELD score. MELD is a system of score that allows us to measure the severity of the chronic liver disease, being able to find that at a higher score in this scale, there will exist a higher financial expense, in which the incomes of the transplant center will not be enough to supply what it’s within the process and the recovery, which reflects in an unfortunate way with a financial disincentive for performing transplants on high MELD receptors [56].

Several studies demonstrate that patients that have developed an illness with an extreme severity and have a high MELD score are considered of high cost. In the same way and in relation with the functional state and physical capability, those extremely dependent patients were also classified as high cost. This is supported because, in the pre-surgical and post-surgical results, as the medium of LOHS (Length of Hospital Stay), the duration in ICU (Intensive Care Unit), and the readmission rates in 30 days were slightly elevated for patients of high cost. In that way, it’s recommended that, if there exists an improvement in the pre-surgical results of patients with liver transplant with a high MELD score and a physical capacity severely damaged, no further use of costs and resources would be required. With this, post-surgical costs would be reduced [59, 61].

In relation with this MELD score, it has also been seen that the sickest patients, with MELD scores superior to 28, have a survival similar to patients transplanted with a low MELD, and once, out of the immediate post-transplant period, the costs have no difference between high and low MELD scores, mostly explained not only by the success of the transplant but for the costs avoided by the recovery of the patients of their serious diseases [60].

The cost factors in any other type of surgical procedure, especially in general and vascular surgery, are determined by the pre-surgical risk factors of the patient and not by the post-surgical complications, while, in the liver transplant, the pre-surgical factors impulse the costs, but in the post-surgery, the complications are the principal generators of costs [56].

We can also add that the complications of the liver transplant not only represent by themselves an additional cost, but also because they show an increment in the cost of the care associated with them. Because of this, even a short stay does not mean lower costs if there is a complication [60].

It’s important to mention that medical literature indicates that the difference in costs is not affected by the quality of the supplier of the treatment, but that the characteristics of the health system do influence as one of the most important explanations of the differences in costs of the liver transplant [57].

The type of graft is also considered another factor to take into account in the post-transplant costs, since the DCD (Donation after Circulatory Death) liver transplants
have become more common in the past years, coming to represent up until 17% of all transplants in 2013–2014. However, due to the prolonged warm ischemia time, these allografts are more sensitive to severe reperfusion injuries than DBD (Donation after Brain Stem Death) liver, which would bring as consequence that the receptors of DCD would frequently show lower results of survival, graft rejection rates, post-transplant complications, and health-related quality of life (HR-QoL). Not only this but also ischemic cholangiopathy (IC) is a particular preoccupation in the receptors of DCD and relates with a higher increment of the morbidity, a reduction of HR-QoL, and generally it requires a new transplant. Not because of what is mentioned above, we may stop pointing out that with a strict selection of organs and with highly capable transplant team, the DCD results can be compared with the DBD patients [62].

Another factor to take into consideration while evaluating the costs of the hepatic post-transplant is the age, when the liver disease is presented at an early age, it determines the functional hepatic deterioration, which forces to search alternative treatments as it is the hepatic transplant.

In an analysis done by Showstack and his workmates, it was demonstrated that there exist other two factors that influence the increment of the prices that are related with the older age of the donor, the older age of the receptor, the alcoholic liver disease, Child-Pugh cirrhosis class C, and that patients previous to the transplant have been hypnotized [7, 63, 64].

Indirectly, it is also mentioned in the bibliography that an allograft of a high risk index from the donor, the post-transplant discharge to a rehabilitation center, the hepatic disease by itself plus the preparations for the transplant could weaken the patient, putting them in a low nutritional and immunological state. This could lead to a higher risk of posterior hospitalization after the transplant, with which the post-transplant costs would increment [60].

### 4.3.2 Some numbers of the post-LT costs

There is no existent data that show the exact post-transplant costs, factors have been mentioned that can influence the increment of this expenses, as well as the causes of why it can increase the costs.

An analysis done by a study mentions that at after 90 days of the hepatic transplant, the economic re-entry supposed 43,785 dollars of extra costs in comparison with the patients that did not re-enter so that the readmissions are associated with the variation of the center and a better utilization of resources [59].

The database of the American University Health System Consortium facilitates the financial data on the economic impact of the hospitalization re-entries for hepatic transplant for every hospitalization registered, mentioning that the average price of the index hospitalization for transplant can be $121,161 (interquartile range (IQR), $94,777–$169,361) besides, the average price associated with the hepatic transplant until 90 days after medical discharge including the admission of the transplant can reach $168,666. The subsequently readmitted patients have elevated prices in their income index ($127,088) in contrast with the patients that were not readmitted ($116,250) [59].

These hospitalization readmissions after the transplant generate a significant economic impact and highlight the obligation to improve the attention at long term in this section of high-risk patients, even more because this data can reflect only one part of the long-term risks associated with chronic immunosuppression, graft rejection, and disease recurrence [59].
Other studies that talk about post-transplant costs mention that the average incremental expense per quality-adjusted life year from the moment in which the patient is included in the donors waiting list up to 27 months after the transplant, especially for primary biliary cholangitis (PBC) patients, alcohol-related liver disease (ARLD), primary sclerosing cholangitis (PSC), is of £29,000 sterling pounds (£1000–£59,000), £48,000 (£12,000–£83,000) and £21,000 (£23,000–£60,000), respectively. The estimations between cost-effectiveness were lower for patients with ALD during the period of 27 months than for patients with PBC or PSC. In a way, this reflects the costs of the most patients with ALD evaluated for each transplant. Although it is data that not only includes the post-transplant but also suggests an estimation of these expenses [63].

Bonsel et al. published the analysis results of price effectivity of the hepatic transplant done in Netherlands in 1980 in nonalcoholic cirrhotic patients, estimating the costs 2 years from the post-transplant in 226,967 Hfl (approximately £130,000 in actual price). They described that the cost of additional quality-adjusted life year for life was around 51,000 Hfl and 133,000 Hfl (£29,000 and £76,000 in actual prices). Even though these results are transcendental for the practice in United Kingdom, it is probable this cannot be directly generalized with other situations because, as an example, the characteristics of the transplant programs in United Kingdom, United States, and other South American countries are very distinct by the number of transplants done in each country [65].

Also, the costs of the hepatic post-transplant could vary depending on the different immediate complications that could be presented finding in the studies that evidence exists showing that the centers in the higher quartile of biliary complication rates, after the liver transplant, spent $22,895 extra per transplant in comparison to the centers in the lower quartile of complications [58, 60].

According to another study, the increment of the MELD score is also related to higher costs ($4309 per MELD point). It’s also related to a reduce in the net income of the transplant center ($1512 per MELD point). It is possible that the contractual reimbursement agreements that are not indexed by disease severity do not reflect the increment in the costs resulting from the MELD system. The increasing severity of the disease, seen with higher MELD scores, is related to attention costs exorbitantly higher for the transplant center. In the generator elements of the incensement of the cost in patients with high MELD scores, we can see higher costs for accommodations and food, as well as an increment in the use of laboratory, radiology, and pharmacy services. All this shows that, apart from existing important increment of the use of necessary resources for treating patients with high MELD scores, the hospital admissions for treating all these necessities could lead to a nonsignificant increase, resulting in a net loss for the transplant center [64].

5. Cost and post-LT survival from acute versus chronic liver disease

Survival rates in post-LT patients for acute liver disease are similar to those in post-LT patients for other indications. This is demonstrated by some studies. Kumar et al. [66] mention that these rates in the patient transplanted for acute liver disease are around 80% at the first year and 75% at 5 years, while Roberts et al. [67] indicate that for patients transplanted for any other cause, these rates are at 85% per year and 74% at 5 years.
Regarding the costs involved in LT for acute liver disease versus another pathology, especially chronic pathology, van Agthoven et al. [68] conducted a study where they compared the costs of these two variables, showed that the economic resources invested in patients for LT for acute disease were € 90,000 while this value amounted to € 107,000 in those with patients with chronic pathology. It is worth mentioning that these costs were estimated up to 1 year post-transplant, it is also important to allude that one of the most important parameters that marked these costs were the days of pre-transplant hospitalization, which can be in the case of chronic pathologies up to 12 days versus 1 or 2 days in acute pathologies [68].

Kumar et al. [66] in their study indicate that some other causes of the increase in these costs may be associated with the development of complications in the immediate postoperative period, with infections being the most common, the development of complications is also associated with the etiology for which the transplant was performed, finding better results in those patients with Wilson's disease versus those who presented acute liver failure due to acetaminophen [66].

Something to consider is that the transplant itself already generates an increase in expenses, since Kumar et al. [66] in their study were able to demonstrate that the costs at days 30, 60, and 365 after a liver transplant versus standard care (that is, in a non-transplanted patient) are 5 times higher, as an example, per year the costs in transplantation were calculated at $ 198,000 against $48,000 in the non-transplanted [66].

6. Conclusion

The LT is the therapeutic option of choice for patients with terminal, acute, or chronic liver diseases, should be recommended when the estimate of survival after LT exceeds or exceeds life expectancy without the procedure or when significantly improves quality of life; however, the selection of candidates should be as judicious as possible, aiming at the best use of resources (for example, grafts) although what is the best use may have different interpretations.

Prioritization using prognostic models allows an adequate allocation due to the limited number of donors. Currently, in many countries, the severity and risk of death from chronic liver disease are estimated by the MELD score; however, the model has limitations, not reflecting with accuracy the severity of some of the complications of chronic liver disease, however, when is the opportune time to indicate The LT and that people should be included in the list are issues that continue to arouse interest and controversies.

The evaluation and waiting list waiting processes for LT are complex and costly, and although the protocols for evaluating and including potential recipients depend solely on each center, there are common problems that should be considered during the decision-making process: (a) disparity between the number of patients on the waiting list and the number of organs available—increases the waiting list length of stay and the morbidity and mortality of potential recipients, with possible waiting list existing for clinical worsening or death, (b) competition among other transplant centers in the same area not only by candidates but also by organs, (c) the epidemiological behavior of chronic liver disease, specific to each area.

About LT and post-LT and considering the different factors that influence the results, it is important to know the costs invested in this way, it is possible to develop and apply strategic decisions aimed at optimizing the available resources and improving the services provided in the pursuit of excellence.
Regarding LT in acute pathologies, the available evidence is scarce, however, by the data exposed would seem to be cost-effective; however we need more evidence to generate conclusions to improve existing policies.

We hope that the evidence presented: (a) contributes to the knowledge of cost management—a fundamental important part for care, in the dimensions of quality and efficiency; (b) allow reflection on the economic analyses of high-cost procedures in the face of the socio-hospital context of health in different countries.
References


Economic Evaluations of Liver Transplantation as Tools for Decision-Making and Implications...
DOI: http://dx.doi.org/10.5772/intechopen.104903

2018;18(Suppl. 1):172-253. DOI: 10.1111/ajt.14559


