

## Retrospective Cohort Study

## Frequency of and reasons behind non-listing in adult patients referred for liver transplantation: Results from a retrospective study

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## Abstract

### BACKGROUND

Few studies have evaluated the frequency of and the reasons behind the refusal of listing liver transplantation candidates.

### AIM

To assess the ineligibility rate for liver transplantation and its motivations.

### METHODS

A single-center retrospective study was conducted on adult patients which entailed a formal multidisciplinary assessment for liver transplantation eligibility. The predictors for listing were evaluated using multivariable logistic regression.

### RESULTS

In our center, 314 patients underwent multidisciplinary work-up before liver transplantation enlisting over a three-year period. The most frequent reasons for transplant evaluation were decompensated cirrhosis (51.6%) and hepatocellular carcinoma (35.7%). The non-listing rate was 53.8% and the transplant rate was 34.4% for the whole cohort. Two hundred and five motivations for ineligibility were collected. The most common contraindications were psychological (9.3%), cardiovascular (6.8%), and surgical (5.9%). Inappropriate or premature referral accounted for 76 (37.1%) cases. On multivariable analysis, a referral from another hospital (OR: 2.113; 95% CI: 1.259–3.548) served as an independent predictor of

non-listing.

## CONCLUSION

A non-listing decision occurred in half of our cohort and was based on an inappropriate or premature referral in one case out of three. The referral from another hospital was taken as a strong predictor of non-listing.

**Key Words:** Contraindication; Eligibility; Evaluation; Referral; Personalized medicine

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**Core Tip:** Because of organ shortage and the need to optimize graft survival, patient candidates for liver transplantation must undergo an intensive multidisciplinary work-up to determine their suitability for registration on the waitlist. Few studies have evaluated the ineligibility rate for liver transplantation and its motivations. In this single-center, retrospective cohort study, the observed non-listing rate was 53.8% and about one out of three non-listing reasons was an inappropriate or premature referral. The external referral was a predictor of non-listing, so the betterment of the education and the training of referring physicians is recommended.

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## INTRODUCTION

Because of organ shortage and the need to optimize graft survival, patient candidates for liver transplantation must undergo an intensive multidisciplinary work-up to determine their suitability for registration on the waitlist[1]. The primary purpose of the evaluation process is to select candidates with a projected 5-year post-transplant survival rate of more than 50%[2]. The American Association for the Study of Liver Diseases guidelines[3] consider the following medical and non-medical non-listing reasons for liver transplantation: A Model for End-stage Liver Disease (MELD) Score < 15 (without other exceptions)[4], severe cardiac or pulmonary disease[5,6], Acquired Immuno-Deficiency Syndrome[7], ongoing alcohol or illicit substance abuse[8], hepatocellular carcinoma (HCC) with metastatic spread[9], uncontrolled sepsis[10], anatomic abnormality that precludes liver transplantation[11], intrahepatic cholangiocarcinoma[12], extra-hepatic malignancy[13], acute liver failure (ALF) with sustained intracranial hypertension[14], hemangiosarcoma[15], persistent noncompliance or the lack of an adequate social support system[16,17]. Few studies have evaluated the ineligibility rate for liver transplantation and its motivations. This study aims to assess the ineligibility rate for liver transplantation and its motivations among potential candidates for liver transplantation.

## MATERIALS AND METHODS

This is a retrospective cohort study that has been conducted at Fondazione Policlinico Universitario A. Gemelli IRCCS (Rome, Italy). All adult patients with liver diseases who were referred for a formal multidisciplinary assessment of eligibility for liver transplantation from 1 January 2015 to 31 December 2017 were included in the study. The primary outcome was the percentage of evaluations that resulted in non-listing for liver transplantation (non-listing rate).

Our transplant center is included in the transplant program of the Lazio region; according to the program's rules[18], only patients with a MELD sodium (MELD Na) score  $\geq 15$ [19] or with the HCC within the up-to-7 criteria[20] are eligible for liver transplant waitlist. Moreover, our transplant center serves as a referral center for patients in the Abruzzo and Molise regions in a "hub-and-spoke" network. Hence, we admit a high percentage of patients who are referred from other hospitals (approximately 30%).

All patients were identified from a clinical referral database that contains information on all patients who are referred for liver transplant evaluation. We collected demographic and baseline clinical data on patients who were waitlisted and non-waitlisted for liver transplantation during the study period. In patients who suffered from more than one disease that led to liver dysfunction, we considered all possible components. In patients with more than one reason behind non-listing, we recorded all the non-listing reasons. The reasons behind the non-listing of patients were categorized as follows: Contraindications, incorrect indication, patient decision, and complications during the evaluation process.

### Multidisciplinary evaluation process

The evaluation work-up was carried out on either an outpatient or an inpatient basis, according to the patient's clinical

conditions. All patients underwent an evaluation of their complete medical history and physical examination, including risk-appropriate cardiopulmonary evaluation. Laboratory work-up included the following: Complete blood count, coagulation tests, blood chemistry, ABO-Rh blood group determination, tumor markers, thyroid function, serologic tests for hepatitis A virus (HAV), hepatitis B virus (HBV), hepatitis C virus (HCV), human immunodeficiency virus (HIV), cytomegalovirus, Epstein-Barr virus, Herpes-simplex virus, Herpes-zoster virus, Syphilis, Toxoplasma, Rubella, molecular HBV-DNA, and HCV-RNA assays, both tuberculin skin test and QuantiFERON test for latent tuberculosis infection and both bacterial and fungal culture on blood, urine, stool and throat swab.

The cardiovascular work-up included electrocardiography, echocardiography, exercise or pharmacologic stress myocardial perfusion imaging by single-photon emission computed tomography (CT), followed by coronary angiography if it was indicated. Respiratory work-up included acid-base-balance, spirometry, and pulmonary artery systolic pressure estimation by echocardiography. The patients underwent total body CT scan with contrast medium to assess the anatomical variants of abdominal vessels, the possible presence of arcuate ligament syndrome, the possible presence and staging of portal vein thrombosis, the diagnosis and staging of HCC, and the search for lesions or occult abscesses in other districts. They also underwent portal vein Doppler ultrasound, supra-aortic vessels and vascular access Doppler ultrasound, electroencephalogram, gastroscopy, and colonoscopy if their age was more than 50 years. The nutritional consultant and the dietitian carried out nutritional assessment and education. Additionally, the women underwent a Papanicolaou smear screening test, transvaginal echography, and mammography, while the men underwent a prostate-specific antigen screening test. All patients underwent alcohol disorder evaluation conducted by a dedicated consultant (Addolorato G) and assessment by a dedicated psychologist (Calia R); subsequent psychiatric consultation was performed on a case-to-case basis. The dental evaluation included digital panoramic radiography, visits, and extractions if they were needed. In conclusion, patients underwent anesthesia and surgical assessment.

Patients with a diagnosis of ALF[21] were evaluated according to an accelerated protocol for possible listing in case of the urgent need for transplantation (status 1, according to the United Network for Organ Sharing). The accelerated protocol includes only a recapitulation of medical history and physical examination, complete blood count, coagulation tests, blood chemistry, ABO-Rh blood group determination, serologic tests for HAV, HBV, HCV, HIV, Cytomegalovirus, Epstein-Barr Virus, hepatitis E virus, electrocardiography, echocardiography, urgent cardiology consultation, and total body CT scan with a contrast medium.

### Statistical analysis

Continuous data were expressed by mean  $\pm$  SD and categorical data were expressed by frequencies and percentages. Independent samples student's *t*-test and  $\chi^2$  test were used for group comparisons wherever it was appropriate. Multivariable logistic regression was used to evaluate the predictors for listing. The differences were reported as statistically significant if the *P* value was less than 0.05. Statistical analysis was performed using SPSS version 17.0 (SPSS Inc., Chicago, IL).

## RESULTS

In the 2015–2017 timeframe, 327 adult patients were referred to our center for liver transplant evaluation. Most patients (75%) were male and their mean age was 54.6 years. Since for 13 of the patients, a listing decision had not yet been taken as of 31 December 2017, our study cohort included 314 patients for whom the evaluation process for being registered in the liver transplantation waitlist was completed (Table 1). The most common reason behind the indication of listing was decompensated cirrhosis in 162 (51.6%) patients, followed by HCC in 112 (35.7%) patients, confirmed or suspected to be ALF in 34 (10.8%) patients, and other indications in 6 (1.9%) patients (5 patients for polycystic liver disease and 1 patient for portal hypertensive biliopathy). Most patients (87.3%) had liver cirrhosis; the most common etiologies were alcoholic liver disease (41.4%), HCV (22.3%), and non-alcoholic steatohepatitis (13.7%). Other etiologies are described in Table 2.

Among the 314 evaluated patients, 145 (46.2%) patients were listed. Their final outcome was transplantation in 108 (34.4%) patients, still on the waitlist as of 31 December 2017 in 21 (6.7%) patients, and delisting in 16 (5.1%) patients (9 patients because of complications during waitlist, 3 because of HCC progression, 2 because of non-compliance and 2 after liver function improvement). In 169 patients, the decision to non-listing for the 2015–2017 period was made and, hence, the non-listing rate was 53.8% in our cohort.

Table 3 reports the reasons behind non-listing. The presence of contraindications accounted for 44.4% of the non-listing reasons; in particular, liver transplant contraindications were more frequently psychological (9.3%), cardiovascular (6.8%), and surgical (5.9%). An inappropriate or premature referral summed up for 37.1% of non-listing reasons and included 16.1% of cases where the patient had a low MELD Na score (below < 15), 10.2% of cases of recovery after conservative management for confirmed or suspected ALF and 7.8% cases of HCC beyond the up-to-7 criteria that were not amenable for downstaging. Moreover, there were 7.8% of cases where patients refused transplantation, 2.9% where people chose another center, and 1.5% where patients lost to follow-up. Finally, 6.3% of patients developed complications during the evaluation process and subsequently died. In 30 patients, there was more than one reason behind non-listing. Hence, we recorded 205 non-listing reasons out of our cohort of 169 patients.

According to patient features between the listed and non-listed patients (Table 2), we showed that male sex, the presence of HCC, past-HBV infection, and the presence of TIPS were significantly more frequent in patients who were listed, while a working diagnosis of confirmed or suspected ALF or a referral from another hospital were significantly more frequent in patients who were non-listed. In the multivariable analysis (Table 4), only the referral from another hospital (OR: 2.113; 95%CI: 1.259–3.548) and past HBV infection (OR: 0.373; 95%CI: 0.164–0.852) were confirmed to be

**Table 1 Adult patients evaluated for liver transplantation by year**

	2015	2016	2017	2015-2017
Non listed	29	60	80	169 (53.8%)
On waitlist (on 31/12) <sup>1</sup>	17	28	21	21 (6.7%)
Drop-out from waitlist	5	5	6	16 (5.1%)
Transplanted	30	36	42	108 (34.4%)
Total (column)	81	129	149	314

<sup>1</sup>These data were provided only to illustrate the distribution of patients in the individual years of the study. For the final calculation of the three-year study period, only those patients who were on the active waitlist as of 31 December 2017 were considered.

**Table 2 Clinical features of patients**

	All patients (n = 314)	Listed (n = 145)	Non-listed (n = 169)	P value
Age (yr)	54.6 ± 11.5	54.4 ± 10.1	54.7 ± 12.6	NS
Male sex	236 (75.1%)	118 (81.4%)	118 (69.8%)	0.018
Alcohol	130 (41.4%)	61 (42.1%)	69 (40.8%)	NS
HCC	112 (35.7%)	63 (43.4%)	49 (29%)	0.008
Active HBV	35 (11.1%)	19 (13.1%)	16 (9.5%)	NS
Past HBV	32 (10.2%)	22 (15.2%)	10 (5.9%)	0.007
HCV	70 (22.3%)	36 (24.8%)	34 (20.1%)	NS
PBC/PSC	23 (7.3%)	15 (10.3%)	8 (4.7%)	NS
Autoimmune	9 (2.9%)	3 (2.1%)	6 (3.6%)	NS
Non-Alcoholic Steatohepatitis	43 (13.7%)	25 (17.2%)	18 (10.6%)	NS
Other indications <sup>1</sup>	27 (8.6%)	14 (9.6%)	13 (7.7%)	NS
Confirmed or suspected ALF <sup>2</sup>	34 (10.8%)	8 (5.5%)	26 (15.3%)	0.011
Portal vein thrombosis	52 (16.6%)	28 (19.3%)	24 (14.2%)	NS
TIPS	20 (6.4%)	14 (9.7%)	6 (3.6%)	0.027
Referred from another hospital	102 (32.5%)	33 (22.8%)	69 (40.8%)	0.001

<sup>1</sup>Include 6 hepatitis D virus coinfection, 5 polycystic liver disease, 3 re-transplantation, 3 iron overload, 2 secondary biliary cirrhosis, 2 Budd-Chiari Syndrome, 2 Alagille Syndrome, 1 Caroli Syndrome, 1 Wilson disease, 1 drug-induced liver disease, 1 portal hypertensive biliopathy.

<sup>2</sup>Include: 10 drug-related, 6 indeterminate, 5 hepatitis B virus, 4 hepatitis A virus, 2 hepatitis E virus, 2 iatrogenic, 1 autoimmune, 1 malignant infiltration, 1 amanita phalloides, 1 Hemolysis Elevated Liver enzymes and Low Platelet count syndrome, 1 acute hepatic artery thrombosis.

Data has been presented as the number of patients (%) or mean ± SD. Analysis has been conducted by either a  $\chi^2$  test or independent samples student's *t*-test. HCC: Hepatocellular carcinoma; HBV: Hepatitis B virus; HCV: Hepatitis C virus; PBC: Primary biliary cholangitis; PSC: Primary sclerosing cholangitis; ALF: Acute liver failure; TIPS: Transjugular intrahepatic portosystemic shun; NS: Not significant.

significant predictors of non-listing and listing, respectively.

## DISCUSSION

In this study, the observed non-listing rate was 53.8%. Few studies have evaluated the frequency of and the reasons behind a candidate's refusal to enlist for liver transplantation. A single-center retrospective cohort study on 309 adult patients, evaluated in Singapore in the 1990–2001 timeframe, reported a non-listing rate of 65.7% [22]. The transplant center of Pisa (Italy), by adopting a step-by-step approach (preemptive evaluation, preliminary evaluation, and complete evaluation), obtained a non-listing rate of 73.7% in the 1996–2004 timeframe [23]. Another single-center retrospective cohort study among 314 adult patients completely evaluated in the British Columbia transplant center, Canada, in the 1997–2001 timeframe reported a non-listing rate of 46.8% [24]. The non-listing rate of Mayo Clinic (United States) in 2005, after the institution of the MELD scoring system for organ allocation, was found to be 53.1% [25]. A cohort study on 337

**Table 3** Reasons behind non-listing for liver transplantation

Non-listing categories	Non-listing motivations	N°			
Contraindications	Psychological <sup>1</sup>	19	9.3%	91	44.4%
	Cardiovascular <sup>2</sup>	14	6.8%		
	Surgical <sup>3</sup>	12	5.9%		
	Ongoing alcohol abuse <sup>4</sup>	10	4.9%		
	Infectious <sup>5</sup>	10	4.9%		
	Obesity (BMI > 35)	9	4.4%		
	Respiratory <sup>6</sup>	7	3.4%		
	Extrahepatic malignancy <sup>7</sup>	6	2.9%		
	Malnutrition <sup>8</sup>	4	1.9%		
Incorrect indication	MELD Na < 15 <sup>9</sup>	33	16.1%	76	37.1%
	Recovery after conservative management for confirmed or suspected ALF	21	10.2%		
	HCC beyond up-to-7 criteria and not amenable to downstaging	16	7.8%		
	Low Mayo Risk Score	4	2.0%		
	HCC successfully treated (T0)	2	1.0%		
Patient decision	Refused transplantation	16	7.8%	25	12.2%
	Chose another center	6	2.9%		
	Lost to follow-up	3	1.5%		
Complications during evaluation		13	6.3%	13	6.3%
Total		205	100%	205	100%

<sup>1</sup>6 cases of psychiatric comorbidities, 5 cases of neurological comorbidities, 3 cases of persistent non-compliance, 5 cases of the lack of an adequate support system.

<sup>2</sup>8 cases of ischemic heart disease, 4 cases of valvular heart disease, 1 case of arrhythmia, 1 case of pulmonary hypertension.

<sup>3</sup>5 cases of portal vein thrombosis Yerdel III-IV, 6 cases of previous gastrointestinal surgery with arterial axil alteration, 1 case of high-risk re-transplantation.

<sup>4</sup>abstinence period < 6 months and negative evaluation by alcohol-disorders specialist.

<sup>5</sup>4 cases of pneumonia, 2 cases of sepsis, 2 cases of HIV infection, 1 case of active tuberculosis, 1 case of osteomyelitis.

<sup>6</sup>5 cases of severe chronic obstructive pulmonary disease, 1 case of severe restrictive pattern, 1 case of interstitial lung disease.

<sup>7</sup>2 cases of breast cancer, 1 case of ovarian cancer, 1 case of lung cancer, 1 case of pancreatic cancer, 1 case of lymphoma.

<sup>8</sup>Based on the opinions of the nutritional consultant and the subsequent multidisciplinary (transplant hepatologist, transplant surgeon, and anesthesist) decision.

<sup>9</sup>After the antiviral treatment or alcoholic abstinence.

MELD-Na: Model for end-stage liver disease-sodium; ALF: Acute liver failure; HCC: Hepatocellular carcinoma; BMI: Body mass index.

adult patients evaluated in London Ontario, Canada, in the 2009–2011 timeframe documented a non-listing rate of 49.3% [26]. According to the report by Mount Sinai Medical Center in New York, its non-listing rate was 58% in the 2000–2012 timeframe, reaching a rate of 82% in the HIV-positive population[27]. These older studies refer to an era in which the effect of anti-HBV and anti-HCV antiviral treatments had not yet been routinely applied; in recent years, waitlist registrations for HBV and HCV patients have been drastically reduced because of decompensation, persisting only registrations because of HCC, HDV co-infection or HBV-related ALF[28,29]. Our study confirms a non-listing rate of approximately 50% in a population predominantly suffering from alcohol-based and metabolic liver disease.

In our study, about one out of three non-listing reasons was inappropriate or premature referral. This is in line with other experiences[22–27] including those reported in a study in Tampa (United States) that was conducted among 242 evaluated candidates who were not listed for liver transplantation during the 2004–2006 period; retrospectively, the most common reasons behind non-listing were early referrals, psychosocial factors, and medical contraindications[30]. On the one hand, early referral undoubtedly entails a cost (for patients, family members, and healthcare providers) and subtracts the availability of resources from other candidates. On the other hand, it provides some benefits such as the optimization of patient care and monitoring, strengthens the doctor-patient relationship, and improves their understanding of the surgery. As per the reports by Mayo Clinic, many patients who were initially refused for liver transplant listing because of too early referral or because of psychosocial reasons, were subsequently re-presented and listed for liver transplantation. The authors concluded that early referral was beneficial for patients because the management of end-stage liver disease could consequently be initiated, and the psychosocial issues could be timely manner. Despite these

**Table 4** Multivariate analysis of predictors for listing

Variable	P value	OR (95%CI)
Referred from another hospital	0.005	2.113 (1.259–3.548)
Past HBV infection	0.019	0.373 (0.164–0.852)
HCC	0.068	0.623 (0.374–1.037)
Male sex	0.067	1.699 (0.964–2.994)
TIPS	0.116	0.439 (0.157–1.226)
ALF/Severe acute hepatitis	0.310	1.584 (0.651–3.852)

Analysis has been conducted by using multivariate logistic regression. HBV: Hepatitis B virus; HCC: Hepatocellular carcinoma; TIPS: Transjugular intrahepatic portosystemic shunt; ALF: Acute liver failure.

observations, it is currently unclear whether early referrals influence (either positively or negatively) clinical outcomes and liver transplantation programs.

Moreover, it is unclear whether non-listing rates relate to the appropriateness of referrals from providers and/or to the effectiveness of the screening of referrals in the liver transplantation program. According to the multivariable analysis, the referral from another hospital was a significant predictor of non-listing. Given that our center has decided not to provide a preemptive evaluation, a possible explanation behind this decision is related to the heterogeneity of the spoke centers regarding the balance of potential contraindications to liver transplant. A potential perspective of our study is to implement better training of the spoke centers to optimize the referral process.

The main limitation of our study is that this is a single-center study and its external validity may be limited. A potential perspective of our study is to perform a multicenter study, possibly endorsed by a scientific society, to overcome this limitation and provide data that better reflect the national (or preferably international) state-of-the-art of liver transplant evaluation.

## CONCLUSION

In conclusion, even in the post-Direct Antiviral Agents era, a final decision of ineligibility for liver transplantation was observed in half of our cohort. Inappropriate or premature referral occurred in one case out of three, but this did not necessarily amount to a flaw. Since the referral from other hospitals was considered a strong predictor of non-listing, the betterment of the education and the training of referring physicians is recommended.

## FOOTNOTES

**Author contributions:** Biolato M designed the study and wrote the paper; Marrone G, and Tarli C collected the data; Liguori A and Miele L analyzed the data; Calia R, Addolorato G, Pompili M, Agnes S, Gasbarrini A, and Grieco A revised the manuscript with an important intellectual contribution.

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## REFERENCES

- 1 **European Association for the Study of the Liver.** EASL Clinical Practice Guidelines: Liver transplantation. *J Hepatol* 2016; **64**: 433-485 [PMID: 26597456 DOI: 10.1016/j.jhep.2015.10.006]
- 2 **Neuberger J,** Gimson A, Davies M, Akyol M, O'Grady J, Burroughs A, Hudson M; Liver Advisory Group; UK Blood and Transplant. Selection of patients for liver transplantation and allocation of donated livers in the UK. *Gut* 2008; **57**: 252-257 [PMID: 17895356 DOI: 10.1136/gut.2007.131730]
- 3 **Martin P,** DiMartini A, Feng S, Brown R Jr, Fallon M. Evaluation for liver transplantation in adults: 2013 practice guideline by the American Association for the Study of Liver Diseases and the American Society of Transplantation. *Hepatology* 2014; **59**: 1144-1165 [PMID: 24716201 DOI: 10.1002/hep.26972]
- 4 **Merion RM,** Schaubel DE, Dykstra DM, Freeman RB, Port FK, Wolfe RA. The survival benefit of liver transplantation. *Am J Transplant* 2005; **5**: 307-313 [PMID: 15643990 DOI: 10.1111/j.1600-6143.2004.00703.x]
- 5 **Donovan RJ,** Choi C, Ali A, Heuman DM, Fuchs M, Bavry AA, Jovin IS. Perioperative Cardiovascular Evaluation for Orthotopic Liver Transplantation. *Dig Dis Sci* 2017; **62**: 26-34 [PMID: 27830409 DOI: 10.1007/s10620-016-4371-3]
- 6 **Lentine KL,** Costa SP, Weir MR, Robb JF, Fleisher LA, Kasiske BL, Carithers RL, Ragosta M, Bolton K, Auerbach AD, Eagle KA; American Heart Association Council on the Kidney in Cardiovascular Disease and Council on Peripheral Vascular Disease; American Heart Association; American College of Cardiology Foundation. Cardiac disease evaluation and management among kidney and liver transplantation candidates: a scientific statement from the American Heart Association and the American College of Cardiology Foundation: endorsed by the American Society of Transplant Surgeons, American Society of Transplantation, and National Kidney Foundation. *Circulation* 2012; **126**: 617-663 [PMID: 22753303 DOI: 10.1161/CIR.0b013e31823eb07a]
- 7 **Mah A,** Wright A. Infectious Considerations in the Pre-Transplant Evaluation of Cirrhotic Patients Awaiting Orthotopic Liver Transplantation. *Curr Infect Dis Rep* 2016; **18**: 4 [PMID: 26743200 DOI: 10.1007/s11908-015-0514-5]
- 8 **Addolorato G,** Bataller R, Burra P, DiMartini A, Graziadei I, Lucey MR, Mathurin P, O'Grady J, Pageaux G, Berenguer M. Liver Transplantation for Alcoholic Liver Disease. *Transplantation* 2016; **100**: 981-987 [PMID: 26985744 DOI: 10.1097/TP.0000000000001156]
- 9 **Clavien PA,** Lesurtel M, Bossuyt PM, Gores GJ, Langer B, Perrier A; OLT for HCC Consensus Group. Recommendations for liver transplantation for hepatocellular carcinoma: an international consensus conference report. *Lancet Oncol* 2012; **13**: e11-e22 [PMID: 22047762 DOI: 10.1016/S1470-2045(11)70175-9]
- 10 **Fischer SA,** Lu K; AST Infectious Diseases Community of Practice. Screening of donor and recipient in solid organ transplantation. *Am J Transplant* 2013; **13** Suppl 4: 9-21 [PMID: 23464994 DOI: 10.1111/ajt.12094]
- 11 **Yerdel MA,** Gunson B, Mirza D, Karayalçin K, Olliff S, Buckels J, Mayer D, McMaster P, Pirenne J. Portal vein thrombosis in adults undergoing liver transplantation: risk factors, screening, management, and outcome. *Transplantation* 2000; **69**: 1873-1881 [PMID: 10830225 DOI: 10.1097/00007890-200005150-00023]
- 12 **Lee DD,** Croome KP, Musto KR, Melendez J, Tranesh G, Nakhleh R, Taner CB, Nguyen JH, Patel T, Harnois DM. Liver transplantation for intrahepatic cholangiocarcinoma. *Liver Transpl* 2018; **24**: 634-644 [PMID: 29514406 DOI: 10.1002/lt.25052]
- 13 **Chapman JR,** Webster AC, Wong G. Cancer in the transplant recipient. *Cold Spring Harb Perspect Med* 2013; **3** [PMID: 23818517 DOI: 10.1101/cshperspect.a015677]
- 14 **Bernal W,** Hyrylainen A, Gera A, Audimoolam VK, McPhail MJ, Auzinger G, Rela M, Heaton N, O'Grady JG, Wendon J, Williams R. Lessons from look-back in acute liver failure? A single centre experience of 3300 patients. *J Hepatol* 2013; **59**: 74-80 [PMID: 23439263 DOI: 10.1016/j.jhep.2013.02.010]
- 15 **Konstantinidis IT,** Nota C, Jutric Z, Ituarte P, Chow W, Chu P, Singh G, Warner SG, Melstrom LG, Fong Y. Primary liver sarcomas in the modern era: Resection or transplantation? *J Surg Oncol* 2018; **117**: 886-891 [PMID: 29355969 DOI: 10.1002/jso.24979]
- 16 **Dew MA,** Rosenberger EM, Myaskovsky L, DiMartini AF, DeVito Dabbs AJ, Posluszny DM, Steel J, Switzer GE, Shellmer DA, Greenhouse JB. Depression and Anxiety as Risk Factors for Morbidity and Mortality After Organ Transplantation: A Systematic Review and Meta-Analysis. *Transplantation* 2015; **100**: 988-1003 [PMID: 26492128 DOI: 10.1097/TP.0000000000000901]
- 17 **Ladin K,** Daniels A, Osani M, Bannuru RR. Is social support associated with post-transplant medication adherence and outcomes? A systematic review and meta-analysis. *Transplant Rev (Orlando)* 2018; **32**: 16-28 [PMID: 28495070 DOI: 10.1016/j.tre.2017.04.001]
- 18 **Centro regionale trapianti Lazio.** Liver transplantation Regional Program Regulations. Jun 1, 2016
- 19 **Kim WR,** Biggins SW, Kremers WK, Wiesner RH, Kamath PS, Benson JT, Edwards E, Therneau TM. Hyponatremia and mortality among patients on the liver-transplant waiting list. *N Engl J Med* 2008; **359**: 1018-1026 [PMID: 18768945 DOI: 10.1056/NEJMoa0801209]
- 20 **Mazzaferro V,** Llovet JM, Miceli R, Bhoori S, Schiavo M, Mariani L, Camerini T, Roayaie S, Schwartz ME, Grazi GL, Adam R, Neuhaus P, Salizzoni M, Bruix J, Forner A, De Carlis L, Cillo U, Burroughs AK, Troisi R, Rossi M, Gerunda GE, Lerut J, Belghiti J, Boin I, Gugenheim J, Rochling F, Van Hoek B, Majno P; Metroticket Investigator Study Group. Predicting survival after liver transplantation in patients with hepatocellular carcinoma beyond the Milan criteria: a retrospective, exploratory analysis. *Lancet Oncol* 2009; **10**: 35-43 [PMID: 19058754 DOI: 10.1016/S1470-2045(08)70284-5]
- 21 **European Association for the Study of the Liver;** Clinical practice guidelines panel, Wendon, J; Panel members, Cordoba J, Dhawan A, Larsen FS, Manns M, Samuel D, Simpson KJ, Yaron I; EASL Governing Board representative, Bernardi M. EASL Clinical Practical Guidelines on the management of acute (fulminant) liver failure. *J Hepatol* 2017; **66**: 1047-1081 [PMID: 28417882 DOI: 10.1016/j.jhep.2016.12.003]

- 22 **Wai CT**, Prabhakaran K, Kaur M, Lee YM, Dan YY, Sutedja DS, Aw MM, Quak SH, Mak K, Isaac J, Lee KH, Lim SG. Successful listing of patients for liver transplant was related to participation of referring doctor in the transplant program. *Transplant Proc* 2004; **36**: 2230-2231 [PMID: 15561201 DOI: 10.1016/j.transproceed.2004.06.046]
- 23 **De Simone P**, Carrai P, Baldoni L, Petruccelli S, Coletti L, Morelli L, Filipponi F. Quality assurance, efficiency indicators and cost-utility of the evaluation workup for liver transplantation. *Liver Transpl* 2005; **11**: 1080-1085 [PMID: 16123969 DOI: 10.1002/Lt.20484]
- 24 **Alali J**, Ramji A, Ho JK, Scudamore CH, Erb SR, Cheung E, Kopit B, Bannon CA, Chung SW, Soos JG, Buczkowski AK, Brooks EM, Steinbrecher UP, Yoshida EM. Liver transplant candidacy unsuitability: a review of the British Columbia experience. *Can J Gastroenterol* 2006; **20**: 95-99 [PMID: 16482235 DOI: 10.1155/2006/879103]
- 25 **Aranda-Michel J**, Dickson RC, Bonatti H, Crossfield JR, Keaveny AP, Vasquez AR. Patient selection for liver transplant: 1-year experience with 555 patients at a single center. *Mayo Clin Proc* 2008; **83**: 165-168 [PMID: 18241626 DOI: 10.4065/83.2.165]
- 26 **Arya A**, Hernandez-Alejandro R, Marotta P, Uhanova J, Chandok N. Recipient ineligibility after liver transplantation assessment: a single centre experience. *Can J Surg* 2013; **56**: E39-E43 [PMID: 23706857 DOI: 10.1503/cjs.004512]
- 27 **Martel-Laferrrière V**, Michel A, Schaefer S, Bindal S, Bichoupan K, Branch AD, Huprikar S, Schiano TD, Perumalswami PV. Clinical characteristics of human immunodeficiency virus patients being referred for liver transplant evaluation: a descriptive cohort study. *Transpl Infect Dis* 2015; **17**: 527-535 [PMID: 25929731 DOI: 10.1111/tid.12395]
- 28 **Flemming JA**, Kim WR, Brosgart CL, Terrault NA. Reduction in liver transplant wait-listing in the era of direct-acting antiviral therapy. *Hepatology* 2017; **65**: 804-812 [PMID: 28012259 DOI: 10.1002/hep.28923]
- 29 **Belli LS**, Perricone G, Adam R, Cortesi PA, Strazzabosco M, Facchetti R, Karam V, Salizzoni M, Andujar RL, Fondevila C, De Simone P, Morelli C, Fabregat-Prous J, Samuel D, Agarwal K, Moreno Gonzales E, Charco R, Zieniewicz K, De Carlis L, Duvoux C; all the contributing centers (www.eltr.org) and the European Liver and Intestine Transplant Association (ELITA). Impact of DAAs on liver transplantation: Major effects on the evolution of indications and results. An ELITA study based on the ELTR registry. *J Hepatol* 2018; **69**: 810-817 [PMID: 29940268 DOI: 10.1016/j.jhep.2018.06.010]
- 30 **Kemmer N**, Alsina A, Neff GW. Social determinants of orthotopic liver transplantation candidacy: role of patient-related factors. *Transplant Proc* 2011; **43**: 3769-3772 [PMID: 22172844 DOI: 10.1016/j.transproceed.2011.08.076]





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