Heart Transplantation in Iran; A Comprehensive Single-Center Review of 15-Year Performance


Background: Heart transplantation in Iran was first performed in July 1993. Since then, Shariati Hospital, affiliated to Tehran University of Medical Sciences, has been representing the most active center of cardiac transplantation in Iran and one of the major sites in the Middle East. This is a comprehensive review of our 15-year practice registry to make a scheme of our record and achievements.

Methods: Clinical data on all consecutive transplanted patients from the Department of Cardiac Surgery, Shariati Hospital, Tehran, Iran over the last 15 years were reviewed. Descriptive and analytical statistics were extracted in regard to recipients, donors, surgical characteristics, and current status of the patients on follow-up.

Results: Totally, 90 patients were transplanted since 1993; 11, 32, and 47 in three five-year periods, respectively. The mean age of the recipients was 29.30±13.17 years. Motor-vehicle accident was the main cause of brain death of donors (48.8%). The most common indication for surgery was idiopathic dilated cardiomyopathy (75.5%). The mean survival rate has been 6.66±0.87 years. One-year and five-year survivals had a rising trend through the five-year periods. Acute allograft rejection and infection were the two major events complicating our transplants.

Conclusion: This study shows that despite a vast variety of obstacles, we have passed the primitive milestones. The number of transplants is increasing at a higher rate in recent years, and patients' survival rates and outcomes seem to be improving.

Keywords: Graft rejection • heart transplantation • survival rate • tissue and organ harvesting • tissue donors

Introduction

Heart transplantation has been the definite treatment for severe heart failure in recent decades.1,2 The first successful heart transplantation in Iran was performed in Shariati Hospital, affiliated to Tehran University of Medical Sciences, in July 1993. Since then, this center has been the major site of cardiac transplantation in the country with a record of 90 transplanted patients in a 15-year period.3 As a result of improving techniques and experiences, the number of heart transplantations is rising on a higher speed during the recent years, and the outcome seems to be more hope-giving compared with the early years.

In this study, we performed a comprehensive review of our heart transplantation registry, which includes the largest number of transplanted patients reported in Iran so far.

Patients and Methods

Records of all consecutive patients who had undergone heart transplantation at the Department of Cardiac Surgery, Shariati Hospital, Tehran, Iran...
Heart transplantation in Iran from its inception in July 1993 up to the end of June 2008 were reviewed. All operations were performed by a team of academic staff including senior heart surgeons. Data on age, sex, cause of heart failure and indication for transplantation, surgical technique, duration of intensive care unit (ICU) stay, early and late complications, immunosuppressive regimen, and current living status were gathered both totally and divided in three five-year periods. We recognize a patient to have pathologically documented acute rejection when the endomyocardial biopsy shows cellular inflammatory process of grade IIIA (grade 2R, moderate rejection) or greater according to the Billingham Standardized Cardiac Biopsy Grading accepted and released by the International Society of Heart and Lung Transplantation (ISHLT). Data from donors were also considered in regard to age, sex, and cause of brain death.

Descriptive and analytical statistics were then assessed by Statistical Package for Social Sciences (SPSS) version 15.0. The results were presented as mean±SD and charts. Early mortality (in-hospital death) was defined as death within 30 days post-transplantation. For calculation of one-year and five-year survival rates (if applicable) Kaplan-Meier survival curves were plotted by Medcalc software version 9.3.7.0 and the results were presented as mean±95% confidence intervals (CI).

## Results

### Basic characteristics

The registry was comprised of 90 consecutive transplanted patients during the defined time span. There has been an ascending trend of transplant numbers through the three five-year periods (Table 1). The main criteria for introduction of a patient into the waiting list for transplant reception were: end-stage heart failure without any other feasible medical or surgical management option, life expectancy of less than six months if untreated, and patient’s informed consent.

All 90 transplanted hearts were harvested from beating-heart, brain-dead patients. Although donor selection was made among a vast variety of the city (Tehran) hospitals by a coordinating audit team, the harvest operation was performed at only three university centers: 36 (40.0%) at Shariati Hospital, 33 (36.6%) at Imam Khomeini Hospital, and 21 (23.3%) at Masih Daneshvari Hospital. The major cause of donors’ deaths was motor-vehicle accident with a total number of 44 cases (48.8%), followed by subarachnoid hemorrhage due to brain artery aneurysm (16 cases, 17.7%), trauma with mechanisms other than motor-vehicle accident (14 cases, 15.5%), chemical/drug intoxication (seven cases, 7.7%), brain tumor (six cases, 6.6%), and other miscellaneous causes (three cases, 3.3%). Demographics of donors are presented in Table 1.

There was no significant difference between the three periods in terms of the recipients’ age ($P=0.89$), as well as of the recipients’ sex ratio ($P=0.83$). The most common cause of transplantation was idiopathic dilated cardiomyopathy (68 cases, 75.5%), followed by ischemic dilated cardiomyopathy (nine cases, 10.0%), postpartum dilated cardiomyopathy (three cases, 3.3%),

### Table 1. Basic characteristics according to the transplant periods.

<table>
<thead>
<tr>
<th></th>
<th>Total ($n=90$)</th>
<th>1st five years ($n=11$)</th>
<th>2nd five years ($n=32$)</th>
<th>3rd five years ($n=47$)</th>
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</thead>
<tbody>
<tr>
<td><strong>Donors</strong></td>
<td></td>
<td></td>
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<tr>
<td>Age (years)</td>
<td></td>
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<tr>
<td>Mean±SD</td>
<td>25.87±11.24</td>
<td>30.18±12.13</td>
<td>25.96±11.49</td>
<td>24.75±10.86</td>
</tr>
<tr>
<td>Range</td>
<td>5 – 51</td>
<td>18 – 48</td>
<td>10 – 51</td>
<td>5 – 47</td>
</tr>
<tr>
<td>Sex (male %)</td>
<td>63 (70%)</td>
<td>7 (63.6%)</td>
<td>21 (65.6%)</td>
<td>35 (74.5%)</td>
</tr>
<tr>
<td><strong>Recipients</strong></td>
<td></td>
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<tr>
<td>Age (years)</td>
<td></td>
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</tr>
<tr>
<td>Mean±SD</td>
<td>29.30±13.17</td>
<td>27.63±9.97</td>
<td>29.78±12.32</td>
<td>29.37±14.52</td>
</tr>
<tr>
<td>Range</td>
<td>1.5 – 74</td>
<td>12 – 46</td>
<td>11 – 54</td>
<td>1.5 – 74</td>
</tr>
<tr>
<td>Sex (male %)</td>
<td>63 (70%)</td>
<td>7 (63.6%)</td>
<td>22 (68.8%)</td>
<td>34 (72.3%)</td>
</tr>
<tr>
<td><strong>Procedure technique</strong></td>
<td></td>
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<tr>
<td>Orthotopic heart</td>
<td>87 (96.66%)</td>
<td>10 (90.90%)</td>
<td>30 (93.75%)</td>
<td>47 (100.00%)</td>
</tr>
<tr>
<td>Classic</td>
<td>53 (58.88%)</td>
<td></td>
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<tr>
<td>Bicaval</td>
<td>34 (37.77%)</td>
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<tr>
<td>Heterotopic heart</td>
<td>2 (2.22%)</td>
<td>1 (9.09%)</td>
<td>1 (3.12%)</td>
<td>0 (0.00%)</td>
</tr>
<tr>
<td>Heart-lung</td>
<td>1 (1.11%)</td>
<td>0 (0.00%)</td>
<td>1 (3.12%)</td>
<td>0 (0.00%)</td>
</tr>
</tbody>
</table>
3.3%), hypertrophic cardiomyopathy (three cases, 3.3%), coronary artery disease (two cases, 2.2%), restrictive cardiomyopathy (two cases, 2.2%), congenital heart disease (one case, 1.1%), Adriamycin dilated cardiomyopathy (one case, 1.1%), and dilated cardiomyopathy due to aortic insufficiency (one case, 1.1%).

The mean duration of ICU stay was 7.2±3.6 days. Baseline immunosuppressive therapy protocol in our center was a triple regimen consisting of corticosteroid (methylprednisolone), cyclosporine (Sandimmune® or Neoral®), and azathioprine (Imuran®) which were initiated at the day of surgery and continued up to the time of discharge, when the azathioprine was changed to mycophenolate mofetil (CellCept®). This triple regimen was taken for a one-year period, after which the corticosteroid would be tapered off gradually and the two remaining drugs would be continued throughout the life time. In the case of finding abnormalities in liver function test (LFT) due to use of cyclosporine, it was replaced by tacrolimus as an alternative. Acute allograft rejection was managed by a course of intravenous methylprednisolone pulse therapy. For resistant rejections, in which ejection fraction or the pathologic grade of myocardial biopsy did not improve, anti T-lymphocyte globulin (ATG) was administered as the second line.

Mortality and survival

At the time of preparation of this paper, totally 42 of all our transplanted patients were alive, representing an overall current survival of 46.6%. The mean survival has been 6.66±0.87 years. Early mortality rate of whole the 15-year period has been 21.1%. However, one-year and five-year survival rates have been 57.1±5.4% and 40.4±6.7%, respectively (Figure 1).

Five-year survival was calculated for 43 patients whose surgeries were before five years ago. Figure 2 shows the changes of early mortality, one-year survival rate, and five-year survival rate through the three predefined five-year courses.

Complications

Totally, 30.8% of the biopsy specimens showed features of overt rejection. Twenty-one patients (23.3%) had at least one episode of acute rejection in their follow-up visits, for whom pulse-therapy was initiated immediately.

Fungal infections were reported in five patients (5.5%), herpetic involvement in four (4.4%), cytomegalovirus (CMV) infection in six (6.6%), and sternal wound infection in three patients (3.3%). Sepsis occurred in three patients (3.3%), which led to death in two patients eventually.

Discussion

The first success on heart transplantation was achieved on December 3, 1967 by Christian Barnard in Cape Town, South Africa.6 That movement triggered a wave in the world of surgery toward more transplantation. Many patients for whom this operation was performed, died in the first six months.7 It was the advent of cyclosporine that made cardiac transplantation a reliable procedure that saved lives of thousands of people all over the world.8 Nowadays, heart transplantation is the treatment of choice for end-stage heart failure.1

Heart transplantation was not established in Iran due to a complex of obstacles such as absence of legal support and rules, lack of technical experience, and also nonexistence of a centralized recipient-donor filing and matching system. In the summer of 1993, our cardiac surgery team under the leadership of Dr. Mohammad-Hossein Mandegar, took the risk of the first heart transplantation in Iran and accomplished it in Shariati Hospital. This was continued by more surgeries in some academic centers in the country.9

The number of heart transplants has been rising at a much higher rate during the recent years rather than the first decade. It could be partly due to the approval of the “Organ Transplantation and Brain Death Law” by the Iranian Parliament in 2000.10 On the other hand, as a result of better and faster communication facilities, finding the best-choice recipient in the huge waiting list and donor-recipient matching has become easier. Although

Figure 1. Kaplan-Meier survival curve for the whole registry from July 1993 through June 2008.
people’s culture and common sense have been improved in this regard, there should be more serious efforts, especially by the mass media and educational centers to help them accept the fact and process of organ donation.

Head trauma (including motor-vehicle accident) was the leading cause of our donors’ death followed by cerebrovascular events. This is exactly the same as the entire International Society for Heart and Lung Transplantation (ISHLT) registry record and also as the Asia-Australia record.11 Although the proportion of head trauma as a cause of donors’ brain death is declining all over the world during the recent years, unfortunately this does not seem to be true in our country.12,13

Idiopathic cardiomyopathy is the number one cause of surgery among the others. That conforms to the demographics of other countries,11 but it is different from the list of patients nominated for heart transplantation in which ischemic cardiomyopathy is the major etiology of cardiac dysfunction. It can be resulted from the great number of ischemic old patients who die awaiting transplantation.14

The evaluated mortality and survival rates (early, one-year, and five-year) are inferior to the overall estimated rates of the entire ISHLT territory.11,15 This fact may be resulted from our limitations in finding the best matched donors in our awaiting patients. In addition, the process of continuous follow-up for transplant patients has its own problems and barriers in Iran such as connection failure between the patient and medical center, poor socioeconomic and cultural status of patients, and high expense of medical equipment and services for a desirable follow-up of this group. Nevertheless, it seems that there has been a promising trend toward better outcomes in recent years as a result of improvement in all the factors mentioned above. Although statistically insignificant ($P=0.83$), fortunately early mortality rate dropped during the second five-year in comparison with the first period, extended with a mild increase into the third period. Both one-year and five-year survival rates had a raising trend between the second and first periods, as well as third and second periods for the one-year survival rate ($P=0.87$ for one-year survival and $P=0.56$ for five-year survival). Early mortality rates within the first and second five-year periods are compatible with those published earlier as a histopathologic investigation from the Department of Pathology,16 but it seems that one-year and five-year survival rates were overestimated in the old study, probably because the authors did not have access to the comprehensive heart transplantation database of the hospital.

Allograft rejection and infections are the two most important and major complications after heart transplantation.2 Acute allograft rejection was approved by endomyocardial biopsy in 23.3% of the patients, representing a comparable rate to regional and international statistics. However, clinically diagnosed rejection should be added to the above rate to result in a true percentage of patients encountered and treated for at least one episode of acute rejection following the transplantation.

This study shows that despite a vast variety of obstacles in the hard court of heart transplantation, we have passed the primitive milestones. Of course, our experiences have made a reliable scaffold for stepping through and achieving better outcome in the future.
Acknowledgment

The authors would like to appreciate all surgeons and academic staff taking trouble to make heart transplantation accessible and of high-quality in Iran. We also would like to acknowledge Mrs. Fatemeh Ahmadi who has been the coordinator of the waiting list and interhospital connections for selection of donors and recipients throughout the 15 years.

References

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