ORIGINAL ARTICLE

Liver transplant candidate unsuitability: A review of the British Columbia experience

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BACKGROUND: Every centre has contraindications to liver transplantation and declares patients unsuitable for medical or nonmedical reasons. To date, there has been no published review of any centre's experience.
METHODS: A retrospective chart review was completed from 1997 to 2001, inclusive of all patients referred for liver transplant to the British Columbia Transplant Society who were declared unsuitable for transplantation, as well as the reasons for unsuitability.
RESULTS: One hundred fifty patients were considered to be unsuitable for transplantation. During this period, 167 transplants were performed and 737 patients were referred for candidacy. Data were missing on three patients; analysis was performed on the remaining 147. Patients' ages ranged from 15 to 72 years, and 33.3% were female. The most common primary liver disease was hepatitis C (n=53, 35%), followed by alcoholic liver disease (n=35, 24%) and autoimmune liver diseases (n=23, 16%). Medical contraindications constituted 74 patients (49.0%) and the most common reasons for unsuitability were no need of a liver transplant (29 patients [39%]), exclusion due to hepatoma or extrahepatic malignancy (20 patients [27%]) and multisystem failure (12 patients [16%]). Nonmedical contraindications constituted 73 patients. Failure to meet minimal alcohol criteria comprised the largest group (n=39, 53.4%) followed by inadequate social support (n=12, 16.4%), failure to follow up medical assessment (n=10, 13.7%) and drug abuse (n=6, 8.2%).
CONCLUSIONS: Although many patients were declined for transplantation, the proportion is relatively small compared with the number of referred patients. Nonmedical reasons, including failure to meet alcohol criteria and lack of social support, remain a significant reason for unsuitability in British Columbia. Community intervention before transplant referral is recommended.

Key Words: *Alcohol; Liver; Social support; Transplantation; Unsuitable*

Greffe du foie et inadmissibilité des candidats : revue de l'expérience en Colombie-Britannique

CONTEXTE : Il y a des contre-indications à la greffe du foie dans tous les centres de transplantation, et un certain nombre de patients sont déclarés inadmissibles pour des motifs médicaux et non médicaux. Jusqu'à maintenant, aucun centre n'a fait l'objet d'un examen publié en la matière.
MÉTHODE : Nous avons procédé, de 1997 à 2001, à un examen rétrospectif des dossiers, y compris de celui de tous les patients qui ont été dirigés vers la British Columbia Transplant Society en vue d'une greffe du foie mais qui ont été refusés, ainsi qu'à un examen des motifs invoqués.
RÉSULTATS : Cent cinquante patients ont été jugés inadmissibles. Durant la période examinée, il y a eu 167 transplantations et 737 demandes d'examen de candidature. Il manquait des données sur trois patients; l'analyse a donc porté sur les 147 autres malades. L'âge des patients variait de 15 à 72 ans, et 33,3 % des candidats étaient des femmes. L'affection initiale la plus fréquente était l'hépatite C (n=53; 35 %), suivie de la maladie hépatique alcoolique (n=35; 24 %) et des maladies autoimmunes du foie (n=23; 16 %). Des contre-indications médicales ont été invoquées dans 74 cas (49,0 %), et les motifs les plus fréquents étaient la non-nécessité d'une greffe du foie (29 cas; 39 %), la présence d'un hépatome ou d'une tumeur maligne extrahépatique (20 cas; 27 %) et l'insuffisance plurisystémique (12 cas; 16 %). Des contre-indications non médicales ont été invoquées dans 73 cas. Le non-respect des critères minimaux, relatifs à l'alcool a justifié le plus grand nombre de refus (n=39; 53,4 %), suivi de l'insuffisance de soutien social (n=12; 16,4 %), de l'impossibilité de suivi médical (n=10; 13,7 %) et de la consommation de drogues (n=6; 8,2 %).
CONCLUSIONS : Même si beaucoup de patients ont été déclarés inadmissibles, la proportion est relativement faible par rapport au nombre de patients dirigés. Des motifs non médicaux, notamment le non-respect des critères minimaux, relatifs à l'alcool et l'insuffisance de soutien social, justifient un nombre assez important de refus en Colombie-Britannique. Il faudrait donc prévoir des interventions communautaires avant d'adresser les demandes de transplantation.

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Since the early 1960s, liver transplantation has evolved from an experimental procedure with uncertain patient outcomes to an accepted therapy for end-stage liver disease. In the modern era of liver transplantation, patients can expect a one-year survival rate of at least 85% and a three-year survival rate of between 75% and 80% (1). This impressive survival benefit stands in stark contrast to the natural history of end-stage decompensated cirrhosis, of which there has been little improvement in survival over almost 20 years, with one- and six-year survival rates of 60% and 21%, respectively, reported in the mid-1980s (2) and a 30% to 40% one-year survival rate reported in the new millennium (3). Successful liver transplant recipients can also expect to enjoy an excellent quality of life with a view to returning to the workforce in the majority of cases (4,5).

Despite the clear benefits of liver transplantation for those with end-stage liver disease, the reality in Canada is that there is a tragic disparity between the need for liver transplantation and the availability of donor organs. Out of necessity, each transplant centre in Canada and the United States has both medical and nonmedical conditions that are considered to be contraindications to the procedure (6), and each year, many patients are declared to be unsuitable for transplantation. Understandably, a declaration of transplant unsuitability generates strong emotional feelings among both patients and referring physicians. To date, no centre in either Canada or the United States has published a review of the reasons for transplant unsuitability of referred patients. It was with a sense of accountability to the referring physicians that we decided to review the reasons for transplant unsuitability in British Columbia (BC) over a five-year period. It was also thought that a review of transplant unsuitability would be educational and provide guidance to referring physicians of BC. Because the liver transplant situation in BC is similar to other regions, our experience is probably generalizable to the rest of Canada.

METHODS

A retrospective chart review of all patients referred to the BC Transplant Society, from 1997 to 2001 inclusively, was conducted to determine the specific reasons why patients were declared unsuitable for transplantation. Medical or nonmedical reasons for transplant unsuitability were determined for each patient. To further determine whether significant differences existed based on disease etiology, unsuitable patients were grouped into five categorical variables: unsuitable for medical reasons; failure to meet minimal criteria for alcohol use (ie, a minimum period of abstinence for at least six months and consultation with an alcohol rehabilitation specialist); substance abuse (ie, the use of street drugs); noncompliance with medical treatment and medical recommendation; and lack of social support.

Statistical analysis consisted of both descriptive statistics and analytical statistical methods to compare the five categories of unsuitability with liver disease etiology. A χ^2 test was used for these categorical variables. To decrease the likelihood of an alpha error due to multiple comparisons analysis, a Bonferroni correction was applied and an alpha level of significance (P value) was considered to be less than 0.005 for a two-tailed test. All statistical analysis was performed with an SPSS version 11.0 (SPSS, USA) statistical software program.

RESULTS

During the five-year period from 1997 to 2001 inclusively, 150 patients referred to the BC Transplant Society Liver Transplant Program were declared ‘unsuitable’ for liver transplantation. During this same period, 167 liver transplants were performed (163 cadaveric transplants and four live donor transplants), and 737 patients were referred for liver transplant assessment. Data on 147 patients (98%) were available for analysis. Three patients had missing data and it was not possible to determine the reason for transplant unsuitability. Demographic characteristics of the 147 patients reviewed are summarized in Table 1. In brief, 66% were male, the majority were Caucasian (70%), the age range was 15 to 72 years, and most were between the ages of 41 and 50 years (34%). In terms of the referring diagnosis of primary liver disease (Table 1), the clear majority had either hepatitis C virus (HCV) (35%) or alcoholic liver disease (24%). Close to 10% of this group had a diagnosis of acute liver failure, whereas the rest suffered chronic liver disease. Although this review was limited to those liver transplant candidates who were declined for transplantation, for comparative purposes, it was noted that of the 167 patients who did proceed to liver transplantation, 35% had HCV (27.5% of these had a secondary diagnosis of past alcohol abuse), 20% suffered autoimmune liver disease (primary biliary cirrhosis, autoimmune hepatitis or primary sclerosing cholangitis) and 9.5% had alcoholic cirrhosis.

Medical reasons for unsuitability

Overall, 74 patients (50.3%) were considered to be unsuitable for liver transplantation on the grounds that their medical situation precluded transplantation (Table 2). This did not necessarily mean that all patients within this subgroup were expected to have a poor outcome. Patients could be declined because of a lack of need for transplantation, either because their liver disease improved or because they suffered from chronic liver disease in the absence of significant decompensation. In fact, the majority of patients within this medically unsuitable group (39%) were turned down for liver transplantation because they did not require transplantation. Of the remaining patients with end-stage liver disease who were declined because of medical unsuitability, the majority (27%) were excluded because of malignancy. This group included those who were found to have extrahepatic malignancy during the transplant candidacy assessment and those with hepatocellular carcinoma (HCC) that was beyond the accepted criteria. The accepted criteria for HCC at the BC Transplant Society during this time period were based on the Milan Criteria (7) (ie, 5 cm or greater for a solitary HCC and, in the case of multicentric HCC, no more than three HCC, with the largest being at least 3 cm). Aside from neoplastic considerations, of those with decompensated liver disease who were declined for transplantation on medical grounds, the development of multisystem organ failure (16.2%) was a significant reason for unsuitability, followed by cardiac disease (8.1%). In all cases in which patients were excluded on the basis of extrahepatic, nonmalignant disease, the decision to do so was based on input from independent consultation with appropriate medical specialists.

Nonmedical reasons for transplant unsuitability

Seventy-three patients (49.7%) were declined for liver transplantation based on nonmedical reasons (Table 3). The single most common reason for unsuitability on nonmedical grounds was failure to meet minimal criteria for alcohol and nonalcohol substance abuse (ie, street drug use). Together, this group

TABLE 1
Demographic characteristics of 147 patients deemed to be unsuitable for transplant

	n (%)
Age (years)	
≤ 20	3 (2)
21–30	7 (4.8)
31–40	19 (13)
41–50	50 (34)
51–60	31 (21)
≥ 61	37 (25)
Ethnicity	
Caucasian	103 (70)
South Asian*	13 (8.8)
First Nations	14 (9.5)
Asia-Pacific†	11 (7.5)
African-Canadian	2 (1.4)
Race not stated	4 (2.7)
Referring diagnosis	
Hepatitis C‡	52 (35)
Alcoholic liver disease	35 (24)
Acute liver failure	14 (9.5)
Hepatitis B	12 (8.2)
Primary sclerosing cholangitis	8 (5.4)
Autoimmune hepatitis	8 (5.4)
Primary biliary cirrhosis	7 (4.8)
Cryptogenic cirrhosis	5 (3.4)
Miscellaneous	6 (4.1)

**Indo-Canadian; †Oriental ; ‡Includes one patient with hepatitis C and hepatitis B coinfection*

TABLE 2
Medical reasons for transplant unsuitability among 74 patients

Medical reason	n (%)
Did not require transplantation	29 (39.2)
Malignancy*	20 (27)
Multisystem organ failure	12 (16.2)
Cardiac disease	6 (8.1)
Respiratory disease	2 (2.7)
Infectious disease	2 (2.7)
Psychiatric disease	2 (2.7)
Endocrine disease	1 (1.4)

**Includes extrahepatic malignancy and hepatocellular carcinoma extending beyond acceptable criteria*

TABLE 3
Nonmedical reasons for transplant unsuitability among 73 patients

Nonmedical reason	n (%)
Alcohol*	39 (53.4)
Inadequate social support	12 (16.4)
Did not follow up	10 (13.7)
Substance abuse†	6 (8.2)
Declined transplantation	5 (6.8)
Other	1 (1.4)

**Did not meet minimal criteria for alcohol; †Nonalcoholic substance abuse (ie, street drug use)*

constituted 62% of patients declined for nonmedical reasons. Not all patients who were declined for liver transplantation for reasons related to alcohol had a primary diagnosis of alcoholic cirrhosis. Some were referred with other liver disease (eg, HCV) and had coincidental alcohol problems. Other causes for nonmedical unsuitability included lack of social support (16.4%) and failure to follow up with the BC Transplant Society, which was considered to be noncompliance with medical assessments (13.7%); a small minority (6.8%) declined liver transplantation after initial referral. All patients who were declined for nonmedical reasons related to alcohol, substance abuse or lack of social support were seen by the BC Transplant Society's clinical psychologist, social worker, and in the case of alcohol/substance abuse, independent drug and alcohol counsellors or rehabilitation specialists.

Analysis of selected reasons for transplant unsuitability with liver disease etiology

In a brief analysis, patients with HCV were significantly more likely to be declared unsuitable for transplantation on nonmedical grounds than those with other liver diseases (P=0.003). Alcoholic cirrhotics patients, on the other hand, were more likely to be unsuitable for transplantation because of medical reasons (P=0.002). Analyzing specific variables, patients with HCV were more likely to have been found to be unsuitable because of no social support (P=0.003) than non-HCV patients, whereas alcoholic cirrhotic patients had a nonsignificant trend toward an increased noncompliance (P=0.017). Alcoholic cirrhotic patients were also highly likely to be unsuitable because of failure to meet minimal listing requirements regarding alcohol than those with other liver diseases (P<0.001). Although this may appear intuitive, it was noted that 19 patients with HCV and one patient with HBV had a secondary diagnosis of alcohol abuse listed in their BC Transplant Society chart.

DISCUSSION

Over a five-year period, 150 patients referred for liver transplant candidacy were declared to be unsuitable. Although 29 of the patients were considered to be unsuitable for the simple reason that they did not need a liver transplant, the majority undoubtedly suffered early mortality after having been declared unsuitable. The number of patients who were considered unsuitable for transplantation may seem large to some in the medical community; however, we note that during the same five-year period, the BC Transplant Society performed only 167 liver transplants, yet 737 new patients were referred for consideration of a liver transplant. This great disparity between the need for liver transplantation and the availability of donor allografts underscores the need for transplant centres to adopt a utilitarian ethic with regard to donor allocation (8). Within reason, consideration must be given to those candidates who have a reasonable likelihood of achieving a good, long-term outcome, and there is little rationale for a 'palliative transplant' to provide individuals with 'a few extra years' or to 'take a chance' on a marginal candidate at the expense of candidates with a greater likelihood of post-transplant success. Contraindications to transplantation and unsuitable candidates are, therefore, both necessary and inevitable.

Although most in the medical community are willing to accept that a patient in need of liver replacement can be declined on medical grounds, some have difficulty with the idea of unsuitability on nonmedical grounds. All transplant centres in Canada and the United States, however, have exclusionary criteria based on nonmedical grounds, and common contraindications include failure to comply with alcohol abstinence requirements and failure to abstain from street drug use, among others. Adherence to nonmedical criteria can be as important to the viability of the liver transplant process as the maintenance of medical criteria, and exclusion of poor candidates for these reasons is consistent with principles of utility in liver transplantation (6,8). In the review of our experience, we found that almost 50% of unsuitable cases were because of nonmedical reasons. Failure to meet minimum criteria with regard to alcohol abstinence and counselling constituted the single largest nonmedical reason for unsuitability. Although patients referred with a liver disease etiology of alcoholic cirrhosis were the most likely to be unsuitable because of alcohol, patients with other primary liver diseases, most notably HCV, could also be declared unsuitable for this reason. The minimal acceptable criteria of the BC Transplant Society for alcohol abstinence (six months) and counselling are very consistent with the policies of other programs in Canada and the United States, and are also consistent with the current practice guidelines of the American Association for the Study of Liver (9). They are also based on reported evidence (10) determined in the early years when prohibition to offer transplantation to these patients was ending. Our own experience, as well as the experience of others (10-13), has been that failure to meet these criteria results in recidivism, suboptimal post-transplant outcomes and post-transplant alcoholic hepatitis. We do concede that what constitutes an ‘acceptable’ outcome in the case of alcoholic liver disease is influenced by subjective value systems. An example of this is the report of Pageau et al (11), who thought that liver transplantation was an appropriate indication even for alcohol recidivism. They reported, however, that the risk of alcohol recidivism at their centre was 32% after three years, with 13% of this group developing post-transplant alcoholic hepatitis and close to 11% returning to heavy drinking. Another interesting aspect of our review was that patients with a primary diagnosis of alcoholic cirrhosis were more likely to be unsuitable for medical reasons in addition to failure to meet alcohol minimal criteria. Although these patients may be at greater risk of extrahepatic poor health – and a study from the Starzl Institute (14) has found that alcoholic patients have a worse post-transplant outcome for nonalcoholic medical reasons, confirming that this is not a healthy population to begin with – it is also important to point out that some patients referred with alcoholic cirrhosis actually improve during follow-up, to the point that transplantation is no longer required. In this situation, ‘medically inappropriate’ for transplantation indicates lack of medical need. Because most patients referred with a diagnosis of alcoholic liver disease have long-standing histories of alcohol abuse, this is certainly one area in which early community intervention, before end-stage liver disease develops, appears to be needed and would, in the long term, probably reduce the number of transplant referrals.

Other nonmedical reasons for unsuitability include substance abuse with street drugs, noncompliance with medical follow-up and lack of social support. Of these, exclusion because of lack of social support continues to be a point of contention among the referring physicians. Admittedly, we are unaware of any studies that have reported the effect of lack of social support on post-transplant outcomes. At the BC Transplant Society, rigorous efforts are made to accommodate these patients with resources from the community and governmental social services. Our experience, however, is that postoperative or post-transplant medical follow-up is pragmatically difficult for individuals who are very socially isolated and that this problem is compounded if the individual’s housing situation is unstable. Overall, we found that patients with a referring diagnosis of HCV were more likely to be unsuitable for nonmedical reasons. Because HCV is the most common reason for both transplantation and referral to the BC Transplant Society, this observation does not have prognostic implications for our program, but is merely a reflection of the wide social demographic spectrum of HCV disease.

Another interesting aspect of our review is the relatively large proportion of patients who were unsuitable for transplantation because they did not need one (39% of the group that was unsuitable on medical grounds). Some of these patients had significant decompensation but improved with follow-up (eg, alcoholic liver disease, acute liver failure); however, others had liver disease but were not end stage. It is the latter group that is of some concern. The mandate of the BC Transplant Society in the pretransplant aspect of patient care is limited to assessment for transplant candidacy. Primary hepatological care needs to be continued by the local specialists and family physicians. Perhaps greater physician education as to the natural history of liver disease and features of decompensation are required. This is underscored by the fact that the BC Transplant Society returns patients with chronic but well-compensated liver disease back to the referring physician. It is conceivable that, at some point, some of them may need to be re-referred for transplant assessment.

CONCLUSIONS

We undertook this review to provide both feedback and accountability to the referring physicians of BC with regard to patients who have been declared unsuitable for transplantation. Although this number may appear to be large, compared with the total number of referred patients over the same time interval, the proportion of patients we deemed unsuitable is relatively small. Specific areas, such as alcohol rehabilitation, appear to be amenable to community intervention before transplant referral.

DEDICATION: This paper is dedicated to the memory of the late Ms Cecilia San Pedro-Perez, our long-time Liver Transplant administrative assistant.

DISCLOSURE: This work was presented in a poster presentation at Canadian Digestive Diseases Week, March 2004, Banff, Alberta.

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