Why Is Heart Transplantation Not Performed in Japan?
Refutation of Dr Yoshio Watanabe’s Arguments Against Heart Transplantation

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Key words: heart transplantation organ transplantation brain death cardiomyopathy donor

INTRODUCTION

Dr Juroh Wada of Sapporo Medical College, Sapporo, Japan performed the first heart transplant in Japan in 1968. However, for a number of reasons the procedure has never been repeated in this country. First, the “Wada transplant” aroused considerable criticism. Dr Wada was accused of murder by a citizens’ group on the grounds that the donor, a 20-year-old drowning victim, may have been alive rather than brain dead when the heart was removed; these charges were dropped after a 2-year criminal investigation. Dr Wada was also criticized for transplanting the heart to a recipient who may not have been a suitable candidate for transplantation — the patient had rheumatic valvular disease of the heart. These criticisms, coupled with a growing distrust of physicians among the Japanese population, have prevented the procedure from being repeated.

However, encouraged by subsequent success with and growing use of heart transplantation in Europe and the USA, the Research Committee on Brain Death, Ministry of Health and Welfare, Japan (Chair: I. Takeuchi), in 1985 established criteria for diagnosing brain death. In 1988, the Committee on Bioethics of the Japan Medical Association published the “Final Report on Brain Death and Organ Transplantation,” which endorsed the “Takeuchi criteria” as the minimum necessary for diagnosing brain death, and declared that in addition to the already recognized cardiac death, brain death (the irreversible loss of brain function) could be considered the death of an individual. However, the general public, religious organizations, philosophical groups, and particularly the bar association were strongly opposed to the recognition of brain death, arguing that

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a person is not dead if the heart is beating. This is the second reason why heart transplantation has not been performed in Japan since 1968.

In an attempt to overcome this confusion, the Japanese government formed the Provisional Commission for the Study of Brain Death and Organ Transplantation. After 2 years of deliberation, this committee presented its final report in January 1992, with opposing opinions appended. The decision of the committee was that organ transplantation should be performed in Japan, and that the transplantation of organs from brain-dead donors should be sanctioned once various essential organizational reforms had been undertaken and provisions for establishing coordinating systems had been made.

On April 12, 1994, the Bill of Organ Transplantation, which defines brain death as death, was brought before the Diet. This procedure was necessary because the removal of the heart from brain-dead donors is illegal and subject to prosecution under the current Japanese legal system. The bill is expected to be approved. However, a group led by Dr Yoshio Watanabe, Cardiovascular Institute, Fujita Health University School of Medicine, Aichi, Japan, a renowned cardiologist, is campaigning against the bill. This is the third reason why further heart transplants have not been performed in Japan.

In this article, we will comment on the opinions of Dr Watanabe; however, we first mention the responses made to questions about heart transplantation raised by the Japanese Circulation Society, and the consequences of these responses.

**JAPANESE CIRCULATION SOCIETY’S VIEWS ON HEART TRANSPLANTATION AND RESULTING ACTIONS**

In May 1988, the Japanese Circulation Society approved the establishment of the Research Committee on Cardiac Transplantation (Chair: H. Toshima). This committee conducted a survey on heart transplantation, sending a questionnaire to the members of the Board of Trustees of the Internal Medicine Group of the society, and then to general society members aged ≤40. The results of this survey, shown in Table I, indicated that the majority of those surveyed were in favor of heart transplantation providing that certain conditions were met; however, 3 of the 149 members of the Board of Trustees (2.0%) and 40 of the 1778 members aged ≤40 (2.2%) stated that heart transplantation should not be performed under any circumstances. From these results, the committee concluded that although some physicians opposed heart transplantation, the majority were in favor of it. Subsequent committee activities were conducted based on this conclusion. However, 45% of those on the Board of Trustees and 56.5% of the members aged ≤40 thought that heart transplantation should be resumed “only
Table I. Results of a Survey on Heart Transplantation Conducted among Members of the Board of Trustees and General Members (aged ≤ 40 years) of the Japanese Circulation Society*

<table>
<thead>
<tr>
<th>Question</th>
<th>Number of trustees (%)</th>
<th>Number of members (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Concerning the resumption of heart transplantation:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>A  Heart transplantation should not be resumed under any circumstances.</td>
<td>3 (2.0)</td>
<td>40 (2.2)</td>
</tr>
<tr>
<td>B  It is alright to resume heart transplantation if certain conditions are met, those conditions being:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1) That it be done in accordance with the final report of the Committee on Bioethics of the Japan Medical Association.</td>
<td>60 (40.3)</td>
<td>578 (32.5)</td>
</tr>
<tr>
<td>2) That it be done only after the criteria for determining that a patient is brain dead have been investigated further, and broad consensus as to what constitutes brain death has been achieved.</td>
<td>67 (45.0)</td>
<td>1005 (56.5)</td>
</tr>
<tr>
<td>3) Other</td>
<td>11 (7.4)</td>
<td>108 (6.1)</td>
</tr>
<tr>
<td>C  I do not agree with either statement.</td>
<td>3 (2.0)</td>
<td>21 (1.2)</td>
</tr>
<tr>
<td>D  Other</td>
<td>5 (3.4)</td>
<td>26 (1.5)</td>
</tr>
<tr>
<td>Total number of respondents</td>
<td>149</td>
<td>1778</td>
</tr>
</tbody>
</table>

* The response rate of members of the Board of Trustees was 88.7%, whereas that of members aged ≤ 40 was 35.7%.

after the criteria for determining that a patient is brain dead have been investigated further, and broad consensus as to what constitutes brain death has been achieved." This indicates that questions about brain death have clearly become a major impediment to heart transplantation in Japan.

Nevertheless, the Japanese Circulation Society, the majority of whose members are internists, decided on the basis of these survey results that their role with respect to heart transplantation was to assume responsibility for determining which patients are suitable heart transplant recipients. For this purpose, the society established the "Study Group on Heart Transplantation Indications" (Chair: H. Toshima) in 1990. The study group was given the task of deciding which patients were suitable candidates for heart transplantation, by impartially scrutinizing data on patients desiring heart transplants submitted by the physicians in charge of these patients. The basis for this decision was that only those patients whose prognosis was extremely poor without heart transplantation and for whom only heart transplantation could be expected to have a therapeutic effect should be selected. The group began its work in January 1992 and by June 1994 had screened 31 patients. Of these, 27 were selected as suitable candidates for heart transplantation. However, to date 10 of the 27 have died, 4 others have improved after receiving a transplant in the USA, one has improved on β-blocker therapy, and the remaining 12 are still waiting for a heart transplant.

It is regrettable that although many cardiologists want to perform heart transplants in patients with heart failure when there is no other means of saving
the patient's life, they are prevented from doing so by opposition based on emotional thinking. In July 1994, Dr Watanabe stated "I am very displeased and concerned that the physicians who promote heart transplantation have not once presented a rebuttal to my arguments. I cannot help thinking that this is because their logic is not sound enough to refute me after all". However, the only reason that we have kept silent is that there does not seem to be any logic in Dr Watanabe's assertions which is worth refuting and we do not intend to engage in a meaningless, emotional dispute.

**Is it illogical to consider brain death the death of the person?**

Dr Watanabe opposes heart transplantation for a variety of reasons. For example, he cites the problem of organs being rejected after transplantation and he raises moral questions concerning organ donors. However, the basis for his opposition is the idea that brain death is not the death of the person. He expresses this idea plainly: "Because heart removal would necessarily bring about final death of the person unlike the many other organs used for transplants". He refutes the following argument, which is considered one of the bases for the concept of brain death: Once a person lapses into total brain death (loss of function of the entire brain including the brain stem), cardiorespiratory arrest follows shortly, so, without question, brain death leads to the death of the entire person. Consequently, the heart of a person in this state is only kept working artificially by a respirator. Dr Watanabe states: "It is incorrect to say that the heart of a patient in a state of brain death is only kept working artificially by a respirator. This is because the heart has the capacity for automatic movement and works spontaneously, as is known from the fact that hearts excised from living organisms continue to beat for any number of hours when perfused via the coronary artery with perfusate containing oxygen, and it is not the case that the heart is made to contract and dilate artificially". However, excised animal hearts kept beating by coronary artery perfusion are different from the hearts of brain-dead humans on a respirator.

The fact that brain death brings on respiratory arrest and inevitably results in the cessation of the heart beat when a respirator is not used is supported by a comment made by Dr Shumway in his keynote address to the 24th Bethesda Conference. Recalling a common practice in the 1960s, Dr Shumway said: "At that time it was common practice for neurosurgeons and neurologists to turn off the respirator on a brain-dead patient, walk away, return in 20 minutes when the heart had stopped, and only then declare the patient dead." As this illustrates, brain death is recognized in medical circles worldwide as the death of the person. Brain-dead patients succumb to cardiac death within an average of 1 week of
brain death, even on a respirator; the brains of such patients are found by autopsy to be completely lysed (N. Kaku, personal communication). Any physician present at the autopsy would probably find this sight extremely memorable. This background forms the basis upon which organ transplantation has become an established treatment for persons with incurable diseases once bona fide donors willing to donate their organs in the event of brain death become available.

In Japan, where brain death is not recognized as death, brain-dead patients are sometimes kept in intensive care until their hearts have stopped completely, and it is estimated that over ¥3,000,000,000 (about US$ 30 million) is spent annually to treat patients following brain death. This huge and, if one agrees that brain death is death of the person, unnecessary expense is due in part to the Japanese universal health insurance system, which puts very little burden on the individual.

Dr Watanabe appeals to the emotions by suggesting that brain-dead pregnant women who give birth cannot be described as being dead. However, the heart of some brain-dead patients who have been found by computed tomography to have low brain density has been kept beating for as long as 101 days (N. Kaku, personal communication). This indicates that when respiration and circulation are maintained by a respirator after brain death, the body of a pregnant woman will continue to function apparently normally. Dr Watanabe insists that persons cannot be considered dead as long as the body is rosy and warm, and the heart is beating. This assertion is purely emotive and cannot be considered a reasonable, logical medical judgment.

Donors

Heart transplantation will become an established medical treatment only when bona fide donors who are willing to donate their hearts after brain death become available. Dr Watanabe makes the point that few people who are willing to donate their hearts would consent to the removal of the hearts of their children. This again is an emotional argument. Dr Watanabe suggests that proponents of heart transplantation in their 50s and 60s, who are too old to be donors, should try to persuade their children (persons of ≤40) to carry a donor card. However, the Japanese diagnostic criteria for brain death do not apply to children aged ≤6 and persons aged ≥18 have the freedom to make their own decision; in such cases parents have no means of forcing their children to agree to becoming donors. Neither should parents be opposed to their children donating organs in the event of brain death if that is what the child has indicated he or she wants.

Table II shows the results of a survey of Japanese Circulation Society mem-
Table II. Results of a Survey of Opinion Regarding Organ Donation

<table>
<thead>
<tr>
<th>Question</th>
<th>Number of society members (%)</th>
<th>Number of medical students (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A  I do not wish to donate my organs under any circumstances.</td>
<td>51 (2.9)</td>
<td>19 (4.1)</td>
</tr>
<tr>
<td>B  While I do not deny that brain death is the death of the person, I do not wish to donate my organs if I become brain dead.</td>
<td>214 (12.0)</td>
<td>44 (9.5)</td>
</tr>
<tr>
<td>C  I wish to donate my organs (heart, liver, kidneys, pancreas, lungs) the moment I am diagnosed as brain dead.</td>
<td>1084 (61.0)</td>
<td>263 (56.7)</td>
</tr>
<tr>
<td>D  Do not know.</td>
<td>361 (20.3)</td>
<td>127 (27.4)</td>
</tr>
<tr>
<td>E  Other</td>
<td>68 (3.8)</td>
<td>11 (2.4)</td>
</tr>
<tr>
<td>Total</td>
<td>1778</td>
<td>464</td>
</tr>
</tbody>
</table>

* Members of the Japanese Circulation Society aged ≤40 years, † Kurume University Medical School students.

bers aged ≤40 and Kurume University Medical School students which investigated opinions regarding post-brain death organ donation. The age of those surveyed is considered ideal for organ donors, and it is important to note that 56.7% of the university students, whose mean age was thought to be approximately 23, and 61.0% of physicians, whose mean age was estimated at 33, agreed with the statement: “I wish to donate my organs (heart, liver, kidneys, pancreas, lungs) the moment I am declared brain dead.” Unfortunately, these wishes cannot be made known because there is no system for distributing donor cards in Japan. It is also unfortunate that Dr Watanabe ignores such data and simply repeats assertions biased by personal opinions.

For organ transplantation to become a reality in Japan, some means of confirming that a person wants to be an organ donor is needed. Therefore the rapid dissemination of organ donor cards or a form on which persons can indicate that they wish to donate their organs is desirable.

**Other Problems**

It is well known that the development of new immunosuppressive agents has dramatically improved the prognosis of heart transplant patients. Nevertheless, it is true, as Dr Watanabe indicates, that heart transplantation causes problems. However, he ignores the statement by Dr Peter Shapiro, Columbia-Presbyterian Medical Center, Presbyterian Hospital, New York, USA, in one of the references he cites, an article introducing a report on the US thoracic medicine field: “These types of problems can be minimized greatly by giving the patients presurgical psychiatric evaluations and postsurgical counseling.”

Dr Watanabe also indicates that major problems with the ecological system,
including the appearance of AIDS, are associated with long-term immunosuppressive therapy following organ transplantation. It is more likely that such problems are associated with gene therapy. However, despite the various associated risks, gene therapy is expected to be very useful and its introduction to the field of medicine has become inevitable. Simultaneously, methods of controlling and minimizing associated risks are being devised. Everything has positive and negative aspects; however, it is our impression that Dr Watanabe amplifies only the negative aspects of heart transplantation and consciously does not examine its positive aspects. This attitude might be described as lacking impartiality.

It has been reported that better matching between the histocompatibility antigens of donor and recipient improves prognosis following heart transplantation.9 However, on the previous occasions that heart transplantation has been proposed in Japan histocompatibility has been ignored by surgeons in the selection of transplant recipients. Nevertheless, the Joint Committee of Japanese Societies Concerned with Transplantation states that when a histocompatibility locus antigen (HLA) test can be done, a recipient with a HLA type that matches that of the donor as closely as possible should be selected.10 We believe that HLA typing of an organ donor after diagnosis of brain death and selection of possible recipients matching that HLA type as closely as possible will minimize postsurgical rejection reactions. In addition, the HLA type of an individual is a matter of natural or divine providence; therefore recipient selection based on HLA type could prevent the criticism that selection of heart transplantation recipients is unfair.

Another important problem is that many Japanese patients are receiving transplants in the USA, UK, and other countries because they cannot obtain them in Japan. To date, 14 and 76 Japanese, respectively, have received heart and liver transplants abroad and are in better health as a result.11 However, there is a shortage of organ donors in all countries and many patients die waiting for a suitable donor. Therefore Japan cannot rely on the provision of organ transplants by other nations indefinitely, and this is another reason why heart transplantation should be made available in Japan.

Dr Watanabe's final allegation, what he calls "the final danger of organ transplantation from brain-dead patients",3 is that ultimately whole-body transplantation will be developed. This is not worthy of rebuttal. Organ transplantation is a medical treatment that is only initiated with the consent of the organ donor, and/or his or her family, and we do not believe that anyone would consent to donating the whole body from the neck down. In addition, it is clear, even from Dr Watanabe's own assertions, that even if an entire body or a brain were to be transplanted, the transplantation would very likely fail due to the rejection reaction.
CONCLUSIONS

Even those who are considered proponents of heart transplantation think of it only as a treatment of last resort. Heart transplantation is a therapy that is an "emergency refuge" for terminal heart failure patients whose prognosis is poor and whose lives can be saved by no other means. As donated hearts depend on the existence of bona fide donors, their number is limited. Consequently, at present heart transplantation in Japan should probably be restricted to patients with intractable cardiomyopathy. Mudge et al.\(^1\) reported that "heart transplantation has been considered in some centers to be a lower risk form of surgical intervention than a high risk revascularization procedure or valve replacement and, hence, is recommended to some patients rather than more conventional surgical interventions." However, we believe that the indications for transplantation should not be expanded in Japan in the manner described in the report by Mudge et al.\(^1\). This statement is supported by the fact that coronary artery disease in Japan is less severe than that in Europe and the USA.\(^13,14\) It is the responsibility of the medical community to monitor transplantation therapy to ensure that it is conducted correctly.

Dr Watanabe emphasizes the negative aspects of heart transplantation, but we would like to draw attention to the positive. A heart from a bona fide donor can dramatically improve the condition of an appropriate transplant recipient and enable the recipient to lead a full, productive life. Dr Watanabe\(^3\) states: "It is hardly a human right to desire the death of another so that one may live." This view is wrong in that heart transplantation is a treatment based entirely upon the goodwill of a donor during life, not upon the right to life of the recipient. There is no way that one could force the donation of organs from people who do not recognize brain death or who refuse to donate their organs in the event of brain death, or patients in a vegetative state. However, when a person is willing to donate organs in the event of brain death and patients can be saved only by heart transplantation, there is no reason to prevent the introduction of medical practices that support heart transplantation.

REFERENCES


