Liver transplantation for alcoholic liver disease among Canadian transplant centres: A national study

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BACKGROUND/OBJECTIVE: Alcoholic liver disease (ALD) is a controversial yet established indication for liver transplantation (LT), and there is emerging evidence supporting a survival benefit in selected patients with severe acute alcoholic hepatitis. The aim of the present survey was to describe policies among Canadian transplant centres for patients with ALD.

METHODS: A survey was distributed to the medical directors of all seven liver transplant centres in Canada.

RESULTS: All seven liver transplant programs in Canada participated in the survey. Every centre requires patients to have a minimum of six months of abstinence from alcohol before listing for LT. Completion of a rehabilitation program is mandatory in one program; the remaining programs do not mandate this if patients have demonstrated prolonged abstinence, and sufficient insight and social supports. No program considers LT for patients with severe acute alcoholic hepatitis, although six of the seven programs are interested in exploring a national policy. Random alcohol checks for waitlisted patients are performed routinely on patients listed for ALD at only one centre; the remaining centres only perform checks if there is clinical suspicion. In the past five years, the mean (± SD) number of patients per centre with graft dysfunction from recidivism was 10±4.36; a mean of 2.5±4.36 patients per centre developed graft failure.

CONCLUSIONS: With minor exceptions, LT policies for subjects with ALD are uniform across Canadian transplant programs. Presently, no centres perform LT for acute alcoholic hepatitis, although there is broad interest in exploring a national policy. Recidivism resulting in graft loss is a rare phenomenon.

Key Words: Alcoholic liver disease; Policy; Liver transplantation

Amongs adult Canadians, alcohol, behind only hepatitis C virus, is the second most common etiology of liver disease resulting in liver transplantation (LT). From 2000 to 2009, 487 of 3928 (12.4%) listed patients in Canada underwent LT for a primary diagnosis of alcoholic liver disease (ALD) (1). While decompensated ALD is an established indication for LT, it remains controversial among factions of society. Although ALD patients experience survival benefits comparable with subjects transplanted for other etiologies of hepatic decompensation, deeply entrenched societal attitudes toward alcoholism render organ transplantation for this patient population a contentious issue in the public forum (2–6).

Because a transplant program must both reflect public values and relentlessly pursue the mandates of beneficence and nonmaleficence to individual patients with organ failure, an inherent conflict may arise in reconciling transplant policies for ALD. The beliefs and perspectives of health care providers comprising the transplant team – although not often assessed or accounted for – undoubtedly weigh into medical decision making, including controversial decisions such as adult recipient listing for LT for ALD. At times, the role of the transplant program to do good and to do no harm may conflict with certain sociocultural perspectives that stigmatize and demonize individuals with alcohol addictions. However, it could be questioned whether what may be perceived to be a health care provider's personal judgment or apparent societal opinions toward alcoholism should influence outcomes of liver organ allocation when patients with ALD would gain clear improvements in longevity and quality of life from a new graft.

LT is life saving and cost effective for selected patients with decompensated cirrhosis, acute liver failure, early hepatocellular carcinoma. Most recent one- and five-year survival rates following LT in Canada approximate 92% and 80%, respectively (1). This success starkly contrasts with outcomes for alcoholic cirrhotic patients with Child-Turcotte-Pugh class C disease, who have one- and two-year survival rates of just 45% and 35%, respectively (7), or adults with severe acute alcoholic hepatitis (defined by...
Discriminant Function >32) who have a >35% mortality rate at four weeks. (8)

With respect to chronic liver disease, generally any patient should be considered for LT if there is evidence of hepatic decompensation (clinically defined as evidence of encephalopathy, jaundice, ascites and/or gastrointestinal bleeding from portal hypertension). A survival benefit is noted for well-selected patients with Model for End-stage Liver Disease (MELD) score >13 or Child-Turcotte-Pugh class B or C, irrespective of underlying etiology (9). All potential transplant candidates undergo a rigorous evaluation at a transplant centre that includes a hepatic and multisystem workup, cross-sectional abdominal imaging and psychosocial assessments by a multidisciplinary team that includes a transplant hepatologist, hepatobiliary surgeon, anesthesiologist, social worker, psychiatrist or psychologist, dietician and physiotherapist, among other allied health professionals.

In practice, the vast majority of LT programs in North America adhere to a so-called ‘six-month rule’ for ALD, in which candidates must abstain from alcohol consumption for a minimum of six months, and successfully demonstrate compliance and insight into their addiction in addition to completing a certified alcohol rehabilitation program. This rule effectively eliminates LT for acute alcoholic hepatitis in Canada despite recent evidence for its impressive survival benefit and safety in well-selected candidates (10-12). It also effectively eliminates the newly presented patient with decompensated end-stage cirrhosis who will not survive six months.

Perhaps current policies and attitudes toward patients with ALD stem from the overall shortage of cadaveric grafts, and the realization that living donation can never satisfy society’s need for livers, especially considering legitimate safety and/or ethical concerns of the latter. In the previous decade, 907 Canadians died while awaiting LT at an estimated mean (± SD) number of patients with recidivism per centre resulting in graft dysfunction was 10±4.36; the mean number of patients with recidivism resulting in graft failure/loss was 2.5±2.08; the number of patients with mild recidivism was estimated to be 30 in one centre, but not quantifiable in the other six programs. All programs agreed in principle that a nationwide dialogue to further unify transplant policies for ALD patients would be helpful.

DISCUSSION

Overall, there is homogeneity among Canadian LT programs with respect to transplantation policies for patients with alcohol-related liver disease. All transplant centres in Canada require at least six months of abstinence from alcohol before listing for LT, and none of the centres currently consider LT for severe alcoholic hepatitis or use validated alcohol assessment tools. Interestingly, there is variability in the use of random alcohol checks and reported recidivism rates despite published data to support this practice (13,14). Serious recidivism resulting in graft dysfunction or loss occurs but is uncommon. Importantly, there is uniform consensus among the seven liver transplant programs in Canada to explore a national transplant policy for patients with ALD, although it is suspected that programs would ultimately desire to maintain their autonomy with respect to their centre’s ultimate policies. While the present survey provides a useful starting point from which to re-evaluate current policy, it did have some limitations including recall bias in estimating the proportion of ALD patients with recidivism post-LT, and lack of standardized measurements of mild recidivism rates post-LT.

The rationale for the ‘six-month rule’ is that many subjects with alcoholic hepatitis will improve spontaneously with supportive care (eg, nutritional supplementation, alcohol withdrawal management, prednisone or pentoxifylline in selected patients, etc) and prolonged abstinence alone, and the majority of hepatic recovery ensues within the first few months (15). An additional reason to justify a mandatory length of sobriety is that prolonged abstinence is a negative predictor of recidivism in the post-LT setting (13,16-18).

In theory, recidivism following LT is relevant because not only could it result in graft loss, but it may have a dire influence on organ donation rates, although it should be noted that there is weak evidence to support this latter hypothesis. Notwithstanding, while rates of alcohol recidivism are approximately 15% to 25% post-LT (14,17,19), the majority of patients with a history of ALD consume minimal amounts that are unlikely to cause graft dysfunction (20). The natural history of ALD following LT is poorly understood for the
obvious reason that there are limited observational data; however, a recent French registry-based study suggested that cirrhosis may recur in as little as 3.5 years (21) and previous Spanish data suggested that patients with recidivism have worse 10-year survival rates (22). The former observation of an accelerated natural history of ALD post-LT in some recipients may be explained by the concurrent overlap of nonalcoholic fatty liver disease, which is highly prevalent in LT recipients. On the other hand, in theory, alcohol may provide some immune protection against rejection, and overall rates of graft loss from recidivism are exceedingly low in multiple publications.

Organ allocation systems are required to fairly and predictably orchestrate organ allotment given the relative deficit of cadaveric grafts compared with the surplus of patients who need them. The MELD model is the most widely used organ allocation system in North America and was formally implemented in the United States (United Network for Organ Sharing) in 2003, and in Canadian liver transplant programs gradually thereafter. In addition to the MELD score being a validated predictor of mortality for subjects with end-stage liver disease or acute liver failure, the model does not overtly discriminate on the basis of age, recipient sex, geographical location, ethnicity or underlying etiology of liver disease, thus satisfying principles of equitable access, universality, transparency and portability.

While organ allocation should be a blinded process to preserve fairness, listing of potential recipients remains under the jurisdic tion of the transplant programs in Canada, and this creates an opportunity for selection bias against those with ALD. Given that there are behavioral elements contributing to most liver diseases (with perhaps the exception of liver conditions that are immune mediated or strongly genetic), the question then becomes, do patients with ALD experience barriers to access LT compared with patients with nonalcoholic liver diseases, and is this distinction fair?

For example, consider the scenario of a patient with nonalcoholic fatty liver disease and etiological risk factors that include obesity, hyperlipidemia and type 2 diabetes mellitus. In this setting, one might argue that this patient could have exerted some control over his or her body weight and glycemic management through dietary modifications and exercise to lower his or her risk of end-stage liver disease. Does this line of reasoning justifiably deny listing this patient for LT years later? Similarly, is a former intravenous drug abuser who acquired hepatitis C infection from inadvertently sharing contaminated needles more entitled to LT than a person with ALD? These ethical arguments suggest there may be some inconsistency in the notion that patients with ALD are responsible for their cirrhosis if we do not apply the same logic to other patient groups. Furthermore, there is evidence of a strong genetic role in the pathogenesis of ALD (23); surely patients in a just society should not be penalized for having a genetic predisposition to a potentially fatal disease.

Decisions on organ allocation for subjects with ALD must be transparent and justifiable to society. The transplant community and the Canadian public at large should re-evaluate the ‘six-month rule’ and weigh mounting evidence of the efficacy of LT for severe acute ALD – effectively much sooner than six months. While successful completion of a rehabilitation program and psychosocial counseling is vitally important for anyone with alcohol addiction, what happens if a patient is too sick to leave the hospital to complete a rehabilitation program? Does that mean he or she dies without an opportunity for LT? Cost-effective arguments against LT in this group are also unlikely to have merit. We have previously shown that subjects with ALD have no increased risk for excess postoperative resource utilization or readmission after LT (24,25). The question with regard to transplant candidacy for patients with ALD should pertain to the likelihood of graft loss from recidivism post-LT and decisions should be evidence-based.

CONCLUSION

Current policies for LT for patients with ALD are similar across Canadian transplant programs, all of which adhere to the ‘six-month rule’, but there is a desire for further debate and exploration of policies to address acute alcoholic hepatitis. Given emerging evidence supporting the efficacy of LT for both severe acute and chronic ALD, it would be in the interest of transplant programs to spearhead a governmentally sanctioned policy discussion into the topic to provide transparency to the public, and establish a medicolegal framework on which to justify medical decisions on listing or not listing patients. In the absence of such an official policy statement, the present article documents what can be considered a reasonable standard of transplant care in this country.

KEY MESSAGES

- Among the seven Canadian liver transplant programs, there is overall strong concordance in transplant policies toward patients with ALD with respect to adherence to the ‘six-month rule’ and no transplantation for severe acute alcoholic hepatitis.
- Canadian transplant policies regarding ALD are consistent with current American and European practices, but there is broad interest, particularly in Europe, toward further evaluation of LT as severe, medically refractory, acute alcoholic hepatitis in light of growing evidence of a survival benefit.

REFERENCES

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