CHAPTER 4

LIVER TRANSPLANTATION

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4.0 INTRODUCTION

Liver transplantation is currently a universally accepted definitive treatment for end stage liver disease. Unfortunately it is a victim of its own success and its further development is being hindered by a marked shortage of cadaveric organs for transplant. The critical shortage of cadaveric organs in Malaysia has led surgeons to source organs from living donors for paediatric cases.

In Malaysia, the first liver transplant was done in Subang Jaya Medical Centre in 1995. In view of the resource limitation, liver transplantation only became available in the public hospital system in 2002. The first liver transplant was undertaken in Selayang Hospital on 10th April 2002.

4.1 STOCK AND FLOW

The number of liver transplants performed from 1993 to 2004 is 75. 61 (81%) were performed locally and 14 (19%) were performed at overseas centres.

Table 4.1.1: Stock and Flow of Liver Transplantation, 1993-2004

Year	93	94	95	96	97	98	99	00	01	02	03	04
New transplant patients	1	1	8	13	3	2	8	3	5	10	5	16
Deaths	0	0	3	4	2	0	4	1	2	5	1	5
Retransplant	0	0	0	0	0	0	0	0	0	0	0	0
Lost to follow up	0	0	0	0	0	0	0	1	0	1	0	2
Functioning graft at 31st December	1	2	7	16	17	19	23	24	27	31	35	44

Figure 4.1.1: Stock and Flow of Liver Transplantation, 1993– 2004

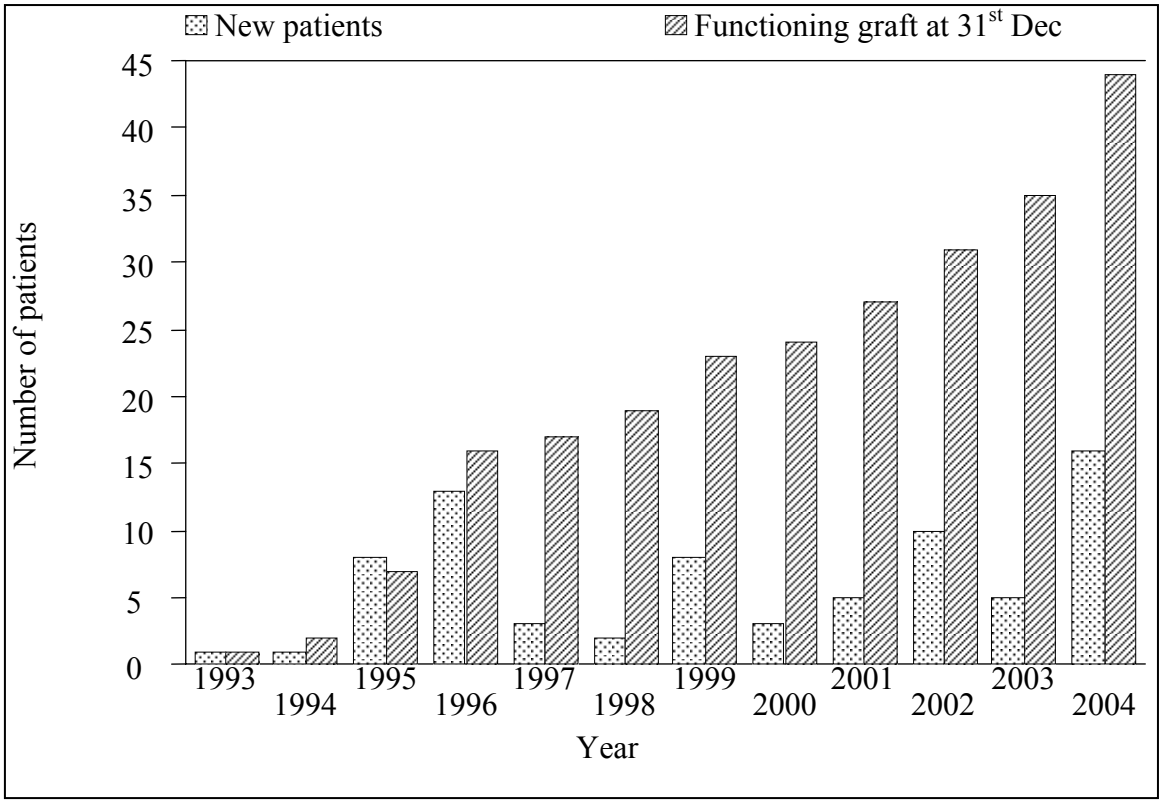

Table 4.1.2: Place of Transplant, 1993-2004

Year	93	94	95	96	97	98	99	00	01	02	03	04	TOTAL
	No.	No.	No.	No.	No.	No.	No.	No.	No.	No.	No.	No.	No.
Local	0	0	8	10	1	1	8	3	5	9	2	14	61
Overseas	1	1	0	3	2	1	0	0	0	1	3	2	14
TOTAL	1	1	8	13	3	2	8	3	5	10	5	16	75

Table 4.1.3: Centres for Liver transplantation, 1993-2004

Year	93	94	95	96	97	98	99
Centre	No.	No.	No.	No.	No.	No.	No.
Subang Jaya Medical Centre	0	0	8	10	1	1	8
Selayang Hospital	0	0	0	0	0	0	0
Australia	1	0	0	3	1	0	0
National University Hospital, Singapore	0	0	0	0	1	1	0
Kings College Hospital, UK	0	1	0	0	0	0	0
Tianjin, China	0	0	0	0	0	0	0
Asian Centre for Liver Disease & Transplantation, Singapore	0	0	0	0	0	0	0
TOTAL	1	1	8	13	3	2	8

Year	00	01	02	03	04	TOTAL
Centre	No.	No.	No.	No.	No.	No.
Subang Jaya Medical Centre	3	5	6	2	7	51
Selayang Hospital	0	0	3	0	7	10
Australia	0	0	0	0	0	5
National University Hospital, Singapore	0	0	0	0	0	2
Kings College Hospital, UK	0	0	0	0	0	1
Tianjin, China	0	0	0	1	1	2
Asian Centre for Liver Disease & Transplantation, Singapore	0	0	1	2	1	4
TOTAL	3	5	10	5	16	75

Table 4.1.4: Distribution of Centres of Follow-up of Transplant Recipients, 2004

Centre	No.	%
Number of patient with functioning graft at 31st December 2004	44	100
Kuala Lumpur Hospital	5	11
SJMC	29	66
Selayang Hospital	8	18
Singapore	1	2
UMMC	4	9

*There are 3 patients who are on follow-up in 2 centres

4.2 RECIPIENTS' CHARACTERISTICS

42 (56%) were males and 33 (44%) were females. The ethnic distribution of the liver transplant recipients are as follows: Chinese 40 (53%), Malays 29 (38%), Indians 4 (6%), Others 2 (3%).

63 (84%) of the transplant recipients were between 1 and 9 years of age at the time of transplant. Biliary atresia was the primary liver disease in 57 (76%) of the recipients. The indications for transplantation in these patients were failure to thrive with growth retardation and poor liver function.

Table 4.2.1: Gender distribution, 1993-2004

Year	**93**	**94**	**95**	**96**	**97**	**98**	**99**	**00**	**01**	**02**	**03**	**04**	**TOTAL**
Gender	No.	No.	No.	No.	No.	No.	No.	No.	No.	No.	No.	No.	No.
Male	0	0	6	5	2	1	3	1	2	7	5	10	42
Female	1	1	2	8	1	1	5	2	3	3	0	6	33
TOTAL	1	1	8	13	3	2	8	3	5	10	5	16	75

Figure 4.2.1: Gender distribution, 1993-2004

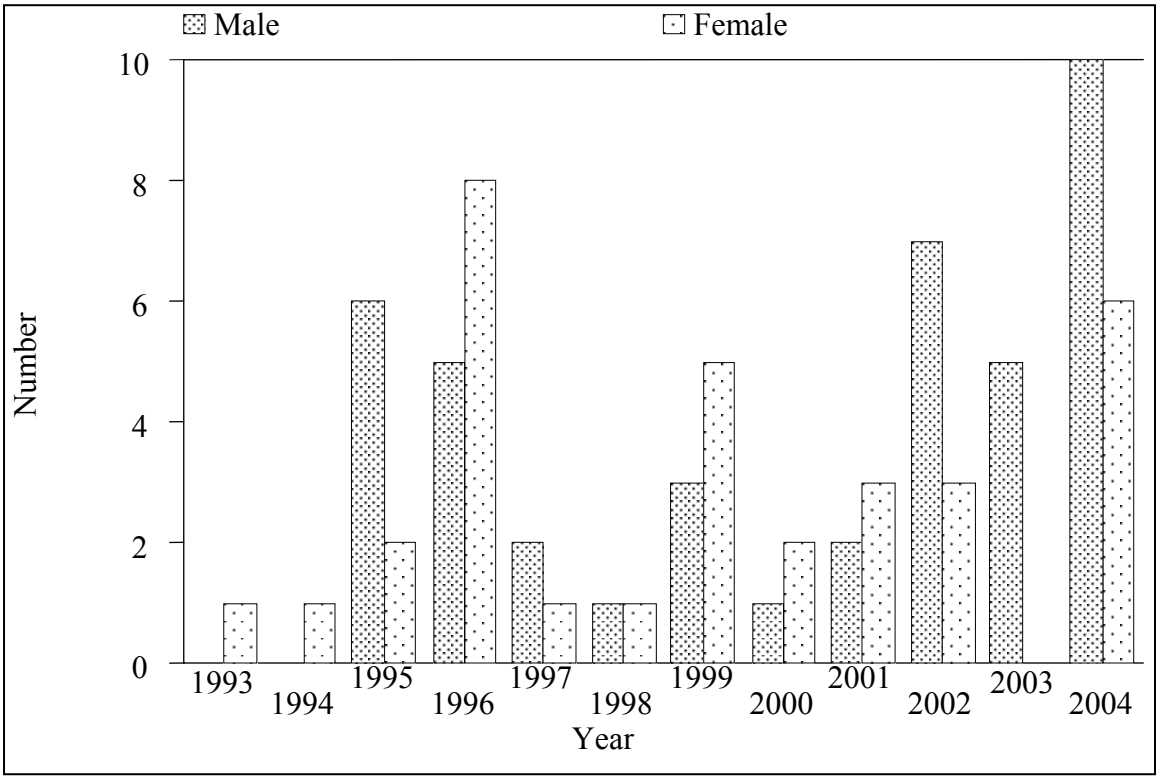

Table 4.2.2: Ethnic group distribution, 1993-2004

Year	**93**	**94**	**95**	**96**	**97**	**98**	**99**	**00**	**01**	**02**	**03**	**04**	**TOTAL**
Ethnic group	No.	No.	No.	No.	No.	No.	No.	No.	No.	No.	No.	No.	No.
Malay	0	1	2	3	1	0	4	1	2	3	1	11	29
Chinese	1	0	6	8	2	1	2	2	3	6	4	5	40
Indian	0	0	0	2	0	1	1	0	0	0	0	0	4
Others	0	0	0	0	0	0	1	0	0	1	0	0	2
TOTAL	1	1	8	13	3	2	8	3	5	10	5	16	75

Figure 4.2.2: Ethnic group distribution, 1993-2004

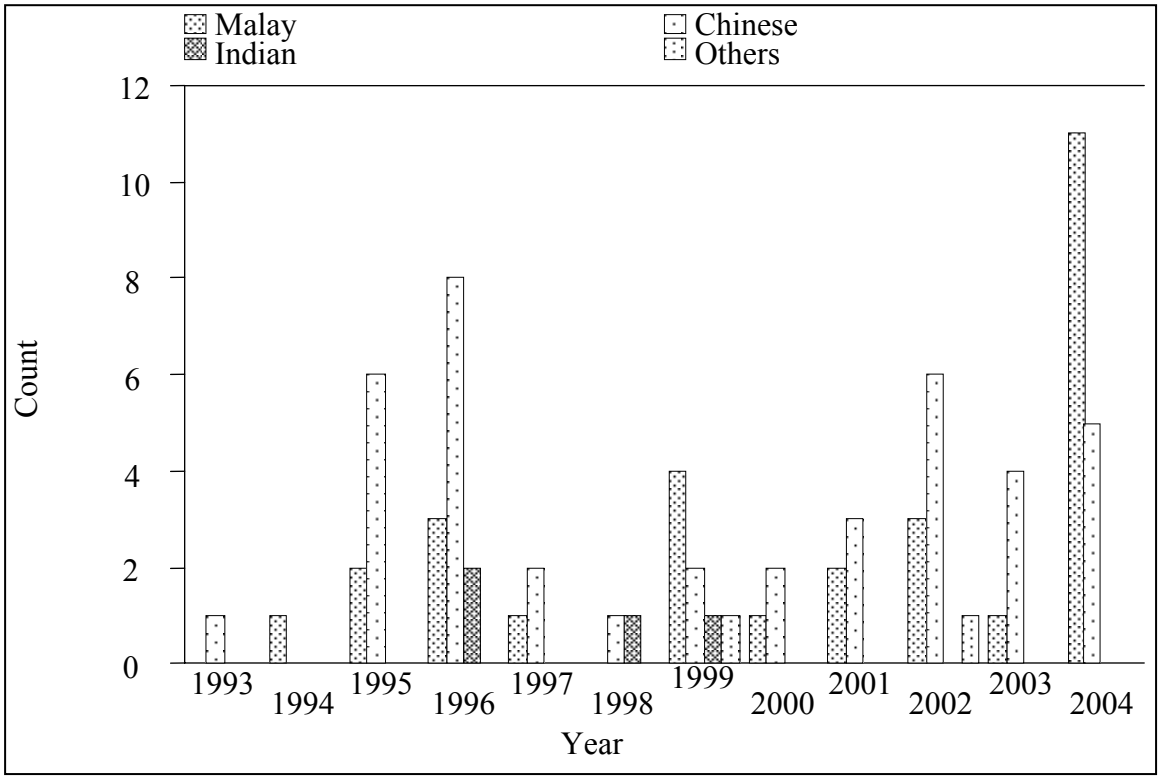

Table 4.2.3: Age distribution, 1993-2004

Year	**1993**	**1994**	**1995**	**1996**	**1997**	**1998**	**1999**
Age group (years)	No.	No.	No.	No.	No.	No.	No.
<1	0	0	0	0	0	1	0
1-4	1	1	3	11	3	1	5
5-9	0	0	3	1	0	0	2
10-14	0	0	1	1	0	0	0
15-19	0	0	0	0	0	0	1
20-39	0	0	1	0	0	0	0
40-59	0	0	0	0	0	0	0
>=60	0	0	0	0	0	0	0
TOTAL	1	1	8	13	3	2	8
Mean	2	4	9	4	2	1	4
SD	-	-	9	4	1	1	5
Median	2	4	6	2	2	1	3
Minimum	2	4	2	2	1	3 months	1
Maximum	2	4	30	14	2	1	15

Year	**2000**	**2001**	**2002**	**2003**	**2004**	**TOTAL**
Age group (years)	No.	No.	No.	No.	No.	No.
<1	0	0	1	0	0	2
1-4	3	4	4	2	9	47
5-9	0	1	4	2	3	16
10-14	0	0	0	0	1	3
15-19	0	0	0	0	1	2
20-39	0	0	1	0	0	2
40-59	0	0	0	0	1	1
>=60	0	0	0	1	1	2
TOTAL	3	5	10	5	16	75
Mean	1	2	6	18	12	7
SD	1	2	7	31	22	14
Median	1	2	4	7	3	2
Minimum	1	1	4 months	1	1	4 months
Maximum	2	5	24	73	74	74

*Age=date of transplant – date of birth

Table 4.2.4: Primary diagnosis, 1993-2004 (N=75)

Year	**1993**	**1994**	**1995**	**1996**	**1997**	**1998**	**1999**
Primary Diagnosis	No.	No.	No.	No.	No.	No.	No.
Biliary atresia	1	1	7	12	3	1	7
Metabolic liver disease	0	0	1	1	0	0	0
Cholestatic liver disease	0	0	0	0	0	1	0
Primary biliary cirrhosis	0	0	0	0	0	0	0
Primary sclerosing cholangitis	0	0	0	0	0	0	0
Autoimmune hepatitis	0	0	0	0	0	0	1
Chronic hepatitis B	0	0	0	0	0	0	0
Chronic hepatitis C	0	0	0	0	0	0	0
Alcoholic liver disease	0	0	0	0	0	0	0
Malignancies	0	0	0	0	0	0	0
Acute liver failure	0	0	0	0	0	0	0
Idiopathic/Cryptogenic	0	0	0	0	0	0	0
Others	0	0	0	0	0	0	0

Year	**2000**	**2001**	**2002**	**2003**	**2004**	**TOTAL**
Primary Diagnosis	No.	No.	No.	No.	No.	No.
Biliary atresia	2	5	6	2	10	57
Metabolic liver disease	0	0	2	0	2	6
Cholestatic liver disease	1	0	0	0	0	2
Primary biliary cirrhosis	0	0	0	0	0	0
Primary sclerosing cholangitis	0	0	0	0	0	0
Autoimmune hepatitis	0	0	0	0	0	1
Chronic hepatitis B	0	0	0	3	2	5
Chronic hepatitis C	0	0	0	0	0	0
Alcoholic liver disease	0	0	0	0	0	0
Malignancies	0	0	1	2	1	4
Acute liver failure	0	0	0	0	1	1
Idiopathic/Cryptogenic	0	0	0	0	0	0
Others	0	0	2	0	1	3

*4 patients have more than one primary disease

Table 4.2.5: Indication for Transplantation, 1993-2004 (N=75)

Year	1993	1994	1995	1996	1997	1998	1999
Indication for Transplantation	No.	No.	No.	No.	No.	No.	No.
Recurrent encephalopathy	0	0	1	0	0	0	1
Uncontrolled bleeding varices	0	0	0	7	1	0	4
Intractable ascites	0	0	0	0	0	0	0
Spontaneous bacterial peritonitis	0	0	0	0	0	0	0
Poor liver function	1	1	7	11	3	1	8
Malignancy	0	0	0	0	0	0	0
Unacceptable quality of life	0	0	0	0	0	0	0
Failure to thrive, growth retardation in paediatric patients	0	0	6	10	3	2	6
Others	0	0	0	0	0	0	0
No data	0	0	0	0	0	0	0

Year	2000	2001	2002	2003	2004	TOTAL
Indication for Transplantation	No.	No.	No.	No.	No.	No.
Recurrent encephalopathy	0	0	1	0	0	3
Uncontrolled bleeding varices	1	1	0	0	2	16
Intractable ascites	0	0	0	0	0	0
Spontaneous bacterial peritonitis	0	0	0	0	0	0
Poor liver function	3	5	9	3	11	63
Malignancy	0	0	0	0	0	0
Unacceptable quality of life	0	0	1	0	0	1
Failure to thrive, growth retardation in paediatric patients	3	5	7	2	10	54
Others	0	0	0	0	1	1
No data	0	0	1	2	2	5

*13 patients had 1 indication for transplantation, 57 had more than 1 indication for transplantation

Table 4.2.6: Recipient blood group, 1993-2004 (N=75)

Year	1993	1994	1995	1996	1997	1998	1999
Blood group	No.	No.	No.	No.	No.	No.	No.
A	0	1	2	0	0	0	3
B	0	0	1	2	0	1	2
AB	0	0	0	1	0	1	0
O	0	0	2	5	1	0	3
No data	1	0	3	5	2	0	0
TOTAL	1	1	8	13	3	2	8

Year	2000	2001	2002	2003	2004	TOTAL
Blood group	No.	No.	No.	No.	No.	No.
A	0	1	3	1	4	15
B	0	1	1	0	1	9
AB	0	0	0	0	1	3
O	3	3	5	1	8	31
No data	0	0	1	3	2	17
TOTAL	3	5	10	5	16	75

4.3 TRANSPLANT PRACTICES

The highest number of transplants carried out was in 2004 but the yearly transplant number shows a variable trend. 85.3% of liver transplants were live donor transplants while 14.7% were cadaveric. 82.8 % of living donors were first degree relatives with mother to child being the most common (Table 4.3.1).

The immunosuppressive medications used are mainly tacrolimus and steroids (Table 4.3.2).

Table 4.3.1: Type of transplant, 1993-2004 (N=75)

Year	**1993**	**1994**	**1995**	**1996**	**1997**	**1998**	**1999**
Type of Transplant	No.	No.	No.	No.	No.	No.	No.
Cadaveric	1	0	0	3	1	0	0
Living related - Mother	0	1	5	2	1	2	5
Living related - Father	0	0	2	7	1	0	2
Living related - Son	0	0	0	0	0	0	0
Living related - Brother	0	0	0	0	0	0	0
Living related - emotionally	0	0	0	0	0	0	0
Living unrelated	0	0	1	1	0	0	1
TOTAL	1	1	8	13	3	2	8

Year	**2000**	**2001**	**2002**	**2003**	**2004**	**TOTAL**
Type of Transplant	No.	No.	No.	No.	No.	No.
Cadaveric	0	0	1	1	4	11
Living related - Mother	2	2	2	2	7	31
Living related - Father	0	2	3	0	1	18
Living related - Son	0	0	0	1	1	2
Living related - Brother	0	0	1	0	0	1
Living related - emotionally	0	0	0	1	0	1
Living unrelated	1	1	3	0	3	11
TOTAL	3	5	10	5	16	75

Table 4.3.2: Immunosuppressive drug treatment at transplantation, 1993-2004 (N=75)

Year	**1993**	**1994**	**1995**	**1996**	**1997**	**1998**	**1999**
Immunosuppressive drugs	No.	No.	No.	No.	No.	No.	No.
Steroids	0	0	2	5	0	2	5
Azathioprine	0	0	0	0	0	0	0
Cyclosporin A	1	1	1	2	0	0	0
Tacrolimus (FK506)	0	0	3	7	2	2	8
Mycophenolate Mofetil (MMF)	0	0	0	0	0	0	0
Rapamycin	0	0	0	0	0	0	0
Monoclonal/Polyclonal antibody	0	0	0	0	0	0	0
Anti IL2R Antibodies	0	0	0	0	0	0	0
Others	0	0	0	0	0	0	0
No data	0	0	4	3	1	0	0
TOTAL patients	1	1	8	13	3	2	8

Year	**2000**	**2001**	**2002**	**2003**	**2004**	**TOTAL**
Immunosuppressive drugs	No.	No.	No.	No.	No.	No.
Steroids	2	5	5	1	12	39
Azathioprine	0	0	0	0	4	4
Cyclosporin A	1	0	0	0	0	6
Tacrolimus (FK506)	2	5	9	5	12	55
Mycophenolate Mofetil (MMF)	0	0	0	0	0	0
Rapamycin	0	0	1	2	0	3
Monoclonal/Polyclonal antibody	0	0	0	0	0	0
Anti IL2R Antibodies	0	0	0	0	0	0
Others	0	0	0	0	0	0
No data	0	0	1	0	4	13
TOTAL patients	3	5	10	5	16	75

*21 patients had 1 type of drug, 37 patients had 2 types, 4 patients had 3 types

4.4 TRANSPLANT OUTCOMES

The 1 year survival rate for the period 1993-1998 and 1999-2004 was 71% and 66% respectively (Table and Figure 4.4.1). The survival rate is lower in the younger age group (< 10 years old) (Table and Figure 4.4.3). The most common known cause of death is sepsis (Table 4.4.4). However 8 cases have unknown cause due to either unavailable source data or death at home.

Table 4.4.1: Patient survival by year of transplant, 1993-2004 (N=75)

Year of Transplant	**1993 - 1998**		**1999 - 2004**	
Interval (months)	% Survival	SE	% Survival	SE
1	82	7	80	6
6	71	9	66	7
12	71	9	66	7

SE=standard error

Figure 4.4.1: Patient survival by year of transplant, 1993-2004

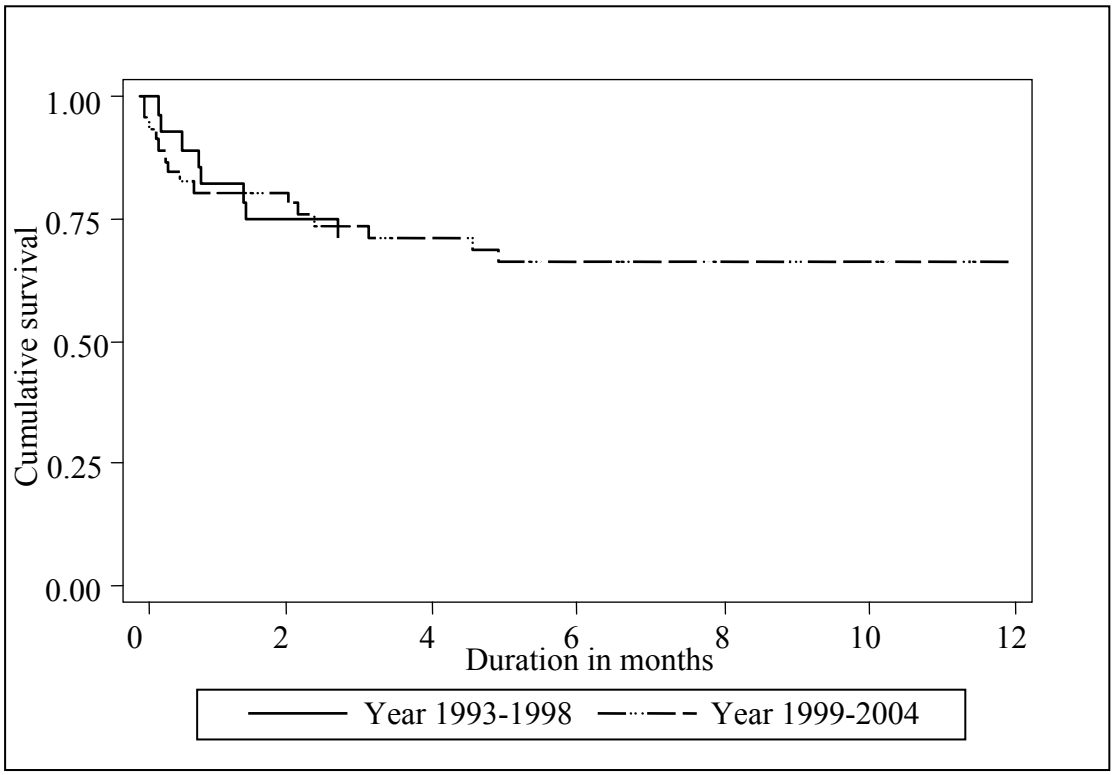

Table 4.4.2: Patient survival by gender, 1993-2004 (N=75)

Gender	**Male**		**Female**	
Interval (months)	% Survival	SE	% Survival	SE
1	80	6	82	7
6	70	7	66	8
12	70	7	66	8

SE=standard error

Figure 4.4.2: Patient survival by gender, 1993-2004

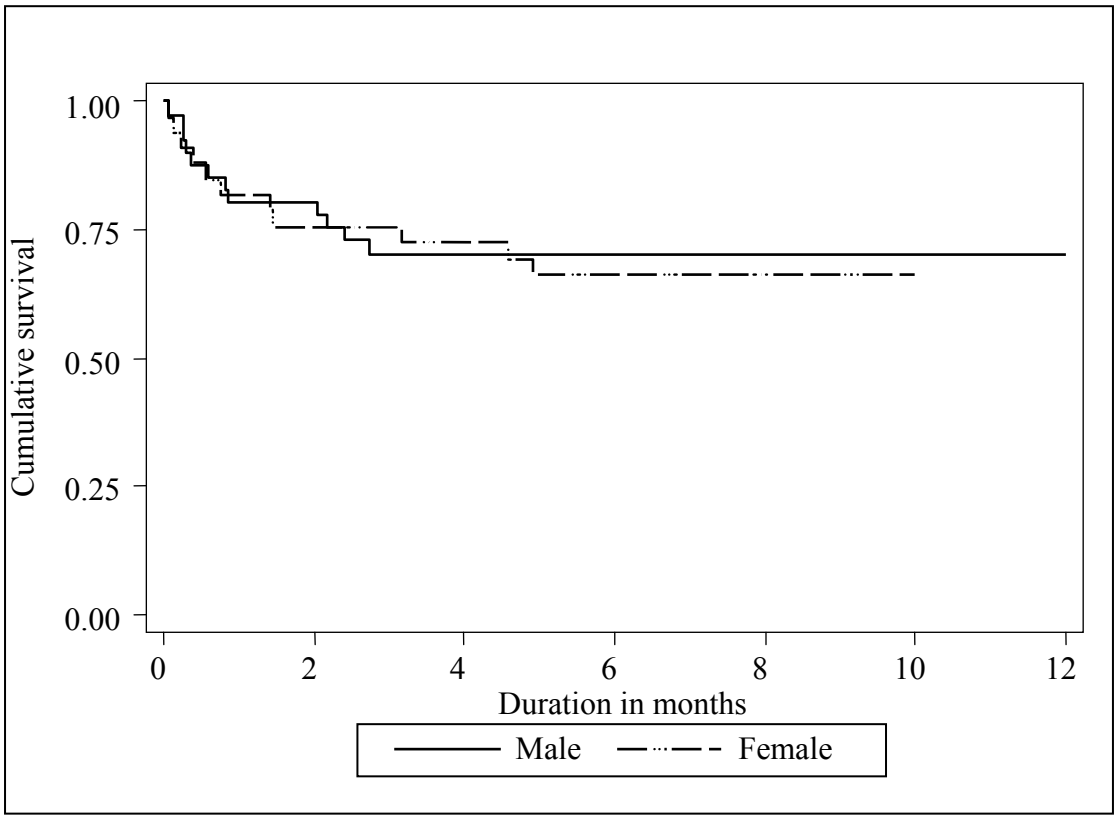

Table 4.4.3: Patient survival by age group, 1993-2004 (N=75)

Age group	**0-9 years**		**>=10 years**	
Interval (months)	% Survival	SE	% Survival	SE
1	79	5	100	-
6	66	6	88	12
12	66	6	88	12

SE=standard error

Figure 4.4.3: Patient survival by age group, 1993-2004

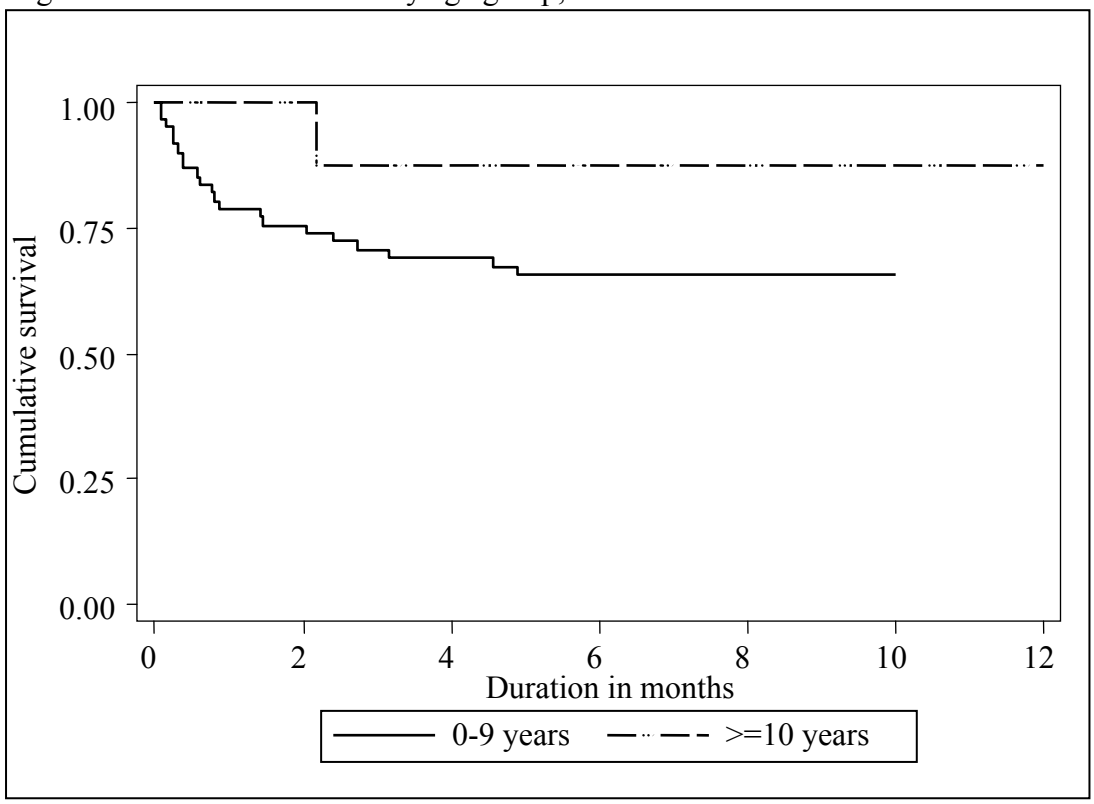

Table 4.4.4: Causes of death, 1993-2004 (N=75)

Year	1995	1996	1997	1998	1999	2000
Causes of death	No.	No.	No.	No.	No.	No.
Bleeding Oesophageal Varices – Post transplant	0	0	1	0	2	0
Chronic graft rejection	0	0	0	0	0	0
Intra-abdominal Bleeding	0	0	0	0	0	0
Ischaemic liver necrosis	0	0	0	0	0	1
Sepsis	0	2	0	0	0	0
Graft Failure	0	0	0	0	0	0
CMV Pneumonia	0	0	0	0	1	0
DIVC	0	0	0	0	0	0
Intracranial Haemorrhage	0	1	0	0	1	0
Pneumonia and Respiratory Failure	0	1	0	0	0	0
Post Transplant Lymphoproliferative Disease and Septicaemia	0	0	0	0	0	0
Unknown	3	0	0	0	0	0
TOTAL*	3	4	1	0	4	1

Year	2001	2002	2003	2004	TOTAL
Causes of death	No.	No.	No.	No.	No.
Bleeding Oesophageal Varices – Post transplant	0	0	0	0	3
Chronic graft rejection	1	0	0	0	1
Intra-abdominal Bleeding	0	0	1	0	1
Ischaemic liver necrosis	0	0	0	0	1
Sepsis	0	3	0	1	6
Graft Failure	0	0	0	1	1
CMV Pneumonia	0	0	0	0	1
DIVC	0	1	0	0	1
Intracranial Haemorrhage	0	0	0	0	2
Pneumonia and Respiratory Failure	0	0	0	0	1
Post Transplant Lymphoproliferative Disease and Septicaemia	1	0	0	0	1
Unknown	0	1	0	2	6
TOTAL*	2	5	1	4	25

*2 patients died with no date of death and cause of death