Selecting candidates for liver transplantation: A medical ethics perspective on the microallocation of a scarce and rationed resource

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Liver transplantation has evolved over the past 35 years from an experimental procedure with high perioperative mortality to an accepted form of treatment with an approximate 85% one-year and 80% three-year patient survival rate. Following the success and acceptance of transplantation in the treatment of end-stage liver disease, there has been a progressive increase in the number of patients seeking a limited supply of donor organs. The ethical focus, on a microallocation level, has therefore changed from that of the 1960s, when the question was whether the procedure should be offered at all, to that of the 1990s and beyond, when the focus is on the proper allocation of a scarce, life-saving resource. The ethical issues concerning fair allocation surrounding liver transplantation are explored, from both the referring physician’s perspective and the perspective of the transplant physician. In particular, the contrasting viewpoints of bioethicists Nicholas Rescher and James Childress, with respect to nonmedical and social criteria in the selection of patients for scarce, life-saving therapies, are explored. Lastly, some alternative ethical models for patient selection are reviewed.

Key Words: Allocation, Ethics, Liver transplantation

Sélection des candidats pour une transplantation hépatique : point de vue d’éthique médicale sur la micro-attribution d’une ressource rare et rationnée

RÉSUMÉ : Au cours des 35 dernières années, la transplantation hépatique est passée du stade de chirurgie expérimentale associée à une mortalité périopératoire élevée à celui d’une méthode thérapeutique reconnue avec un taux de survie d’environ 85% à 1 an et de 80% à trois ans. À la suite du succès de la transplantation dans le traitement des hépatopathies en phase terminale, on observe une augmentation progressive du nombre de patients qui désirent être greffés bien que le nombre des donneurs demeure limité. Dans les années 60, la principale question sur le plan éthique, concernant la micro-attribution, était de savoir si on devait absolument offrir ce type d’intervention, tandis qu’à partir des années 90 le débat s’est déplacé sur la question de l’attribution adéquate d’une ressource rare mais qui sauve la vie. Les questions éthiques au sujet d’une attribution juste dans le contexte de la transplantation hépatique sont examinées, à la fois du point de vue du médecin qui adresse les candidats pour une transplantation et de celui du médecin qui va réaliser la greffe. En particulier, les points de vue opposés des bioéthiciens Nicholas Rescher et James Childress, relativement aux critères sociaux et non médicaux qui prévalent dans la sélection des patients candidats à des thérapies rares et qui sauvent la vie sont analysés. Finalement, d’autres modèles éthiques pour la sélection des patients sont passés en revue.
In many respects, liver transplantation, as it stands today, can be considered a suprasubspecialty, standing in close proximity not only to nontransplant hepatology/gastroenterology but also to the other ‘sister’ solid organ transplant areas of heart, lung and kidney transplantation. Unlike traditional medical and surgical subspecialties, however, the collected solid organ transplant areas are truly multidisciplinary, with the necessary involvement of physicians, surgeons, pharmacy specialists, clinical nurses, social workers and psychologists. Just as transplantation produces unique medical/surgical problems, the field also produces its own unique ethical dilemmas. The main ethical issues regarding organ transplantation can be broadly categorized as follows: macroallocation issues – the allocation of resources at the level of society (eg, would health care dollars spent on transplantation be better spent in other areas of health care?); microallocation issues – the allocation of resources at the level of the individual patient or group of patients (eg, who, if anyone, should be offered a donor organ?); and organ procurement and distribution issues (eg, regional versus national distribution of organs, organs purchased on an international ‘black market’, organs obtained from executed prisoners, etc). Although each of these broad categories is important, the focus of this commentary is on ethical issues at the level of microallocation with regards to liver transplantation. The differing and sometimes conflicting perspectives of both the referring physicians and the multidisciplinary unit that comprises the transplant ‘team’ are examined. The ethical points that arise within the category of microallocation may be generalizable to all solid organ transplant programs; however, it must be noted that renal transplantation differs in that there is an effective and widely available nontransplant alternative that can be offered to patients, namely, the various forms of dialysis. In this regard, liver transplantation is closer to heart and lung transplantation in that there is no viable nontransplant alternative for end-stage disease other than morbidity and death.

BACKGROUND

It has been only 35 years since the first attempt at liver transplantation in a human recipient was reported by Dr Thomas Starzl et al (1), then at the University of Colorado. This first attempt, although preceded by numerous technical expertise developed in animal experiments, ended tragically with the intraoperative death of a three-year-old child. The cases that followed in the 1960s, likewise, were associated with early postoperative mortality (2). As the field of liver transplantation passed from its experimental infancy the problems of surgical technique were largely overcome. Medical complications, chiefly those of adequate immunosuppression, limited graft and patient survival as well as generalizability outside of a few academic centres, remained. Indeed, before 1980, the one-year survival rate post-transplant was less than 50% (3,4). The development and introduction of cyclosporine into clinical practice in the early 1980s (5) heralded the ‘cyclosporine era’ – a period of markedly improved graft and patient survival. Today, with the addition of tacrolimus (formerly FK506) to the immunosuppressive regimen (6,7), patients and clinicians alike can depend on a one-year survival rate of the order of 85% and a three-year survival rate of 75% to 80% for first transplants (8; 1991 to 1994 cohort). In British Columbia, where liver transplantation has been available since 1989, the patient survival rate mirrors that of the rest of North America, with an overall one-year survival rate close to 85% and a five-year survival rate of 70% (analysis based on cohort 1989 to 1996 [personal communication]). These favourable survival statistics are in stark contrast to the poor prognosis of patients with end-stage cirrhosis – one- and six-year survival rates of 60% and 21%, respectively, for decompensated patients (ascites, variceal bleeding, encephalopathy, hypoalbuminemia, coagulopathy) (9).

In addition to a quantitative survival benefit, liver transplantation can provide patients with an improvement in the level of quality of life compared with the pretransplant condition of chronic liver disease (10-12). Hunt et al (12), from Duke University, in a recent survey of post-transplant patients, found that 85% of respondents had Karnofsky scores of 90% to 100%, with no patient reporting a score of less than 80% (normal activity with effort, demonstrating some signs or symptoms of disease). Most importantly, both American (12) and Canadian (13) surveys have found that approximately 60% of liver transplant recipients are able to return to work. Transplant recipients who were unemployed post-transplant tended to be older or on social assistance pretransplant.

Liver transplantation has become, in the late 1990s, first-line treatment for patients with decompensated liver disease of numerous etiologies as well as a form of macroscopic gene replacement therapy for several systemic metabolic diseases (eg, hereditary oxalosis) (14). With medical progress, the list of diseases for which liver transplantation may be of benefit continues to grow, whereas the list of absolute and relative contraindicated conditions continues to shrink. For example, until recently, cirrhosis secondary to chronic hepatitis B infection was an absolute contraindication for transplantation because of the high rate of allograft reinfection and associated poor outcome (15). Today, with the use of high dose hepatitis B hyperimmune globulin (HBIG) and antiviral agents such as lamivudine, transplantation can be offered to patients at centres where these post-transplant therapies are available (16). Similarly, patients with advanced age and alcoholic liver disease, conditions that were formerly considered absolute contraindications for transplantation, may not be excluded solely on medical grounds alone. Several centres have reported that older transplant recipients have no difference in outcome compared with younger recipients (17,18). Similarly, patients transplanted for alcoholic liver disease have a favourable long term outlook (19). Post-transplant recidivism is reportedly low after a proscribed period of abstinence (20,21), and six months appears to be an acceptable period of abstinence.

For all of the above reasons, the number of liver transplants performed has increased almost yearly. To illustrate, using the most recent American data from the United Net-
work of Organ Sharing (UNOS) (22), in 1996, 4058 transplants were performed in the United States compared with only 1713 in 1988, a 2.4-fold interval increment. The number of patients on the waiting list increased from 616 in 1988 to 7467 in 1996, a 12.1-fold interval increment. Most importantly, the number of wait-listed patients dying before transplantation increased from 195 in 1988 to 954 in 1996, a 4.9-fold interval increment. Similarly, in British Columbia, the number of transplants performed increased from three in 1989 to 33 in 1996, whereas the number of new patients referred for transplant assessment (but not necessarily wait-listed) within that period increased from 65 to 120 per year (unpublished data).

Clearly, the ethical focus surrounding liver transplantation has changed from the early 1960s to the present. Whereas in the pioneering years, dismal outcomes led to the question of whether this therapy should be offered at all (at the time some commentators felt that a moratorium was called for [2]), as we approach the new millennium the ethical issue shifts to that of the fair allocation of a scarce and rationed resource.

**ETHICAL PERSPECTIVE: THE REFERRING PHYSICIAN**

Aside from the provision of medical care that conforms to a reasonable standard, the referring physician’s involvement in the transplantation process is essentially to decide whether to refer the patient to the regional transplant centre. Referring a patient for transplant assessment appears to satisfy the tenets of biomedical ethics, chiefly, beneficence, nonmaleficence (do no harm), patient autonomy and justice. After all, the simple act of patient referral may result in potential life-prolonging treatment (beneficence). Aside from possible time and monetary expenses of the patient from travelling to the scheduled appointment or, in the case of patients too ill to be assessed as out-patients, the health care expenses incurred in transferring the patient to the transplant-base hospital for assessment, referral itself seems to be nonmaleficient. Patient autonomy appears to be satisfied, at least as far as the referral process goes, because the patient must agree to appear for the scheduled appointment or agree to transfer. The burden of actual informed consent of course rests with the transplant team. Because transplantation has become the treatment of choice for end-stage liver disease, referral safely places the physician within the medical-legal boundaries of ‘reasonable standard of care’ (23) and fulfils the biomedical principle of ‘justice’ (like treated as like). Failure of the physician to refer an otherwise appropriate patient for transplantation, or a delayed referral, results in obvious maleficence – potentially avoidable mortality and, in the latter case, possible unnecessary posttransplant morbidity with a potential for mortality due to the patient’s debilitated physical state.

Although, in many cases, the burden of deciding that a patient is unsuitable for transplantation lies with the transplant team, referring or attempting to transfer an obviously inappropriate patient (ie, a patient with a known contraindication for transplantation) is not without consequence. The potential for unrealistically raising the hopes and expectations of both patient and family can constitute maleficence. Similarly, the referral may delay the opportunity of a more realistic transplant candidate to be seen and assessed, thereby infringing on the biomedical principle of justice. Finally, shifting or abandoning the burden of duty of care of a nontransplantable patient onto the transplant team may, depending on the context, be perceived as unprofessional behaviour.

**THE TRANSPLANT PHYSICIAN**

Unlike the referring physician, the transplant physician is in a unique and, at times difficult, position. The transplant physician has an obligation to act in the best interests of not only the individual patient who has been referred for assessment, but also the entire cohort of patients who, likewise, are in need of a transplant. Because, as discussed in the ‘Background’, the number of patients seeking liver transplants exceeds the number of organs that can be procured, the transplant physician must weigh the competing interests of any given individual patient against others in the cohort. Liver allografts can be considered a scarce and rationed resource. The ethics of fair allocation of this precious commodity must be considered if the individual patient, as well as society as a whole, is to benefit. Analogy can be drawn to the desperate situation of passengers from a sinking ship in an overloaded lifeboat – not all can be saved. Who should be allocated a scarce, rationed life-saving resource, which in this case is space in the lifeboat? This scenario, which Childress (24) originally described in his paper on the allocation of scarce, life-saving resources and which was retold 24 years later by Weir (25), is based on the experience of the passengers and crew of the ill-fated William Brown, which in 1841 struck an iceberg in the North Atlantic ocean. Patients with end-stage liver disease seeking a transplant are in a similar position to that of the passengers of the William Brown. A more medical analogy to the current transplant situation can be drawn from the American experience with hemodialysis in the late 1960s. During this period, kidney dialysis was in limited supply and in Seattle, Washington a selection committee decided who was to receive this life-saving therapy (26). Unlike, liver transplantation, however, the American dialysis dilemma had an economic solution – federal funds were made available to increase availability.

**THE SELECTION PROCESS**

Deciding who, of many, is an appropriate transplant candidate with the possibility of receiving a liver allograft is, in reality, a two-stage process. In the first stage, which can be considered ‘primary selection’, patients are selected for the waiting list or ‘activated’. When a donor organ becomes available (‘harvested’) the second phase or ‘secondary selection’ process begins. In this phase, the transplant surgeon and physician review the list of patients on the waiting list and a decision is made as to which specific patient will be allocated the donor organ.
PRIMARY SELECTION: DECIDING WHICH PATIENTS WILL BE GRANTED A PLACE ON THE WAITING LIST – ETHICAL MECHANISMS

Medical utility: The principle of utilitarianism is literally that of ‘maximizing happiness, minimizing misery’ (27) or in other words, achieving the best possible outcome. In terms of liver transplantation, this means selecting patients who will benefit the most from the donated organ in terms of graft and patient survival. It also means that patients who are unlikely to survive the immediate postoperative period or who are unlikely to achieve long term survival benefit should not be offered transplantation. It is for this reason that the presence of many coexisting medical illnesses (eg, significant heart disease, active bacterial infections) and primary liver diseases (eg, large primary liver cancers) represents contraindications for transplantation (14). The principle of medical utility may also extend to local technical expertise (surgical expertise for organ transplantation in a patient with a previous complicated intra-abdominal surgery may not be available at a small centre, although it may be available at a large centre) or the local availability of resources (eg, the lack of large quantities of HBIG needed to prevent allograft re-infection may not allow patients with hepatitis B to receive transplants). Furthermore, the principle of medical utility may include nonmedical conditions. An example of this is documented habitual noncompliance in a patient with a disease that can be treated by transplantation. Noncompliance has been associated with increased graft loss (28).

The principle of medical utility may, at times, appear to place the transplant physician in conflict with the traditional values of the ‘good doctor’. Rejecting a respectable, sympathetic patient who would enjoy an improved quality of life and a few extra years of life post-transplant but in whom the probability of long term survival is unlikely (ie, a palliative transplant) may appear to violate the notions of beneficence and benevolence. One has to consider, however, the interests of other patients who would enjoy a long term survival benefit but may be denied the opportunity if the principle of medical utility is not adhered to.

The use of age as a selection criterion for transplantation is a controversial area in transplantation. In the past, many centres had an age cut-off, which was defined arbitrarily (eg, more than 60 or 65 years of age). As previously mentioned, data from several centres (17,18) demonstrated that older patients could have a favourable post-transplant outcome. Furthermore the use of age as a selection criterion has been criticized (29) as unethical because it represents discrimination and because patients should be treated on an individual basis. On the basis of medical utility, however, rejecting a patient on the basis of advanced age may be justified. Although, the cited studies do not appear to demonstrate a difference in post-transplant outcome for the duration of the study (ie, five years), it is not logical to extrapolate these results to 10 to 15 years post-transplant. The question can also be raised as to the upper age limit at which transplantation should be considered realistic (70 years? 80 years?). Because older patients may also have inapparent degenerative conditions of senescence (eg, mild renal impairment, occult coronary, cerebral-vascular disease), which may adversely affect long term outcome on the basis of medical utility, medical utility appears to favour the younger patient. To avoid the inherent unfairness of an arbitrary age limit yet retain some aspect of medical utility it may be best to consider biological age rather than true chronological age.

Ethics of selecting patients based on nonmedical criteria: Despite contraindications, relative and absolute, to transplantation on medical grounds (justified by medical utility), there is still an excess of candidates competing for a limited supply of donor organs. In an attempt to resolve this issue Nicholas Rescher (30) and James Childress (24) presented two opposing viewpoints. Both included a first stage of selection that employed the principles of medical utility and practicality. For Rescher, the practical and utilitarian features of selection for ‘exotic life-saving therapy’ were hospital constituency, research interests (a “progress of science factor”) and predictors of best outcome (prospect of success, relative likelihood of success and life expectancy factors). For Childress, medical acceptability (medical utility) determined the first stage of the screening process for what he considered “scarce life-saving medical resources”. Childress stressed that attempts to determine fine gradations of ‘medical acceptability’ should be avoided (eg, attempting to determine which of the acceptable candidates would have a better outcome than the others).

Where Rescher and Childress differed was in the second stage of selection. For Rescher, utilitarian reasoning extended into the social sphere. Therefore, a “family role factor” that includes the interests of the candidates familial/social dependents should be considered. By using this reasoning, a mother with children would be given higher priority than a single man with no dependents. Rescher extended his concepts of social utility to include “potential future contributions factor” and “past services-rendered factor”. In the former, priority assessment would take into account the candidate’s potential value to society. Rescher argued that “...society invests a scarce resource in one person against another...” and, therefore, society is “entitled to look to the probable prospective ‘return’ on its investment”. In the latter situation, Rescher felt that the “past services” factor would allow for the “recognition and reward of services rendered”. There are, of course, difficulties in attempting to apply social utilitarian principles to scarce life-saving resources – difficulties that Rescher also acknowledged. For instance, a candidate’s ‘potential future contributions’ may not be predictable from present circumstances. There is also the problem of what value systems are to be used to define and measure the value of one individual’s future contributions against another (eg, a criminal defence lawyer versus a pediatric nurse). The debate in the media after ex-alcoholic American baseball icons received liver transplants seems to underscore the difficulties with Rescher’s “past services” factor.

Childress, on the other hand, believed that the importance of psychosocial factors in the selection of patients for scarce life-saving resources should be minimized and should
be considered only when relevant to the medical conditions (eg, a patient's ability to cope with transplantation). Otherwise, he believed that the second stage of selection beyond medical utility should be on the basis of random selection – either 'first come, first served' or by lottery. Childress argued that judgements based on social utility diminish the individual's dignity and reduce it to the mere sum of past and future worth to society. Moreover, Childress pointed out the possible maleficence of determining access to life-saving resources on the basis of social values – psychological and emotional harm to those refused on the basis of lack of social worth. In fairness to Rescher, he also commented on the "desirability of introducing an element of chance" such as random selection of a homogenous group of potential candidates.

In reality, neither the social utilitarian model of Rescher (30) nor the random selection model of Childress (24) has been adopted exclusively for use by any transplant centre. Rather, they form opposite ends of a spectrum, and decisions regarding nonmedical criteria are rarely the sole province of physicians or surgeons but encompass the input of other team members, including nurses, social workers and psychologists. Certainly, social considerations such as education and socioeconomic standing are not of importance in the selection process, a fact confirmed by a recently published survey of Canadian liver transplant medical directors (31). On the other hand, most centres do have either absolute or relative social, lifestyle and behavioural contraindications for transplantation. For instance, 93.5% of surveyed American liver transplant centres consider current addictive drug use to be either an absolute or relative contraindication, almost 70% consider incarceration for a felony to be an absolute or relative contraindication and 67% consider lack of social support to be a relative contraindication (32). With regards to these nonmedical contraindications, some defence on the basis of transplant utility with regards to outcome is usually made, although specific supporting data may be lacking or weak.

SECONDARY SELECTION: DETERMINING WHICH PATIENT ON THE WAITING LIST RECEIVES A PROCURED ORGAN

Once an organ has been harvested some mechanism is needed to determine which of the patients on the waiting list is to receive a transplant. Unlike the 'primary selection' process, considerations of psychosocial issues do not enter the equation. Selection is, again, first on the basis of medical utility. Factors such as ABO blood group match between donor organ and recipient (in liver transplantation, human leukocyte antigen matching is not an issue) and donor-to-recipient size match (a technical consideration) are used. The egalitarian principle of medical urgency is also preeminent, with the view that those most in need (and therefore most likely to die in the short term) should receive a transplant first. Both UNOS and the Canadian Transplantation Society prioritize patients according to medical need; therefore, egalitarianism is medically 'codified' in national policy. Finally, when all other factors remain equal, some element of Childress' random allocation philosophy (24) is applied, with most centres allowing for some consideration as to the time a candidate has been on the waiting list, ie, 'first come, first served'.

ALTERNATIVE ETHICAL PHILOSOPHIES REGARDING PATIENT SELECTION

Application of feminist ethics: Feminist ethics focuses on power imbalances between social groups (eg, men versus women, Caucasian versus non-Caucasian, doctors versus nurses, etc), with a view to addressing these power imbalances (33). Mullen et al (31) suggest that feminist ethics can be applied to a selection of candidates for transplantation. They argue that health care professionals are in a position of power over patients. A way to remedy this power imbalance is to allow transplant recipients, representatives from the public or donor families to participate in the selection process. Although this may appear to mitigate power imbalances, such 'power-sharing' solutions have inherent difficulties. First of all, application of feminist ethics in this context presumes that health care professionals, including doctors, nurses, social workers and psychologists, cannot act fairly – that there is an underlying bias in their decision-making process. It also presumes that nonhealth care professionals are free of these 'power biases' and better able to act in the best interests of the unempowered patients. This may not be true. Second, individuals lacking a sufficient background in the complex health care issues that surround organ transplantation may not be in a position to contribute recommendations that are perceived as appropriate. They may in fact be relegated to the functional status of passive observer. Lastly, all health care professionals are accountable for their actions. This accountability is legislated via the powers conferred upon the governing health care colleges (eg, the Health Professionals Act of British Columbia) (34). Lay members who attend transplant selection meetings are allowed access to privileged patient information, and, in theory, are not governed by the same codes of professional conduct as are health care professionals.

Market place ethics: Liver transplantation is an exceptionally expensive proposition. The total first-year cost to an uninsured American seeking a liver transplant in 1992 was US$302,900 (35). One possible criterion for the selection of candidates is to adopt a market place ethic – organ allocation on the basis of simple ability to pay (26). Such a policy would certainly minimize public health care expenses and may be in accordance with social utilitarianism – those able to pay are already in a high social-economic strata and are, therefore, more likely to contribute economically to society post-transplant rather than becoming a social-economic burden. However, such a market place approach is incongruent with any sense of egalitarianism and social justice. As well, such an approach would be perceived as putting a dollar value on human life. There would also be the inevitable loss of real human dignity as desperate individuals attempted to raise.
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funds in much the same manner as local public charities (eg, church bazaars, appeals to the media). Fortunately, in Canada, the Canada Health Act ensures that Canadians do not have to bear the costs personally; therefore, a market place approach to health care is not an issue. In the United States, most private insurers provide coverage for transplantation and, although Medicaid (public health care for the needy) varies according to state, over the years many states have lost legal attempts to refuse transplant funding (35-37) such that, in the United States, market place ethics is also losing its importance.

Moral reciprocity – Transplantation based on willingness to donate: Another approach is for potential transplant candidates who had previously demonstrated a willingness to donate their own organs (eg, had signed organ donor cards) to be given priority over those who had refused (39). Such a policy would presumably have a positive effect on the current organ shortage in that people would be more inclined to donate organs (albeit for less than altruistic reasons), thereby satisfying utilitarian philosophy. Making selection dependent on willingness to donate also strongly appeals to a sense of justice – ‘treating like as like’. However, such an approach is not without its detractors (40). Such a policy may unjustly penalize those who were undecided about the issue of organ donation or were unaware of the means to declare willingness to donate before their unexpected discovery of need. The question of how willingness to donate would be determined or were unaware of the means to declare willingness to donate before their unexpected discovery of need. The question of how willingness to donate would be determined among prospective transplant candidates is also problematic. The very fact that prospective candidates are aware of their own personal need for an organ would undoubtedly affect their opinion of willingness to donate. The truly selfish would profess their willingness to donate with the knowledge that such an admission would increase their likelihood to receive an organ; honesty would thus be compromised, which would be incongruent with the concept of justice.

CONCLUSIONS

The selection of a few among the many in need of a scarce resource, such as an organ transplant, is a difficult task. No one ethical theory, outside of medical utility on a physiological basis, is completely applicable or can be totally ignored. From a humanistic viewpoint, selection of transplant candidates will inevitably bring about unhappiness to some, no matter who or how candidates are selected. Calabresi and Bobbitt, in the context of the United States Medicaid transplant funding debates but easily generalizable to the microallocation setting, described such a decision as a “tragic choice” – tragic in that the outcome will “ultimately violate some deeply held societal value” no matter what the outcome (41). Despite the inevitable personal tragedies that occur as a result of competition for a scarce and rationed resource, it is necessary to keep in mind that the process of microallocation must both exist and be fair to prevent personal and societal tragedies of even greater magnitude.

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