

CHAPTER 3

HEART AND LUNG TRANSPLANTATION

Editors:

Mr Mohamed Ezani Md. Taib
Dato' Dr David Chew Soon Ping
Dr Ashari Yunus

Expert Panel:

Tan Sri Dato' Dr Yahya Awang (Chair)
Mr Mohamed Ezani Md. Taib (Co-chair)
Datin Dr Aziah Ahmad Mahayuddin
Dr Aizai Azan Abdul Rahim
Dr Ashari Yunus
Dato' Dr David Chew Soon Ping
Dr Hamidah Shaban

Contents

3.0 Introduction

3.1 Stock and Flow of Heart Transplantation

3.2 Recipients' Characteristics

- Demographics and Clinical Status
 - Primary Diagnosis

3.3 Transplant Practices

- Type of Transplant
- Immunosuppressive Therapy and Other Medications
- Duration of Waiting Time on the Waiting List

3.4 Transplant Outcomes

- Post Transplant Complications
 - Patient Survival
 - Causes of Death

List of Tables

Table 3.1.1: Stock and Flow of Heart Transplantation, 1997-2006.....	60
Table 3.1.2: Stock and Flow of Lung Transplantation, 2005-2006.....	60
Table 3.2.1: Distribution of Patients by Gender, 1997-2006.....	61
Table 3.2.2: Distribution of Patients by Ethnic Group, 1997-2006.....	61
Table 3.2.3: Distribution of Patients by Age, 1997-2006.....	61
Table 3.2.4: Distribution of Patients by Primary Diagnosis, 1997-2006.....	61
Table 3.3.1: Distribution of Patients by Heart Procedure, 1997-2006.....	63
Table 3.3.2: Distribution of Patients by Immunosuppressive Used, 1997-2006.....	63
Table 3.3.3: Immunosuppressive Used at Time of Last Follow-up up to 2006.....	64
Table 3.3.4: Duration of Waiting Time on Waiting List, 1997-2006.....	64
Table 3.4.1: Post Transplant Events at Last Follow-up up to 2006.....	65
Table 3.4.2: Post Transplant Malignancies at Follow-up up to 2006.....	66
Table 3.4.3: Non-compliance at Follow-up up to 2006.....	66
Table 3.4.4: Patient Treated for Rejection at Follow-up up to 2006.....	66
Table 3.4.5: Distribution of Patients by Time of Deaths, 1997-2006.....	67
Table 3.4.6: Patient Survival, 1997-2006.....	67
Table 3.4.7: Cause of Death at Discharge, 1997-2006.....	68
Table 3.4.8: Cause of Death at Follow-up, 1997-2006.....	68

List of Figures

Figure 3.1.1: Stock and Flow of Heart Transplantation, 1997-2006.....	60
Figure 3.4.6: Patient Survival, 1997-2006.....	67

3.0 INTRODUCTION

The first heart transplant in Malaysia was carried out at Institut Jantung Negara (IJN) Kuala Lumpur in December 1997. The main limitation to the performance of heart transplants has been the lack of donor organs. Since 2004, IJN in collaboration with Institut Perubatan Respiratori (IPR) of the Ministry of Health has been preparing to perform lung transplantation as well as heart lung transplant and the first lung transplant was carried out in December 2005.

The rest of the report that follows will review the results of heart and lung transplantation in Malaysia till end of 2006.

Only 1 heart transplant and 1 double lung transplant were carried out in 2006.

3.1 STOCK AND FLOW

Table 3.1.1: Stock and Flow of Heart Transplantation, 1997-2006

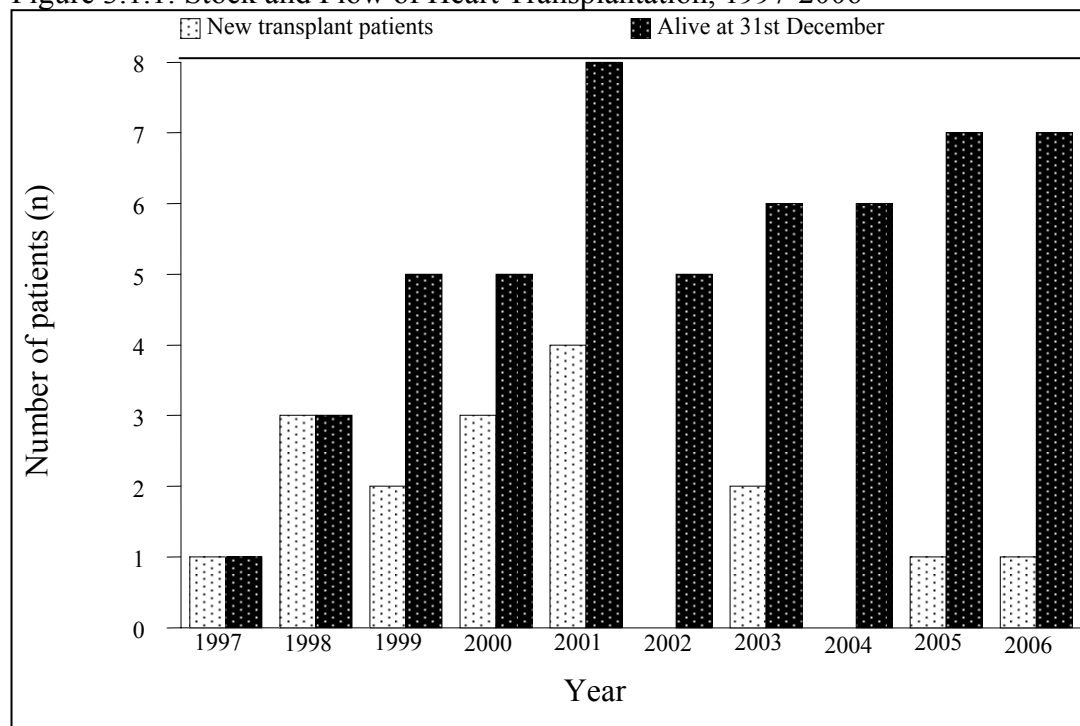
Year	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006
New transplant patients	1	3	2	3	4	0	2	0	1	1
Deaths	0	1	0	3	1	3	1	0	0	1
Retransplanted	0	0	0	0	0	0	0	0	0	0
Lost to follow up	0	0	0	0	0	0	0	0	0	0
Alive at 31 st December	1	3	5	5	8	5	6	6	7	7

N.B. There was no heart transplants carried out in 2004

Table 3.1.2: Stock and Flow of Lung Transplantation, 2005-2006

Year	2005	2006
New transplant patients	1	1
Deaths	0	1
Retransplanted	0	0
Lost to follow up	0	0
Alive at 31 st December	1	1

Figure 3.1.1: Stock and Flow of Heart Transplantation, 1997-2006



3.2 RECIPIENTS' CHARACTERISTICS

A total of 17 heart transplants have been carried out from 1997 to 2006. Two thirds of the recipients were males and over half were Indians. The mean age of recipients was 36 years (range 13-55 years) (Table 3.2.3). The aetiology of heart failure is as listed in Table 3.2.4. Ischaemic cardiomyopathy was the commonest aetiology followed by dilated cardiomyopathy.

Table 3.2.1: Distribution of Patients by Gender, 1997-2006

Year	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	TOTAL
Gender	No.	No.	No.	No.	No.	No.	No.	No.	No.	No.	No.
Male	1	3	0	2	2	0	2	0	1	1	12
Female	0	0	2	1	2	0	0	0	0	0	5
TOTAL	1	3	2	3	4	0	2	0	1	1	17

Table 3.2.2: Distribution of Patients by Ethnic Group, 1997-2006

Year	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	TOTAL
Ethnic group	No.	No.	No.	No.	No.	No.	No.	No.	No.	No.	No.
Malay	0	0	1	1	2	0	0	0	1	0	5
Chinese	0	0	0	1	0	0	1	0	0	0	2
Indian	1	3	1	1	2	0	1	0	0	1	10
TOTAL	1	3	2	3	4	0	2	0	1	1	17

Table 3.2.3: Distribution of Patients by Age, 1997-2006

Year	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	TOTAL
Age, years	No.	No.	No.	No.	No.	No.	No.	No.	No.	No.	No.
0-19	0	0	2	1	1	0	0	0	1	0	5
20-39	0	2	0	0	0	0	0	0	0	0	2
40-59	1	1	0	2	3	0	2	0	0	1	10
>=60	0	0	0	0	0	0	0	0	0	0	0
TOTAL	1	3	2	3	4	0	2	0	1	1	17
Mean	51	40	16	37	38	-	46	-	15	44	36
SD	-	9	1	22	17	-	8	-	-	-	16
Median	51	37	16	44	43	-	46	-	15	44	40
Minimum	51	33	15	13	14	-	40	-	15	44	13
Maximum	51	50	16	55	54	-	52	-	15	44	55

Age=date of transplant-date of birth

Table 3.2.4: Distribution of Patients by Primary Diagnosis, 1997-2006

Year	97	98	99	00	01	02	03	04	05	06	TOTAL
Primary diagnosis	No.	No.	No.	No.	No.	No.	No.	No.	No.	No.	No.
Ischaemic Cardiomyopathy	1	3	0	1	1	0	2	0	0	1	9
Idiopathic Dilated Cardiomyopathy	0	0	2	1	2	0	0	0	1	0	6
Restrictive Cardiomyopathy	0	0	0	0	0	0	0	0	0	0	0
End Stage Valvular Heart Disease	0	0	0	0	1	0	0	0	0	0	1
Hypertrophic Cardiomyopathy	0	0	0	1	0	0	0	0	0	0	1
Others	0	0	0	0	0	0	0	0	0	0	0
TOTAL	1	3	2	3	4	0	2	0	1	1	17

Two lung transplantations were carried out from 2005 to 2006. Both the recipients were Indian males, age 56 year old and 43 year old. Both had idiopathic pulmonary fibrosis. The first patient underwent single lung transplantation and the second patient underwent double lung transplantation.

3.3 TRANSPLANT PRACTICES

The majority of heart transplant patients received orthotopic biatrial and only 2 had orthotopic bicaval procedure (Table 3.3.1).

At the time of transplant all patients received methylprednisolone followed by prednisolone. All also received cyclosporine and azathioprine, but in 3 patients, azathioprine was later replaced by mycophenolate mofetil (Table 3.3.2).

All surviving heart transplant recipients were on Neoral[®]. Only 2/7 patients were maintained on steroids and azathioprine, while 5/7 patients were on mycophenolate mofetil (Table 3.3.3).

Four of the recipients were transplanted when they presented with severe heart failure, before they were formally listed on the waiting list. The other 13 recipients were transplanted from the waiting list and their average waiting time was 9 months (Table 3.3.4). The patient who had heart transplant in 2005 received a Thoratec implantable Ventricular Assist Device (VAD) support for 4.5 months as a bridge to eventual transplant.

The 2 lung transplant patients received Neoral[®] and Mycophenolate Mofetil as immunosuppressive agents.

Table 3.3.1: Distribution of Patients by Heart Procedure, 1997-2006

Year	97	98	99	00	01	02	03	04	05	06	TOTAL
Heart Procedure	No.	No.	No.	No.	No.	No.	No.	No.	No.	No.	No.
Orthotopic Bicaval	1	1	0	0	0	0	0	0	0	0	2
Orthotopic Traditional	0	2	2	3	4	0	2	0	1	1	15
Heterotopic	0	0	0	0	0	0	0	0	0	0	0
TOTAL	1	3	2	3	4	0	2	0	1	1	17

Table 3.3.2: Distribution of Patients by Immunosuppressive Used, 1997-2006

Year	97	98	99	00	01	02	03	04	05	06	Total
Type of immunosuppressive	No.	No.	No.	No.	No.	No.	No.	No.	No.	No.	No.
Steroids											
Prednisolone	1	3	2	3	4	0	1	0	1	0	15
Methylprednisolone	1	3	2	3	4	0	2	0	1	1	17
Calcineurin Inhibitors											
Neoral [®]	1	3	2	3	4	0	1	0	1	0	15
Antimetabolites											
Azathioprine (AZA)	1	3	2	3	4	0	2	0	0	1	16
Mycophenolate Mofetil (MMF)	0	0	0	0	1	0	1	0	1	0	3
TOTAL patients at notification	1	3	2	3	4	0	2	0	1	1	17

Table 3.3.3: Immunosuppressive Used at Time of Last Follow-up up to 2006

Year of follow up*	2004	2005	2006
Type of immunosuppressive	No.	No.	No.
Steroids			
Prednisolone	1	3	2
Methylprednisolone	0	0	0
Calcineurin Inhibitors			
Neoral [®]	1	6	7
Antimetabolites			
Azathioprine (AZA)	1	3	2
Mycophenolate Mofetil (MMF)	3	3	5
TOTAL patients at follow-up	6	6	7

*Data according to year of follow up of transplanted patients

Table 3.3.4: Duration of Waiting Time on Waiting List, 1997-2006

Year	97	98	99	00	01	02	03	04	05	06	TOTAL
Duration (months)*	No.	No.	No.	No.	No.	No.	No.	No.	No.	No.	No.
<5	0	2	1	0	1	0	1	0	0	0	5
5-<10	1	0	1	0	1	0	0	0	1	0	4
10-<15	0	0	0	1	0	0	0	0	0	1	2
15-<20	0	0	0	1	0	0	0	0	0	0	1
20-<25	0	0	0	0	0	0	0	0	0	0	0
25-<30	0	0	0	0	0	0	0	0	0	0	0
30-<35	0	0	0	0	0	0	0	0	0	0	0
35-<40	0	0	0	0	0	0	1	0	0	0	1
TOTAL	1	2	2	2	2	0	2	0	1	1	13
Mean	6	2	4	15	5	-	20	-	9	10	9
SD		0	1	6	5	-	25	-	-	-	10
Median	6	2	4	15	5	-	20	-	9	10	6
Minimum	6	2	3	10	1	-	2	-	9	10	1
Maximum	6	2	5	19	8	-	37	-	9	10	37

*Duration=date of transplant-date added to wait list

3.4 TRANSPLANT OUTCOMES

Hypertension and hyperlipidaemia requiring drug treatment was common post transplant with high incidence in recipients (Table 3.4.1). Two patients were treated for rejection out of the 11 patients who were discharged from hospital (Table 3.4.4).

Six (35%) of the heart transplant recipients died in hospital following transplant (Table 3.4.5). One died of hyperacute graft rejection and another from graft failure. The other 4 died of multiorgan failure with septicaemia (Table 3.4.7).

Four patients had succumbed to late deaths after their heart transplant. One of the deaths occurred within a year (sudden death, cause unclear), while the other 3 deaths occurred more than a year post transplant. The 1 year Kaplan Meier patient survival rate was 59% (Fig 3.4.6). One patient died of small cell lung cancer (he was a smoker, but stopped before his transplant). Another patient died suddenly but autopsy showed cardiac allograft rejection which was due to non-compliance to immunosuppression. Another death in a peripheral hospital was classified as severe bleeding but the actual cause of death was unclear (Table 3.4.8).

The first lung transplant patient survived with good quality of life. Unfortunately, the second patient succumbed 8 weeks after transplantation with cause of death due to Cytomegalovirus infection.

Table 3.4.1: Post Transplant Events at Last Follow-up up to 2006

Year of transplant*	97	98	99	00	01	02	03	04	05	06	TOTAL
Type of post transplant events	No.	No.	No.	No.	No.	No.	No.	No.	No.	No.	No.
Drug-Treated Hypertension	1	2	2	1	3	0	1	0	1	0	11
Bone Disease (Symptomatic)	1	0	0	0	1	0	0	0	0	0	2
Chronic Liver Disease	0	0	0	0	0	0	0	0	0	0	0
Cataracts	0	0	0	0	0	0	0	0	0	0	0
Diabetes	1	2	0	0	0	0	1	0	0	0	4
Renal Dysfunction	1	0	0	0	1	0	0	0	0	0	2
Stroke	0	0	0	0	0	0	0	0	0	0	0
Drug-Treated Hyperlipidaemia	1	2	2	1	3	0	1	0	1	0	11
TOTAL patients at follow-up	1	2	2	1	3	0	1	0	1	0	11

*Data according to year of transplant of patient

Table 3.4.2: Post Transplant Malignancies at Follow-up up to 2006

Year of transplant*	97	98	99	00	01	02	03	04	05	06	TOTAL
Type of post transplant malignancies	No.	No.	No.	No.	No.	No.	No.	No.	No.	No.	No.
Recurrence of pre-transplant tumour	0	0	0	0	0	0	0	0	0	0	0
De Novo solid tumour	1	0	0	0	0	0	0	0	0	0	1
De Novo lymphoproliferative disorder	0	0	0	0	0	0	0	0	0	0	0
Skin	0	0	0	0	0	0	0	0	0	0	0
TOTAL patients at follow-up	1	2	2	1	3	0	1	0	1	0	11

*Data according to year of transplant of patient

Table 3.4.3: Non-compliance at Follow-up up to 2006

Year of transplant*	97	98	99	00	01	02	03	04	05	06	TOTAL
Non-compliance during follow-up	No.	No.	No.	No.	No.	No.	No.	No.	No.	No.	No.
• Yes	0	0	1	0	0	0	0	0	0	0	1
• No	1	2	1	1	3	0	1	0	1	0	10
TOTAL patients at follow-up	1	2	2	1	3	0	1	0	1	0	11
<i>Areas of non-compliance:</i>											
• Immunosuppression medication	0	0	1	0	0	0	0	0	0	0	1
• Patient unable to afford immunosuppression medications	0	0	1	0	0	0	0	0	0	0	1
• Other medication	0	0	0	0	0	0	0	0	0	0	0
• Other therapeutic regimen	0	0	0	0	0	0	0	0	0	0	0
TOTAL patients with noncompliance	0	0	1	0	0	0	0	0	0	0	1

*Data according to year of transplant of patient

Table 3.4.4: Patient Treated for Rejection at Follow-up up to 2006

Year of transplant*	97	98	99	00	01	02	03	04	05	06	TOTAL
Patient treated for rejection	No.	No.	No.	No.	No.	No.	No.	No.	No.	No.	No.
• Yes	0	1	0	0	0	0	0	0	0	0	1
• No	1	1	2	1	3	0	1	0	1	0	10
TOTAL patients at follow-up	1	2	2	1	3	0	1	0	1	0	11
<i>Number of rejection events</i>											
• 1	0	1	0	0	0	0	0	0	0	0	1
• 2	0	0	0	0	0	0	0	0	0	0	0
• 3	0	0	0	0	0	0	0	0	0	0	0
TOTAL patients with rejection	0	1	0	0	0	0	0	0	0	0	1

*Data according to year of transplant of patient

Table 3.4.5: Distribution of Patients by Time of Deaths, 1997-2006

Year of discharge	97	98	99	00	01	02	03	04	05	06	TOTAL
Time of deaths*	No.	No.	No.	No.	No.	No.	No.	No.	No.	No.	No.
<3 months (at discharge)	0	1	0	2	0	1	1	0	0	1	6
3-<6 months	0	0	0	0	0	0	0	0	0	0	0
6 months-1 year	0	0	0	0	0	1	0	0	0	0	1
>1 year	0	0	0	1	1	1	0	0	0	0	3
TOTAL patients who died	0	1	0	3	1	3	1	0	0	1	10

*Time=Date of death–date of transplant

Table 3.4.6: Patient Survival, 1997-2006

Year of Transplant	1997-2005	
Interval	% Survival	SE
6 months	65	12
1 year	59	12
2 year	47	12
3 year	40	12

SE=standard error

Duration =date follow up-date transplant, if alive at discharge

=date of discharge-date of transplant, if dead at discharge

Figure 3.4.6: Patient Survival, 1997-2006

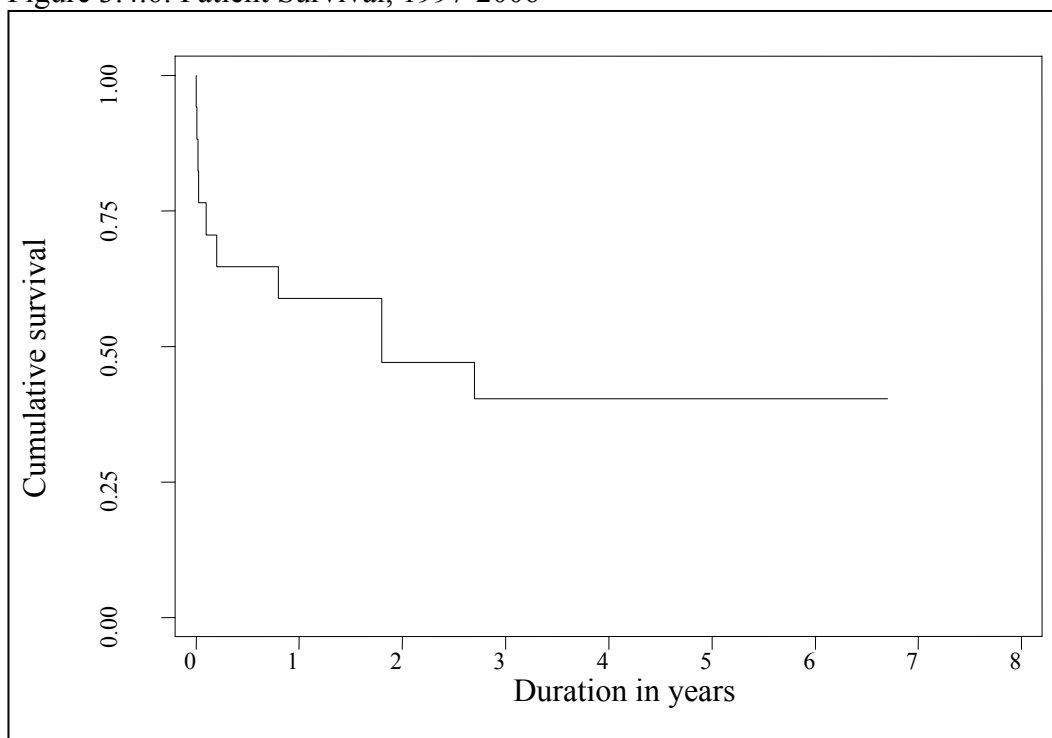


Table 3.4.7: Cause of Death at Discharge, 1997-2006

Year	97	98	99	00	01	02	03	04	05	06	TOTAL
Cause of death	No.	No.	No.	No.	No.	No.	No.	No.	No.	No.	No.
Hyperacute rejection	0	0	0	0	0	0	1	0	0	0	1
Multi organ failure	0	0	0	1	0	0	0	0	0	0	1
Respiratory failure secondary to septicaemia	0	0	0	0	0	1	0	0	0	0	1
Respiratory failure, renal function and liver failure, ARDS, septicaemia	0	0	0	1	0	0	0	0	0	0	1
Septicaemia, multiorgan failure	0	1	0	0	0	0	0	0	0	0	1
Graft failure	0	0	0	0	0	0	0	0	0	1	1
TOTAL patients who died at discharge	0	1	0	2	0	1	1	0	0	0	6

Table 3.4.8: Cause of Death at Follow-up, 1997-2006

Year	97	98	99	00	01	02	03	04	05	06	TOTAL
Cause of death	No.	No.	No.	No.	No.	No.	No.	No.	No.	No.	No.
Severe bleeding	0	0	0	0	0	1	0	0	0	0	1
Lung cancer, small cell type, septicaemia, bronchopneumonia	0	0	0	1	0	0	0	0	0	0	1
Rejection due to non-compliance	0	0	0	0	1	0	0	0	0	0	1
Unknown	0	0	0	0	0	1	0	0	0	0	1
TOTAL patients who died at follow-up	0	0	0	1	1	2	0	0	0	0	4