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REVIEW

Bone marrow and stem cell transplantation: Malaysian experience

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Malaysia conducted the first BMT in the country in 1987. Since then, there have been 1155 transplantations performed in a total of eight transplant centres. A majority of the transplantations were allogeneic, including myeloablative and nonmyeloablative. A vast majority of donors are HLA identical siblings. The mean age of transplanted patients was 26 years. The major reason for transplantation was hematological malignancies. The overall survival was 60% for allogeneic transplantation and 52% for autologous transplantation. The most common cause of death in transplanted patients was the underlying disease followed by infection-related complications. Currently, the government is expanding the existing public cord blood bank as well as the local donor registry.
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The first BMT in this country was conducted on a paediatric patient in 1987 at University Malaya Medical Centre (UMMC; previously known as University Hospital) in Kuala Lumpur, Malaysia. In 1993, the first adult transplantation was performed also at the same hospital. Since then, more BMT centres in Malaysia have been set up; currently, there are totally eight such transplant centres, two of which are government owned, four are private and the remaining two are university-based. Out of the total of eight, three are currently performing paediatric transplantation and almost all hospitals conduct allogeneic transplantation.

The total number of transplantations performed until 2006 was 1155, where the majority of these transplantations were allogeneic (808). Autologous SCT started in 1989, and as of the end of 2006 the total number transplanted were 347. After 1999, the number of transplantations per year has increased significantly. The annual number of transplantations performed ranges from 100 to 150. The calculated new transplant rate per million population in Malaysia until the end of 2005 is shown in Figure 1, which shows a spike after the year 1999 with the opening of more centres.

A majority of the patients are local. There is a aslight female preponderance (48% male subjects, 52% female subjects). The largest ethnic group transplanted was the Chinese (48%) followed by the Malays (37%) and the Indians (7%). The age of transplantation ranges from 1 month to 70 years. The mean age of new transplant patients in 2005 was 26 ± 16 years. Fifty-nine per cent of the transplantations were performed in patients under the age of 19 years. Twenty-seven per cent were transplanted in those in the age group of 20–39 years and 14% in those under 60 years. Only five patients older than 60 years were transplanted, and all are autologous SCT. The young median age reflects the paediatric bias in the registry, as transplantation in Malaysia was first started in paediatric patients.

The predominant transplantation performed is sibling-related transplantation (70.7%), with the remaining autologous. Seventy-nine per cent of the transplant sources were from PBSCs. Cord blood transplantation was first performed at UMMC in 1997 in a paediatric patient, and an unrelated transplantation in 1997 was also performed at the same hospital. The first adult unrelated transplantation was started in 2006, and currently two centres are performing adult unrelated transplantations. Thus far, three adult unrelated transplantations have been performed, with one of the unrelated sources of stem cell being cord blood. An overview of types of transplant is illustrated in Figure 2.

A majority of allogeneic transplantations are for malignant disorders. Most are hematological malignancies; AML being the most common disease (24%), followed by CML (11%) and ALL (11%). Other nonmalignant hematological disorders include thalassemia major (10%) and aplastic anemia (10%). However, with the availability of imatinib, CML is now no longer one of the most common diseases for transplantation. Lymphoma remains the commonest disease for autologous SCT.

The major cause of death from transplantation is relapse and underlying disease. Sepsis is the second commonest cause of death. Up to the end of 2006, 41.4% patients who had undergone transplantation survived. The overall

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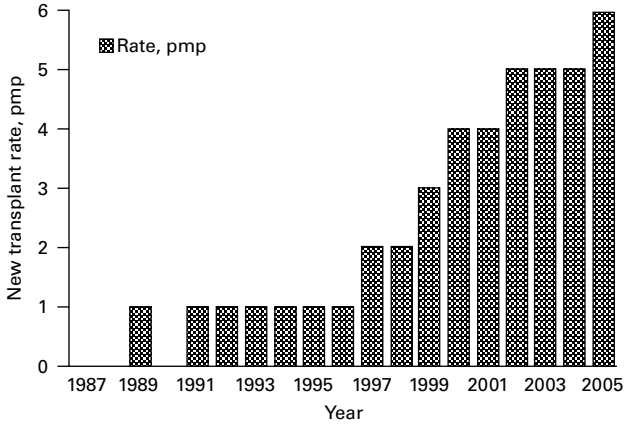

Figure 1 New transplant rate per million population (1987–2005).

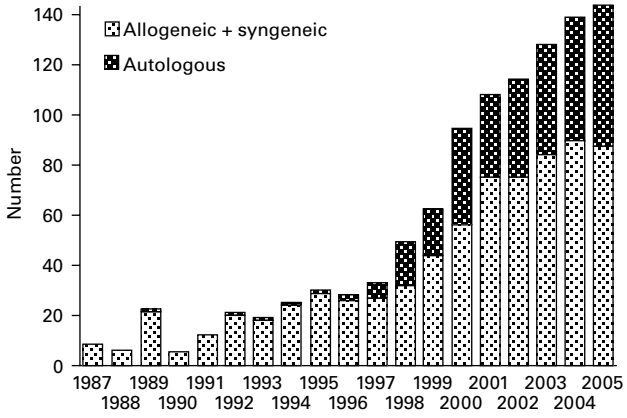

Figure 2 Type of transplant during 1987–2005.

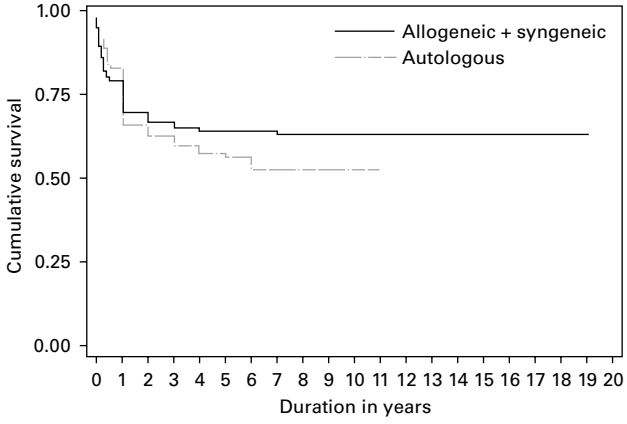

Figure 3 Patient survival by type of transplant.

survival of patients who had allogeneic transplantation was about 60% and that for those who had autologous transplantation was about 52% (Figure 3). Patient's survival by year of transplant is shown in Figure 4. The reason for better survival prior to 1992 was due to the younger transplanted population. There was no difference in survival rate in female and male patients.

Disease-free survival (DFS) of more than 60% was seen in ALL patients and is most likely due to the paediatric

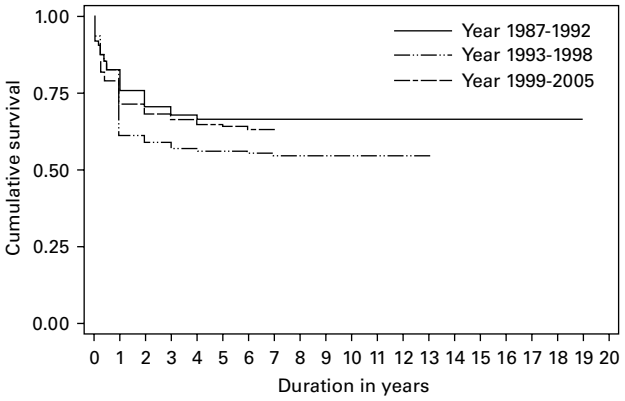

Figure 4 Patient survival by year of transplant.

population. The DFS for AML patients at 10 years is about 60% for allogeneic transplantation and less than 40% for autologous transplantation. This is worse in adults, which is approximately 30% at 10 years. For patients who were transplanted for thalassemia (the majority a younger population), DFS is 70% at 10 years. DFS for CML patients is more than 50% at 10 years. DFS for aplastic anaemia is more than 50% at 10 years. The DFS for allogeneic transplantation is better reported in non-Hodgkin lymphoma (90%), and is 50% at 5 years for autologous transplantation. The number of allogeneic transplantation in non-Hodgkin lymphoma is low, and hence the above data are difficult to interpret.

In 2005, the causes of death due to underlying disease were 39%, infection 25% and GVHD 17%.

Of special interest in Malaysia was the study of the response of each of the different ethnic groups to transplantation. Therefore, a small study was done with the collaboration of two major transplant hospitals (UMMC and Ampang Hospital). A total of 146 adult patients who underwent HLA-matched related allogeneic transplantations were studied from 1999 to 2006. The incidence of acute GVHD was reported to be 63%, with grades II–IV occurring in 50% of the patients. Patient and donor age were found to be significant factors in the development of acute GVHD ($P = 0.04$ and 0.02, respectively). There were no significant ethnic differences, although Indians seemed to have a higher incidence of acute GVHD (86%) compared to the Chinese and Malays (59% for both). However, this is not statistically significant and is most likely due to the relatively small number of Indian patients in the study population. We found no increase in the acute GVHD rate in PBSC patients and BM as a source of stem cells.

Another study presented as a poster at ABMT this year looked at one centre in Kuala Lumpur (Ampang Hospital). They studied 106 adult patients (52% Malays, 30% Chinese and 9% Indians). The major source of stem cells was BM (80%). The median age was 23 years. They found 5-year overall survival to be 60% with event-free survival of 50%. Transplant-related mortality at day 100 is 16%. Extensive chronic GVHD is seen in 34% of Malays, 18% of Chinese and 38% of Indians. The most common cause of death in Malays is GVHD (52%), whereas relapse/underlying disease is the most common cause of death in

the Chinese and Indians (60 and 80%, respectively). Again, the result was not statistically significant owing to the small number of patients.

Currently, the cost of transplantation varies between centres, ranging from RM 500 to RM 100 000, depending on the centres for allogeneic transplantation. The cost of autologous SCT is cheaper, ranging from RM 500 to RM 50 000. The problem faced by the patients is mainly financial, as only two government hospitals provide transplant services on a subsidized basis. Unfortunately, the waiting list is relatively long. For the universities, there are social welfare and other non-government organizations that will assist with fund raising for patients who require financial assistance.

Two of the centres participated in the international registry, one being the European Bone Marrow Transplant Registry (EBMT) and the other the International Bone Marrow Transplant Registry (IBMTR).

Research activities are generally not big. Currently, there are a few ongoing trials that looked at the graft versus host rate in the multi-ethnic population and established the incidence as well as the possible causes.

Most recently, a national transplant registry has also recently been set up by the Malaysian Society of Transplantation and the Ministry of Health Malaysia. The second report of the national transplant registry is now currently available at http://www.mst.org.my.

There is currently a campaign under way by the government to initiate national public cord blood banking. To date, the country has only 800 public cord blood in storage and is thus looking at improving and expanding the services. The government is also promoting the expansion of a national blood and marrow registry. The Malaysian Marrow Donor Registry was launched in December 1999 and is a joint project with the Ministry of Health, Institute Medical Research and the National Cancer Council. To date, there are more than 10 000 donors registered, of which most have been typed. The target was to obtain at least 40 000 registered donors.

The challenges ahead will be the cost involved especially in unrelated SCT, minimizing the risk of transplant-related mortality, especially focusing on the multiracial groups, and to further establish the local registry, both cord blood and marrow.

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Conflict of interest

Dr Gin Gin Gan declared no financial interests.