表7 生体ドナーの続柄

	Age of Recipient		Total
	<18 y.o.	≧18 y.o.	
Mother	1,251	228	1,479
Father	1,000	211	1,211
Son	0	1,256	1,256
Daughter	0	522	522
Brother	9	431	440
Sister	4	318	322
Nephew	0	56	56
Grandmother	44	2	46
Aunt	19	10	29
Cousin	2 (Male 2)	26 (Male 23, Female 3)	28
Uncle	12	9	21
Grandfather	19	0	19
Niece	0	10	10
Father's cousin	2 (Male 1, Female 1)	0	2
Grandson	0	1	1
Cousin's son	0	1	1
Wife	0	528	528
Husband	0	432	432
Brother-in-law	0	20	20
Son-in-law	0	16	16
Sister-in-law	0	8	8
Father-in-law	2	3	5
Nephew-in-law	0	4	4
Mother-in-law	0	3	3
Daughter-in-law	0	2	2
Grandfather-in-law	1	0	1
Uncle-in-law	0	1	1
Common-law husband	0	1	1
Common-law wife	0	1	1
Friend	0	1 (Female)	1
Domino	1 (Male)	38 (Male 19, Female 19)	39
	2,366	4,139	6,505

表9 生体肝移植におけるレシピエントとドナーのABO血液型適合度

	Age of Recipient		Total
	<18 y.o.	≧18 y.o.	
Identical	1,568	2,823	4,391
Compatible	482	922	1,404
Incompatible	316	391	707
	2,366	4,136	6,502

すべて家族性アミロイドポリニューロパチー（FAP）であった。

生体肝移植におけるレシピエントとドナーのABO血液型適合度を**表9**に示す。「dual graft」のうち1例は，ABO一致のドナーとABO適合のドナーの2人から移植されていたので，集計から除いた。このため，**表9**の合計は生体肝移植の総数6,503より1少ない6,502になっている。なお，「dual graft」の他の1例は，ABO適合の2人のドナーから移植されていたので，「適合」に含めた。ABO不適合の頻度は，大人9%，小児13%であった。なお，小児の不適合316のうち，0歳が142と最も多く，以下1歳55，2歳23，3歳19等であった。**表10**に，大人・小児別のABO不適合移植数の年次推移を示す。

移植後の累積生存率，生着率（**表11**）とも，生体肝移植と死体肝移植の間に差がなかった。生体肝移植と脳死肝移植との比較においても差はなかった（**図1**）。以下，疾患（群）別の生存率データについては，10移植以上の疾患（群）については必ず記載し，それ以下の場合は必要に応じて記載することとする。

死体肝移植の予後は，以下の通りであった(**表12**)。

1）再移植は，初回移植に比し予後が有意に悪かっ

表8 ドミノ肝移植数の推移（1989〜2011年）

Year	1989	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	Total
≧18 years	0	0	0	0	0	0	0	0	0	0	3	5	4	1	7	4	2	1	1	4	4	2	0	38
<18 years	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	1
Total	0	0	0	0	0	0	0	0	0	0	3	5	4	1	8	4	2	1	1	4	4	2	0	39

表 10　生体肝移植における ABO 不適合移植数の推移（1989～2011 年）

Year	1989	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	Total
≧18 years	0	0	1	0	0	1	1	0	5	3	5	5	17	13	22	33	47	31	47	42	39	35	44	391
＜18 years	0	0	4	4	11	12	9	11	14	9	13	8	13	21	13	20	24	18	21	18	27	23	23	316
Total	0	0	5	4	11	13	10	11	19	12	18	13	30	34	35	53	71	49	68	60	66	58	67	707

表 11　移植後の累積生存率と累積生着率

	Patient Survival（%）							Graft Survival（%）						
	n	1 year	3 year	5 year	10 year	15 year	20 year	n	1 year	3 year	5 year	10 year	15 year	20 year
Cadaveric Donor	139	81.8	78.7	77.1	70.6			139	81.1	78.0	76.5	69.9		
Heart-beating	136	83.6	80.4	78.8	72.1			136	82.9	79.7	78.2	71.5		
Non-heart-beating	3	0.0						3	0.0					
Living Donor	6,503	83.4	79.3	76.9	71.9	68.2	67.5	6,503	82.9	78.6	76.0	70.2	65.9	64.6

表 12　脳死肝移植におけるレシピエントの累積生存率

		n	Cumulative Survival（%）			
			1 year	3 year	5 year	10 year
Primary or Retransplant	Primary	113	88.3	85.8	83.9	79.0
	Re-transplantation	18	55.6	48.6	48.6	32.4
	Re-re-transplantation	5	80.0	80.0	80.0	80.0
Recipient Age	＜18	19	78.9	78.9	78.9	78.9
	18≦	117	84.4	80.6	78.6	67.0
Indication	Cholestatic Disease	32	93.8	93.8	93.8	84.4
	Hepatocellular Disease	39	84.2	80.0	80.0	
	Vascular Disease	0	—			
	Neoplastic Disease	10	70.0	70.0		
	Acute Liver Failure	22	89.8	83.9	83.9	83.9
	Metabolic Disease	10	100.0	80.0	80.0	80.0

た（p＝0.0003，**図 2**）。

2）小児と大人では，予後に有意な差はなかった（**図 3**）。

3）脳死肝移植の疾患群別の予後を**図 4** に示す。胆汁うっ滞性疾患のうち，胆道閉鎖症は 1 年・3 年・5 年・10 年とも 82.4% であった。症例数は少ないが，原発性胆汁性肝硬変（n＝8）は 1 年・3 年・5 年 100%，10 年 50%，原発性硬化性胆管炎（n＝7）は 1 年・3 年・5 年・10 年とも 85.7% であった。また，肝細胞性疾患のうち，HBV は 1 年・3 年・5 年 77.1%，HCV は 1 年 81.2%，3 年・5 年 73.1% であった。また，腫瘍性疾患のうち，肝細胞癌は 1 年・3 年 70.0% であった。

生体肝移植の予後は，以下の通りであった（**表 13-1**，**表 13-2**）。

1）再移植は，初回移植に比し予後が有意に悪かった（p＜0.0001，**図 5**）。

2）性別では女性の予後が有意に良かった（p＝0.0074，**図 6**）。

3）小児と大人では，後者で有意に予後が悪かった（p＜0.0001，**図 7A**）。10 歳ごとに区切った年齢群で比較した場合も同様に有意差を認めた（p＜0.0001，**図 7B**）。

4）原疾患別の予後を検討した。まず，6 つの疾患

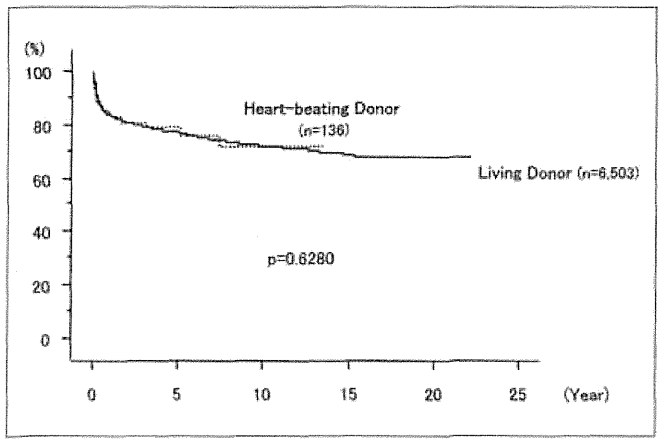

図1 生体肝移植と脳死肝移植における累積生存率

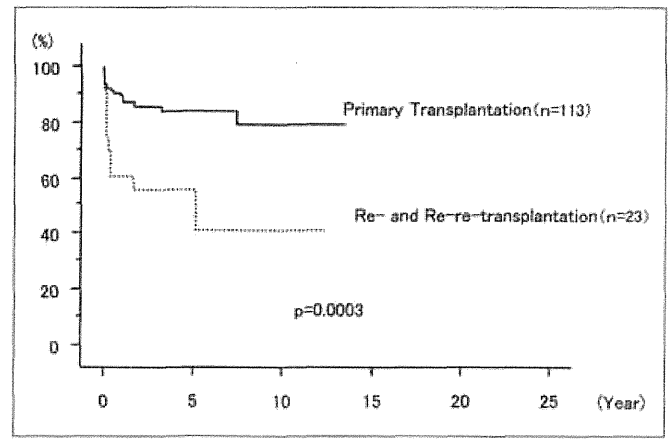

図2 脳死肝移植における初回移植と再移植の累積生存率

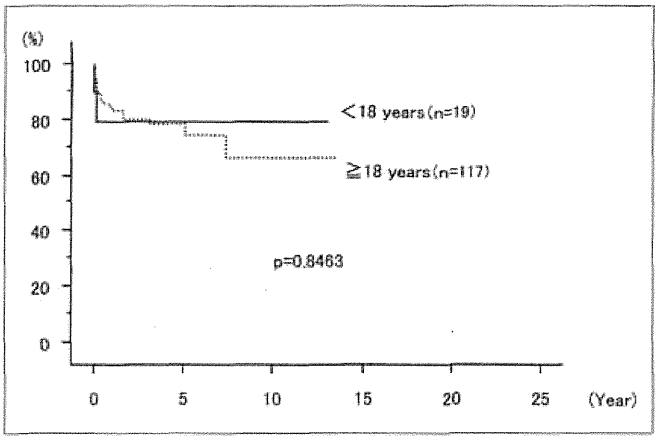

図3 脳死肝移植における年齢別の累積生存率

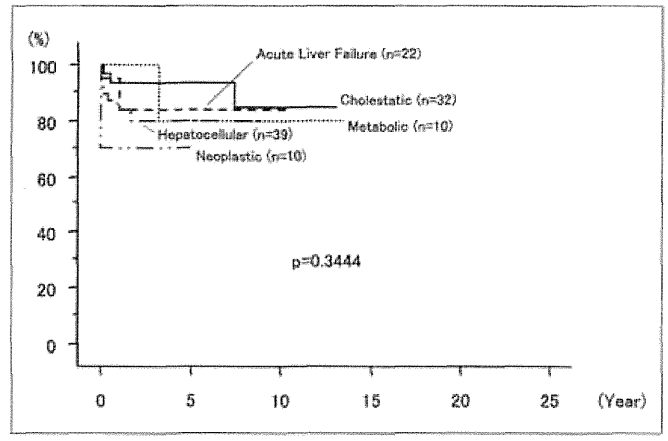

図4 脳死肝移植における疾患群別の累積生存率

群について比較すると，有意な差が認められた（p<0.0001，**図8A**）。個々の疾患群の検討では，胆汁うっ滞性疾患の中で疾患の間で予後に有意差を認めた（p<0.0001，**図8B**）。肝細胞性疾患では，疾患間に生存率の有意な差を認めなかった（**図8C**）。一応HCVとHBVを取り出して比較してみると，後者の予後が有意に良かった（p=0.0057）。腫瘍性疾患では，疾患群内で予後に有意差を認めた（p=0.0071，**図8D**）。腫瘍性疾患のうち，肝血管腫（n=9）の予後は1年・3年88.9%，5年・10年76.2%，胆管細胞癌（n=8）の予後は1年75.0%，3年・5年・10年62.5%であった。急性肝不全の中では，疾患間に生存率の有意な差を認めなかった（**図8E**）。代謝性疾患では，疾患の間に有意差を認めた（p<0.0001，**図8F**）。なお，プロピオン酸血症（n=9）は1年・3年100%，5年・10年83.3%であった。「その他」の疾患群中では，先天性肝線維症は1年・3年・5年・10年・15年・20年とも83.3%，多発性肝嚢胞症は1年78.6%，3年・5年62.9%，10年43.1%であった。症例数は少ないが，特発性門脈圧亢進症（n=8）は1年・3年・5年・10年37.5%，GVHD（n=4）は1年75.0%・3年50.0%，5年25.0%であった。

5）8種のgraft別で予後を比較すると，有意な差があった（p<0.0001，**図9**）。

6）レシピエントのABO血液型は，予後に影響を与えなかった（data not shown）。

7）ドナーの性別は，レシピエントの予後に影響を与えなかった（data not shown）。

8）ドナーの年齢を，10歳ごとに区切った年齢群で比較すると，有意差を認めた（p<0.0001，**図10A**）。HCVの症例に限って比較した場合も同様の結果であった（p<0.0001，**図10B**）。60歳以上のドナーから移植されたHCV症例（n=33）の生存率は特に悪く，1年51.5%，3年48.1%，5年38.5%であった。

表 13-1　生体肝移植におけるレシピエントの累積生存率

		n	Cumulative Survival (%)					
			1 year	3 year	5 year	10 year	15 year	20 year
Primary or Retransplant	Primary	6,338	84.1	80.0	77.5	72.5	68.8	68.0
	Re-transplantation	160	55.6	53.5	51.8	48.1	48.1	
	Re-re-transplantation	5	60.0	60.0	60.0	60.0		
Recipient Gender	Male	3,116	83.5	78.2	75.4	69.6	66.8	66.2
	Female	3,387	83.3	80.4	78.3	74.0	69.8	68.9
Recipient Age	<18	2,366	88.5	86.9	85.7	83.2	80.7	80.2
	18≦	4,137	80.5	75.0	71.8	64.6	56.3	
	~9	1,950	89.5	87.8	87.1	84.7	83.1	82.8
	10~19	512	84.3	83.1	80.0	77.1	69.2	67.4
	20~29	331	80.3	76.1	73.9	68.1	61.7	
	30~39	429	78.5	72.6	69.2	65.3	57.5	
	40~49	777	79.8	75.9	74.6	66.0	60.2	
	50~59	1,700	80.9	74.5	70.5	63.2	60.4	
	60~69	789	80.6	74.6	70.9	60.4		
	70~79	15	80.0	71.1	56.9	56.9		
Indication	Cholestatic Disease	2,623	87.7	86.1	84.9	81.2	77.7	76.9
	Biliary Atresia	1,723	90.9	89.8	88.8	86.2	84.3	84.0
	Primary Biliary Cirrhosis	567	81.1	78.4	76.9	71.0	59.8	
	Primary Sclerosing Cholangitis	171	80.1	75.6	71.7	60.6	50.1	
	Alagille Syndrome	75	93.3	91.9	91.9	87.0	87.0	87.0
	Byler's Disease	35	91.4	88.6	88.6	84.9	57.3	57.3
	Caroli Disease	12	75.0	75.0	75.0	75.0	75.0	
	Congenital Bile Duct Dilatation	12	58.3	58.3	58.3	58.3		
	Hepatocellular Disease	1,161	79.4	75.2	72.6	63.4	59.3	59.3
	HCV	509	77.9	72.4	68.5	58.7		
	HBV	244	83.6	79.3	78.4	71.5		
	Alcoholic	147	80.8	78.4	76.0	48.6		
	Autoimmune Hepatitis	73	76.7	75.2	75.2	75.2		
	NASH	40	79.6	79.6	73.5	49.0		
	Cryptogenic Cirrhosis	136	78.5	74.4	71.5	65.1	60.8	60.8
	Vascular Disease	66	96.9	87.1	87.1	87.1	87.1	87.1
	Budd-Chiari	35	91.4	85.5	82.2	82.2	82.2	82.2
	Congenital Absence of Portal Vein	25	96.0	91.4	91.4	91.4	91.4	
	Neoplastic Disease	1,404	84.3	74.8	69.6	60.5	51.5	51.5
	HCC	1,299	84.5	74.6	69.6	60.4	47.9	47.9
	Hepatoblastoma	61	85.1	81.3	73.1	73.1	73.1	
	Liver Metastasis	18	72.2	72.2	60.2			
	Acute Liver Failure	641	74.2	71.4	69.6	67.3	64.9	64.9
	HBV	144	77.8	74.9	74.0	73.0	73.0	
	Drug-induced	35	76.9	76.9	73.7	73.7	73.7	
	Autoimmune Hepatitis	26	68.8	68.8	68.8	68.8		
	Viral (≠HBV)	24	62.5	62.5	62.5	62.5		
	Unknown	404	73.4	69.9	67.7	64.3	61.0	
	Metabolic Disease	395	89.1	85.9	83.8	82.2	75.6	72.5
	Wilson Disease	111	90.0	89.1	87.2	86.2	73.4	73.4
	Familial Amyloid Polyneuropathy	73	95.9	88.9	83.4	77.4	74.1	
	OTC Deficiency	48	95.8	95.8	95.8	95.8	95.8	
	Citrullinemia	47	95.7	95.7	95.7	95.7	91.2	
	Glycogen Storage Diseases	25	83.3	64.5	64.5	64.5	43.0	
	Methylmalonic Acidemia	22	81.8	81.8	81.8	81.8		
	Primary Hyperoxaluria	15	53.3	53.3	53.3	53.3	53.3	
	Tyrosinemia	13	92.3	76.9	76.9	76.9	76.9	
	CPS Deficiency	12	91.7	91.7	91.7			

表 13-2　生体肝移植におけるレシピエントの累積生存率

		n	Cumulative Survival (%)					
			1 year	3 year	5 year	10 year	15 year	20 year
Graft	Monosegment	103	79.6	77.1	75.1	75.1		
	Lateral Segment	1,635	89.8	88.3	87.7	85.3	83.5	83.1
	Posterior Segment	96	74.9	67.9	65.0	60.2		
	Left Lobe	1,271	79.1	75.4	72.2	68.5	61.7	60.1
	Left Lobe＋Caudate Lobe	1,027	80.6	77.0	73.8	67.7		
	Right Lobe	2,346	83.0	76.9	73.8	65.7	63.4	63.4
	Whole Liver	23	82.6	73.4	73.4	52.4		
	Dual Graft	2	100.0	100.0	100.0			
Donor Age	10～19	64	84.4	81.1	77.3	70.2	70.2	
	20～29	1,670	85.3	82.3	80.1	76.3	72.9	71.6
	30～39	2,248	86.8	83.0	80.8	75.8	73.1	72.6
	40～49	1,326	82.4	78.5	76.5	70.9	66.0	64.8
	50～59	919	78.0	71.7	68.3	62.0	55.2	
	60～69	276	67.0	60.8	55.6	49.7	46.9	
	70～79	2	50.0	50.0	50.0			
ABO Compatibility	Identical	4,391	84.4	80.3	77.8	72.8	69.2	68.2
	Compatible	1,404	84.1	80.1	77.4	72.5	69.7	69.7
	Incompatible	707	75.8	71.9	70.2	65.2	59.6	59.6

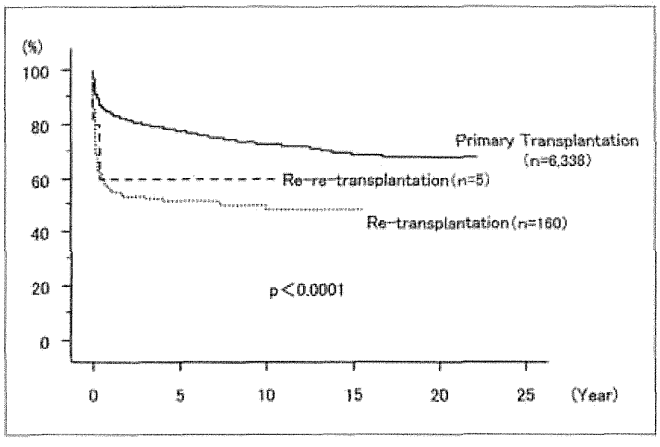

図 5　生体肝移植における初回移植と再移植の累積生存率

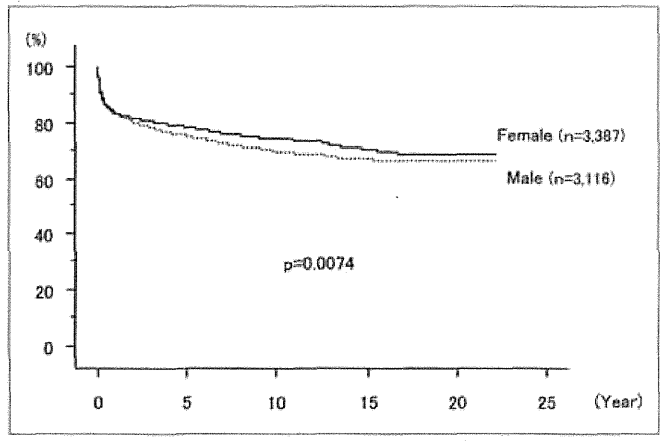

図 6　生体肝移植における性別の累積生存率

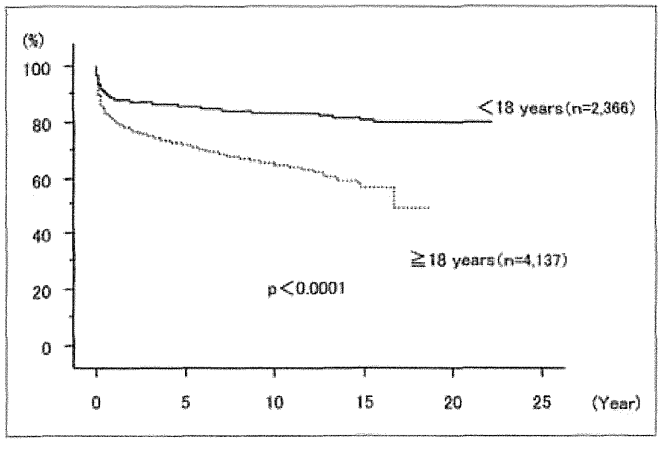

図 7A　生体肝移植における年齢別の累積生存率

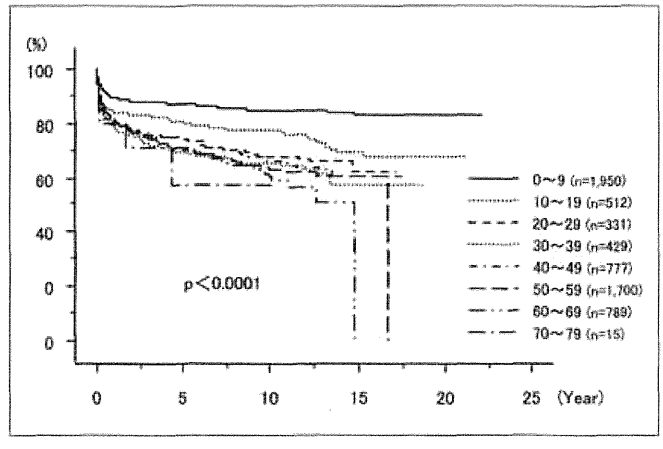

図 7B　生体肝移植における年齢別の累積生存率（10 歳ごとの年齢群比較）

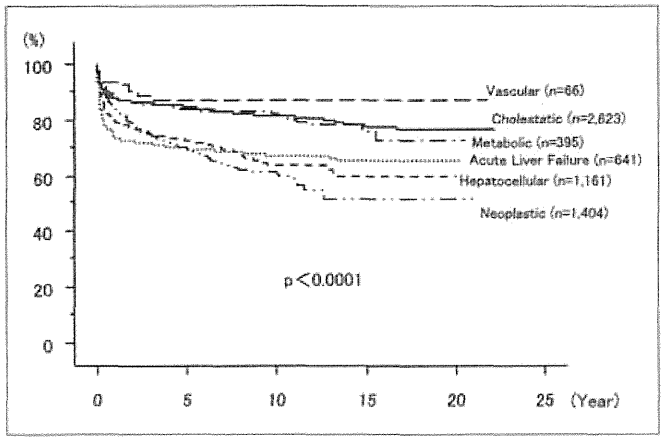

図 8A　生体肝移植における疾患群別の累積生存率

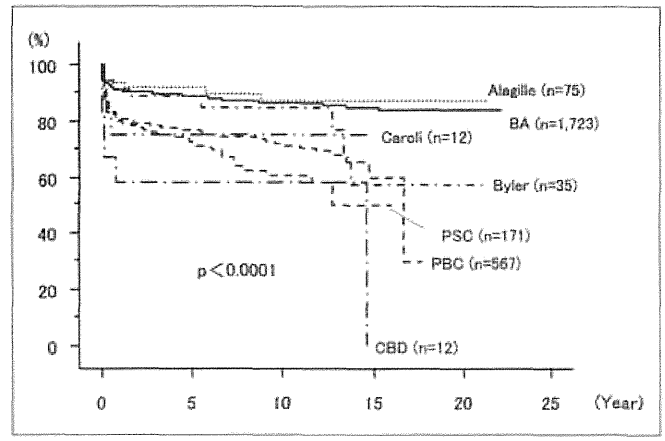

図 8B　生体肝移植における胆汁うっ滞性疾患の累積生存率

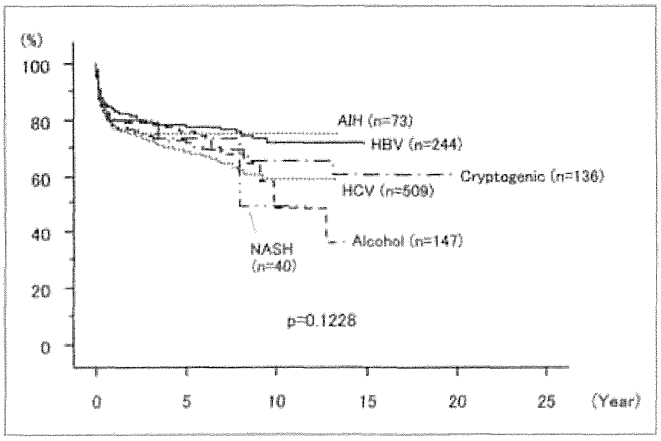

図 8C　生体肝移植における肝細胞性疾患の累積生存率

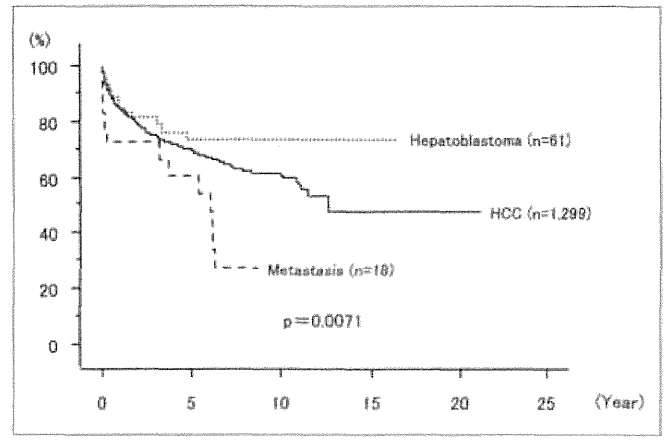

図 8D　生体肝移植における腫瘍性疾患の累積生存率

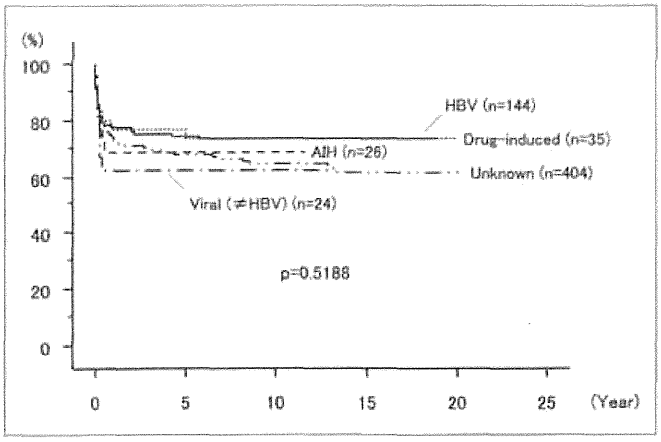

図 8E　生体肝移植における急性肝不全の累積生存率

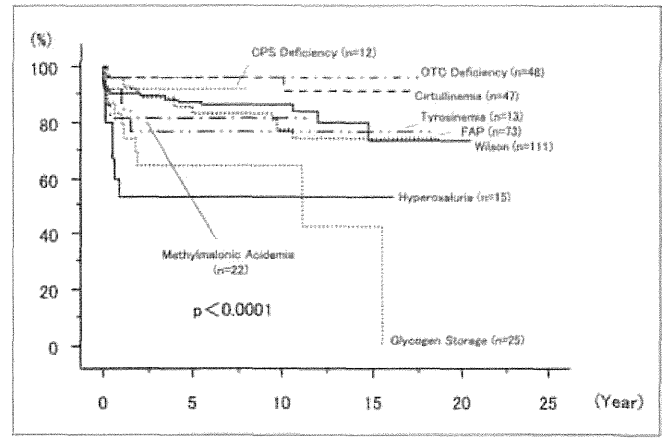

図 8F　生体肝移植における代謝性疾患の累積生存率

9）レシピエントとドナーの ABO 血液型適合度別の予後を見ると，血液型不適合群は，一致群，適合群に比し有意に予後が悪かった（$p<0.0001$，**図 11A**）。不適合群においてレシピエントの年齢別に予後をみると，0 歳（1 年 83.8%，3 年・5 年 83.0%，10 年 80.5%，15 年・20 年 76.9%）1 歳（1 年・3 年 85.5%，5 年・10 年・15 年・20 年 82.9%），2 歳（1 年・3 年・5 年・10 年 91.3%）はほぼ同様に良好であったのに対し，3 歳（1 年 78.9%，3 年・5 年・10 年 67.7%，15 年 33.8%）では明らかに不良であった。0～2 歳と 3 歳を比較す

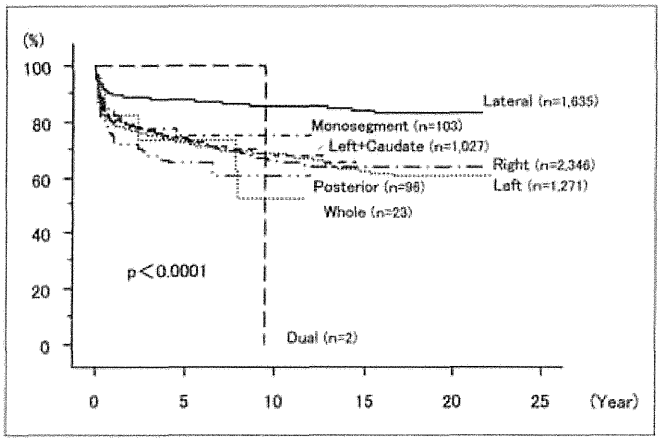

図 9　生体肝移植における graft 別の累積生存率

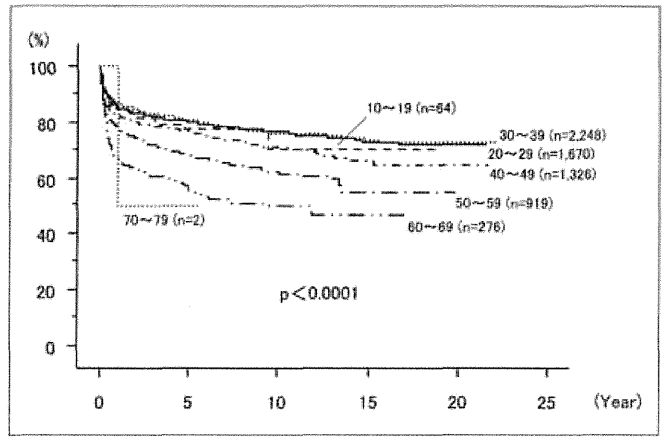

図 10A　生体肝移植におけるドナー年齢別の累積生存率

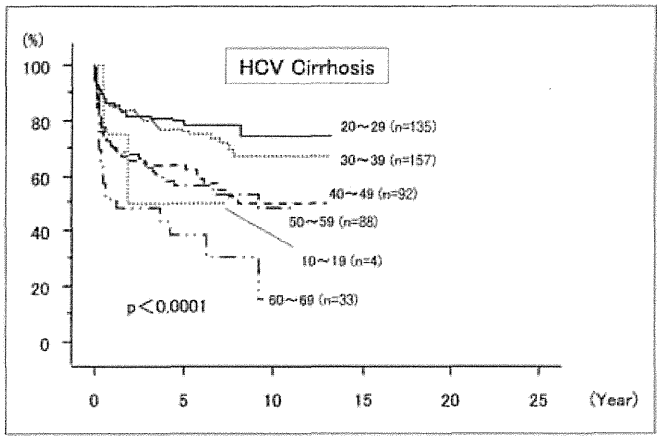

図 10B　生体肝移植におけるドナー年齢別の累積生存率（HCV 症例）

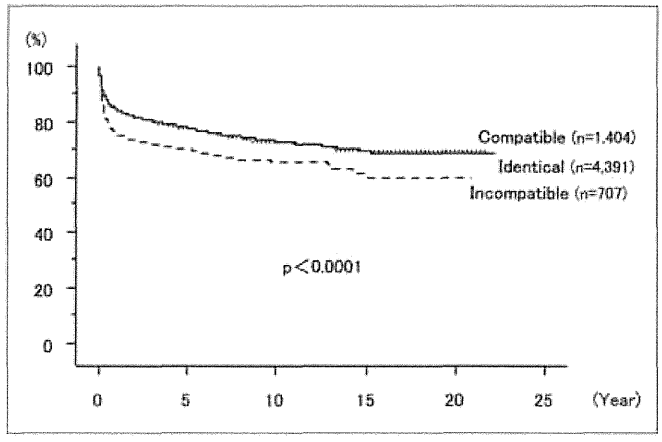

図 11A　生体肝移植における ABO 血液型適合度別の累積生存率

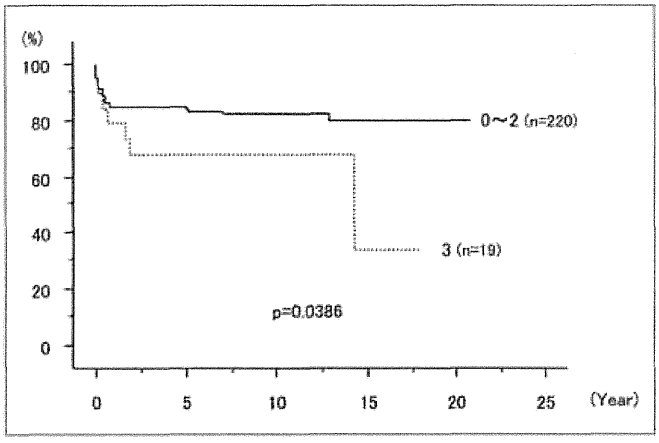

図 11B　生体肝移植の ABO 血液型不適合群におけるレシピエント年齢別の累積生存率（1）

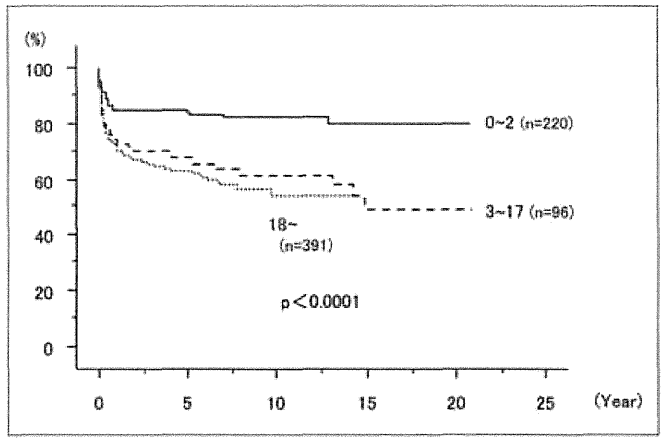

図 11C　生体肝移植の ABO 血液型不適合群におけるレシピエント年齢別の累積生存率（2）

ると，生存率に有意な差を認めた（p=0.0386，**図 11B**）。次に，年齢を 3 群に分けて比較すると，0～2 歳（つまり 36 カ月未満）は 1 年 85.0%，3 年 84.5%，5 年 83.8%，10 年 82.2%，15 年・20 年 80.0% と良好であったのに対し，3～17 歳は 1 年 74.0%，3 年 70.5%，5 年 67.4%，10 年 61.4%，15 年・20 年 49.0%，18 歳以上は 1 年 71.0%，3 年 65.0%，5 年 63.0%，10 年 53.8% と有意に悪かった（p<0.0001，**図 11C**）。

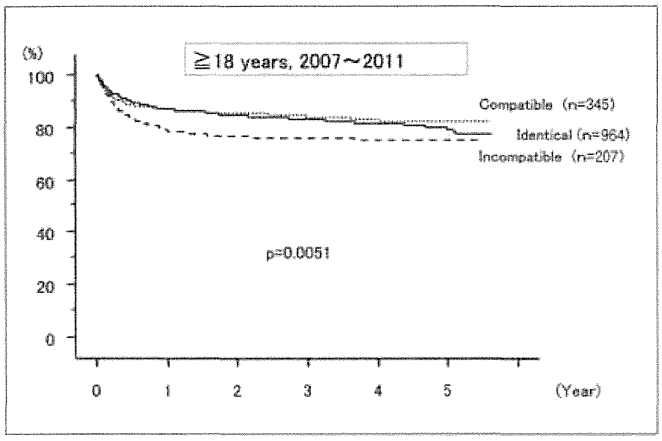

図 11D　生体肝移植（大人）の ABO 血液型適合度別の累積生存率（2007～2011 年）

近年，特に大人において ABO 不適合移植に対する新しい対策が行われ，予後が改善している。そこで，直近の 5 年間（2007～2011 年）の大人の移植例に限って比較してみたが，不適合はまだ一致，適合に比し有意に悪かった（p＝0.0051，**図 11D**）。

IV. おわりに

肝移植研究会が 1992 年以来行ってきた症例登録の第 13 回の集計結果を誌上で公にすることができた。先に挙げたすべての移植施設の皆様のご協力の賜であり，稿を終えるにあたり改めて感謝の意を表したい。

文責：日本肝移植研究会
猪股裕紀洋，梅下浩司，土本伸二

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American Journal of Transplantation 2012; 12: 523–530
Wiley Periodicals Inc.

doi: 10.1111/j.1600-6143.2011.03822.x

Minireview

Current Status of Organ Transplantation in Japan

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To overcome severe donor shortage, Japanese doctors over the years have developed innovative strategies to maximize organs transplanted per brain death donor and expanded the donor pool using living donors. They also used living and marginal organs and drastically improved living donor lung, liver, pancreas and kidney transplantations. Moreover, they initiated ABO blood type incompatible liver transplantation advancements and succeeded in overcoming the blood type barrier in kidney and liver transplantations. Similar efforts are underway for pancreas transplantation. Furthermore, Japanese doctors have developed a nonaggressive step to achieve immunosuppression following organ transplantation by carefully monitoring donor-specific hyporesponsiveness and infectious immunostatus. However, the institution of amendments to allocation systems and the intensification of efforts to decrease living donor morbidity and to increase the number of brain death donors have remained important issues needing attention. Overall, the strategies Japan has adopted to overcome donor shortage can provide useful insights on how to increase organ transplantations.

Key words: Brain death, blood type, incompatible transplantation, living donor liver transplantation.

Abbreviations: ABO-I, ABO-incompatible; CI, calcineurin inhibitor; DDLT, deceased donor liver transplantation; DDLuT, deceased donor lung transplantation; LDLLuT, living donor lobar lung transplantation; LDLT, living donor liver transplantation; LFS, large-for-size; LRKT, living related kidney transplantation, MMF, mycophenolate mofetil; OTPD, organs transplanted per donor; SFS, small-for-size; SPK, simultaneous pancreas kidney transplantation.

Received 02 June 2011, revised 15 September 2011 and accepted for publication 19 September 2011

Introduction

The Japanese organ transplantation experience over recent years has been beset by a severe donor shortage because of the restrictions imposed by the organ transplantation law of 1997. In this law, family consent was required for organ recovery even in executing a documented will of a donor and the donor age must be 15 years or older. This shortage of deceased organ donors has reshaped the current practice and nature of organ transplantation in Japan and catalyzed the development of unique innovations in living donor transplantation.

The revision of the transplantation law in June, 2010 involved a change from the "opt-in" system to the "opt-out" system, leading to the progressive increase in the number of brain death donors and all donors except two concurred by family consent without executing a documented will. Although the restriction of donor age was removed, there has been only one pediatric donor and the allocation system has remained unchanged. Despite these efforts, organ recovery was performed in only 115 brain death donors since the first case in February 1999.

As an overview of the current status of organ transplantation in Japan, first, we present Japanese strategies for maximizing organs transplanted per brain death donor and outcomes, the approaches taken to expand the donor pool using living donors and the innovations introduced to increase the number of transplantation, focusing on efforts to use living and marginal organs to improve transplantation outcomes. Second, we describe and provide insights into the unique features of Japanese living donor lung, liver, pancreas and kidney transplantations (KTs) and ABO blood type incompatible liver transplantation. Finally, we lay out the current challenges and perspectives of organ transplantation in Japan.

This minireview aims to provide important information and useful insights regarding the strategies and innovations Japan has adopted over the years to increase organ transplantation under scarcity of deceased donors.

Japanese strategies for maximizing organs transplanted per brain death donor and outcomes

To maximize organs transplanted per donor (OTPD), the Japan Organ Transplant Network introduced a new system in November 2002. This system involved the partnership of well-trained transplant consultant doctors and local doctors in assessing donor hemodynamics and providing intensive care to donors. Their primary goal is to substantially improve cardiac and lung functions (1). These consultant doctors tirelessly performed bronchial toileting for donors and assisted local anesthesiologists in maintaining optimal circulatory and respiratory conditions during recovery.

With the implementation of this new system, the OTPD in Japan substantially increased to 6.8 in 2008, compared with the United States OTPD of 3.04. As of December 2010, 89 heart, 1 heart–lung, 87 lung, 95 liver and 84 pancreas transplantations were performed from 115 consecutive brain death donors.

For heart transplantations, 90 heart donors included only 21 standard criteria donors for the heart. The remaining 69 heart donors were marginal donors, with high-dose inotrope requirement in 33, with histories of cardiopulmonary resuscitation in 33 and who were older than 55 years without coronary angiogram in 8. None of the 89 heart and 1 heart–lung recipients died of primary graft function. In the 89 heart transplantation patients, 80 were supported with a left ventricle assisting system and the average waiting time was 960 days (range, 29–2772 days). The 10-year posttransplantation survival rate was 95% (Figure 1A). Deaths were caused by infection in two patients at 4 months and 4 years and gastric cancer in one patient at 11 years.

For lung transplantations, 187 procedures have been successfully performed as of December 2010. These transplantations involved deceased donor lung transplantation (DDLuT) in 87 patients, achieving a 10-year patient survival rate of 51% (Figure 1B) and living donor lobar lung transplantation (LDLLuT) in 100 patients (2). Sustained efforts, such as aggressive treatment of donor atelectasis by bronchoscopy or single lung transplantation, have been made to effectively utilize marginal donors. Moreover, lungs were used for transplantation in more than 60% of brain death donors. Presently, more than 130 patients are waitlisted for DDLuT with an average waiting time of 1037 days. The distribution of diagnoses as indication for lung transplantation is unique in Japan (3), with idiopathic pulmonary arterial hypertension (n = 42, 23%) as the most frequent indication, followed by lymphangioleiomyomatosis (n = 36, 19%), idiopathic interstitial pneumonia (n = 30, 16%) and bronchiolitis obliterans (n = 25, 13%). Emphysema (n = 8, 4%) and cystic fibrosis (n = 3, 2%) are rare indications.

The long-term liver (Figure 1D) and kidney (Figure 1E) transplantation outcomes were comparable to those in Western countries.

For pancreas transplantation, 84 procedures from brain death donors and two from donors after cardiac death have been successfully performed. Of the deceased donors, 63% were over 40 years, 59% died of cerebrovascular attack and over 50% required multiple catecholamine treatments at the agonal phase. The recipients were also "marginal" with an average age of 41.5 years, a diabetic period of 28.4 years, a dialysis duration of 7.4 years and an average waiting time of 1482 days. Between 2000 and 2007, the pancreas procurement rate reached 75%.

For simultaneous pancreas and kidney (SPK) transplantation, Japan has achieved a 5-year patient survival rate of 98%, a pancreas graft survival rate of 74% (Figure 1C) and a kidney graft survival rate of 71%.

Expansion of donor pool using living donors

Because of the limited number of donor organs, organ transplantation over the years has transformed into the expansion of the donor pool as part of the innovation in living donor transplantation. Pioneering attempts have been made to use donor after cardiac death in KT, living donor in lung, liver, kidney and pancreas transplantations and marginal donors such as ABO blood type incompatible (ABO-I) kidney, liver and pancreas transplantations to expand the donor pool.

Living donor lung transplantation

LDLLuT has become a realistic option for properly selected candidates to expand the donor pool and has been successful in patients on a ventilator or on extracorporeal membrane oxygenation (4). However, because of possible serious complications in donor lobectomy, LDLLuT has been indicated only for critically ill patients. Moreover, it requires two healthy donors with a compatible blood type. For pediatric lung transplantations, all 21 cases encountered underwent LDLLuTs, because organ recovery was not allowed from brain death donors younger than 15 years until the transplantation law revision. The Japanese experience has revealed higher 5- and 10-year survival rates of 81% and 76% with LDLLuT (n = 100) than the 71% and 51% with DDLuT (n = 87; p = 0.122), respectively (Figure 1B). Long-term improvement in survival has also been achieved using LDLLuT by transplanting two lobes from two donors, taking advantage of the contralateral unaffected lung as a reservoir in case of unilateral chronic rejection (5). To date, there has been no perioperative mortality among living donors.

Living donor liver transplantation

Organ transplantation in Japan saw an initial increase in the number of living donor liver transplantation (LDLT) of up to 570 in 2005, followed by a decrease and status quo of about 450 LDLTs. There were two major LDLT innovations in the last decade: Resolution of graft size mismatch and resolution of blood type mismatch.

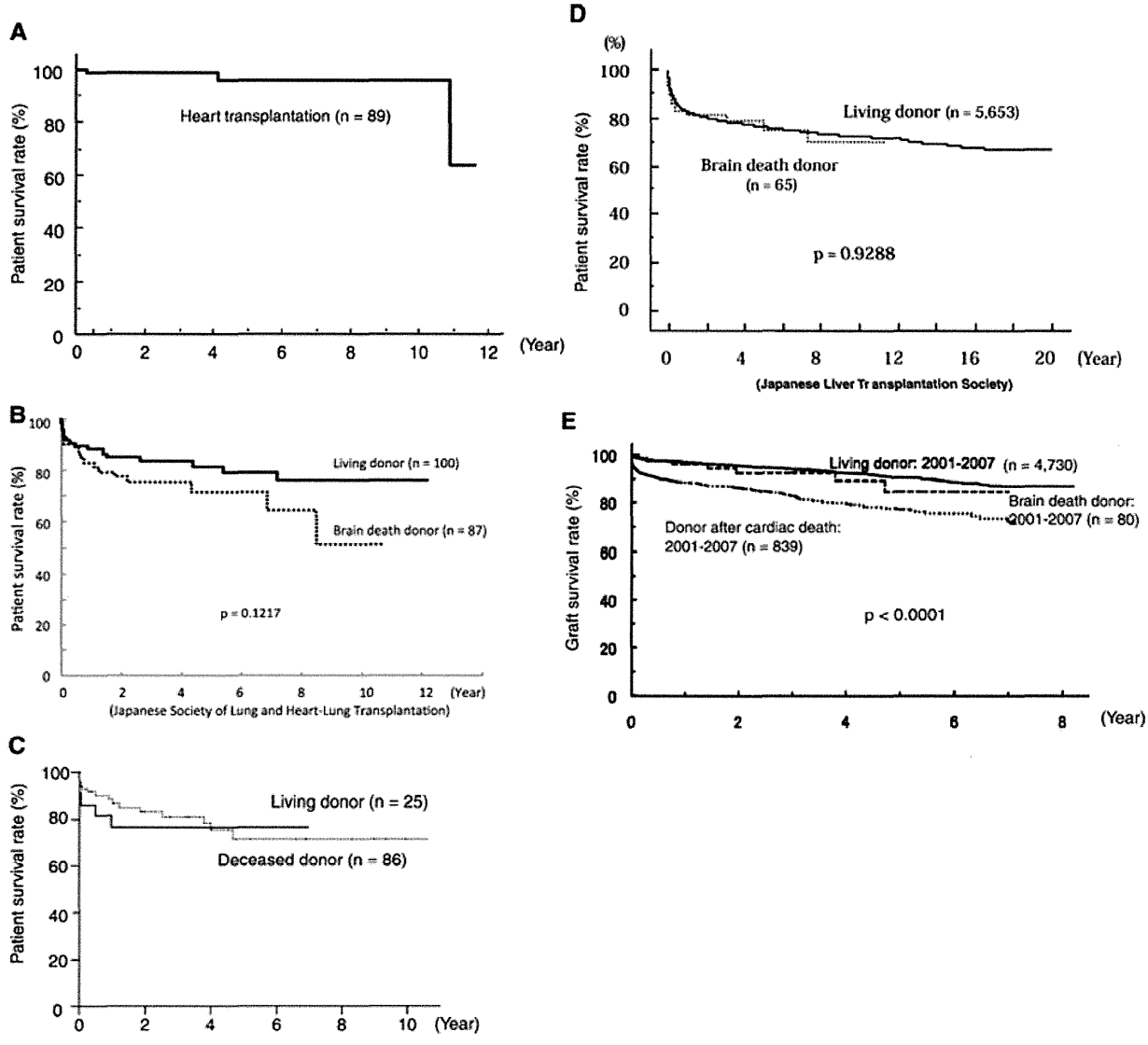

Figure 1: Patient survival rates (%) following organ transplantation in Japan. (A) Patient survival rates (%) in heart transplantation (n = 89): The 10-year patient survival rate was 95%. (B) Patient survival rates (%) in lung transplantation (n = 187): The 10-year patient survival rate was 76% in living donor lobar lung transplantation (LDLLT, n = 100) and 51% in deceased donor lung transplantation (DDLT, n = 87). (C) Graft survival rates (%) in pancreas transplantation in living donor transplantation (n = 25) and deceased donor transplantation (n = 86). (D) Patient survival rates in liver transplantation (n = 5653 as of December 2009): The 10-year survival rate (%) in DDLT (n = 65) was 70% and that in LDLT (n = 3573) was 72% according to the Japanese Liver Transplantation Society. (E) Graft survival rates (%) in kidney transplantation since 2001 (n = 5649): The 5-year graft survival rate of the donor after cardiac death kidney transplantation (n = 839) was 77%, that after brain death donor kidney transplantation (n = 80) was 85% and that after living donor kidney transplantation (n = 4730) was 91%.

The resolution of graft size mismatch involved small-for-size (SFS) and large-for-size (LFS) grafts. Japan has also developed a strategy for a successful LDLT in infants involving the application of hyperreduced left lateral segments (6). Moreover, considerable efforts have been made to improve LDLT using the left lobe following an experience of donor death with LDLT involving a right lobe graft with the middle hepatic vein obtained from a donor with nonalcoholic steatohepatitis (7). In line with all these efforts, the Tokyo group has innovatively included the left caudate lobe to the left lobe graft and developed a patch technique to obtain outflow without congestion (8,9). The Kyoto group achieved further success by portal modulation (10,11).

To assess LDLT-associated complications, the Japanese Liver Transplant Society reviewed the complications in 299 donors among 3565 living liver donors (8.9%; Ref. 12) and reported a case of operation-related mortality

(0.03%). Sustained efforts are underway to reduce donor complications.

Living donor pancreas transplantation

To date, five centers in Japan have performed living related pancreas transplantations in 25 patients (i.e. 21 SPK, 1 pancreas after kidney and 3 pancreas alone transplantations).

The first living donor SPK (LDSPK) transplantation was performed in 16 cases and ABO-I transplantations were performed in six cases (13). In the LDSPK transplantation, donor operation involved right nephrectomy followed by distal pancreatectomy with open laparotomy in eight donors and a laparoscopic procedure in eight donors. Among the 16 cases of LDSPK transplantation, 14 showed no complications, diabetes or renal dysfunction. Only one donor developed a Clavien grade I pancreatic fistula and one donor formed a grade III-a pancreatic cyst. Moreover, 14 patients achieved insulin independency immediately after LDSPK and have maintained insulin independency and shown normal endocrine function. LDSPK transplantation has, thus, far achieved a 3-year patient survival rate of 100%, a 3-year pancreas graft survival rate of 88% and a 3-year kidney graft survival rate of 94%. As of December 2010, the number of LDSPK became 25 (Figure 1C).

Living donor kidney transplantation (LDKT) and donor after cardiac death (DCD) transplantation

As of December 31, 2007, 21 110 KTs were performed (14). Among 12 455 KT recipients whose follow-up data were obtained from transplant centers, 9796 were living donors and 2651 were diseased donors.

Over the last 10 years, the number of KTs has significantly increased, with 1312 KTs performed in 2009 alone, of which 189 cases (14.4%) were deceased donor KTs and only 14 cases (8%) were brain death donor KTs. Until 1997, all deceased donor KTs were DCD KTs.

In the 5649 KTs performed between 2001 and 2007, the 5-year graft survival rates were 77% in DCD KT (n = 839), 85% in brain death KT (n = 80) and 91% in LDKT (n = 4730) (Figure 1E).

KT outcomes have also dramatically improved over the last decade (14). The 5-year graft survival rate in deceased donor KT improved from 66.7% between 1983 and 2000 (n = 2801) to 78% between 2001 and 2007 (n = 919). The 5-year graft survival rate in living donor KT improved from 82% (n = 7089) to 91% (n = 4730). One possible reason for this improvement is the introduction of tacrolimus and mycophenolate mofetil (MMF) in 2001. Interestingly, the outcome of DCD KT in Japan was better than that in Europe or the United States, possibly because the kidney of Japanese could be genetically more tolerant to ischemic injury.

For initial immunosuppression in KT, calcineurin inhibitors (CIs) had been administered because of the unavailability of antithymoglobulin in Japan. Although the incidence of rejection has been low, delayed graft function has been observed in 70–80% of cases. There have been remarkable improvements in KT outcomes from cardiac death donors, but acute rejection and donor age have been identified as independently associated with graft outcome (15). To overcome this problem, KT patients receive intense follow-up even at an additional cost of the medical institution.

Cardiac death organ transplantation

In DCD donation, physicians are allowed to turn off the respirator only after confirming cardiac death. Statements regarding kidney and pancreas recovery from DCD are included in the transplantation law but there are none for liver and lung recovery. However, the law does not prohibit liver and lung recovery from DCD. Three DCD liver transplantations were performed separately in 1964, 1968 and 1993 and two DCD pancreas transplantations were carried out in 1997.

ABO blood type incompatible liver transplantation

Liver: In LDLT in Japan, the chance of transplantation across the ABO blood type barrier is only 10% and 623 ABO-I LDLTs were registered as of the end of 2010. To address this issue, two innovative strategies have been formulated: Hepatic infusion therapy and rituximab prophylaxis (16). The effects of rituximab prophylaxis on ABO-I adult LDLT have been maximized by administering rituximab earlier than 1 week before transplantation (17). The Kyushu group successfully eliminated local infusion treatment by B-cell desensitization with rituximab (18). Although the outcome of ABO-I LDLT was inferior to those of ABO-compatible and identical LDLTs (Figure 2A), outcome in adult ABO-I LDLT has been dramatically improved by rituximab prophylaxis (Figure 2B).

Recently, the Hiroshima group spearheaded the development of a novel concept in preventing antibody-mediated rejection (AMR) in ABO-I transplantation, which involved the elimination of B cells responding to blood group A carbohydrates through blockade of B-1 cell differentiation by CIs (19).

Japanese doctors have also exerted considerable efforts to identify AMR markers to enable early diagnosis and immediate treatment. These markers included edema in the portal tracts with portal hemorrhage and mild neutrophil infiltration as early diagnostic histological features of humoral rejection in ABO-I liver transplantation (Figure 3A; Ref. 20). Diffuse C4d staining in portal capillaries and periportal areas observed in severe AMR has also been identified as a good surrogate marker (Figure 3B).

Kidney: To overcome deceased donor shortage, Japanese doctors have also pioneered in ABO-I LDKT. The first case

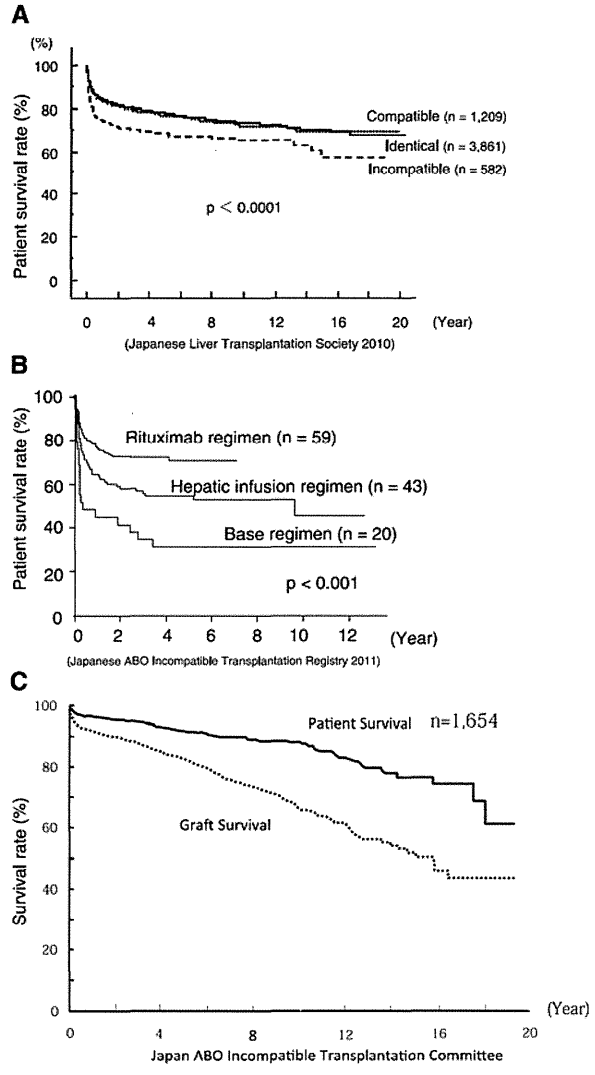

Figure 2: Outcomes of ABO incompatible living donor liver and kidney transplantations. (A) Comparison of patient survival rates (%) among ABO identical, compatible and incompatible living liver transplantations. (B) Adult patient survival rates (%) following ABO-incompatible liver transplantation in three regimens: The survival rate was improved with the introduction of hepatic infusion therapy and further with rituximab. The base regimen consisted of triple immunosuppression with plasma exchange with or without splenectomy. The infusion regimen was composed of base regimens with hepatic infusion. The rituximab regimen consisted of a base regimen with rituximab prophylaxis with or without hepatic infusion. The 5-year patient survival rates were significantly different at 70%, 54% and 31% for the rituximab, hepatic infusion and base regimens, respectively ($p < 0.001$). (C) Patient and graft survival rates (%) after kidney transplantation between blood type incompatible LDKTs.

of ABO-I living related KT (ABO-I LRKT) was performed in 1989 and more than 20% of LRKTs in 2009 were ABO-I (14). Two major innovations for immunosuppression in ABO-I LRKT have been initiated: The introduction of tacrolimus and MMF in 2001 and that of rituximab in 2005. ABO-I LRKTs performed in 876 cases between 2001 and 2007 has achieved relatively high graft survival rate of 86% at 5 years after transplantation (Figure 2C; Refs. 14,21). Recently, Tokyo Women's Medical University has reported a 5-year graft survival rate of 97% for ABO-I LRKT with rituximab. The recent pioneering efforts made for ABO-I LDKT have produced higher graft survival rates and lower incidence rates of AMR than those for ABO-compatible LRKT (22).

Pancreas: For the six ABO-I LDSPK transplantations performed in Japan, pretransplantation rituximab desensitization has achieved insulin independency and withdrawal from hemodialysis without any AMR episode in all patients (13).

Current Challenges and Perspectives

Anti-HLA antibody-related rejection

The recent recognition of the importance of qualitative and quantitative evaluations of anti-HLA antibodies in KTs has led to the development of successful strategies using rituximab and IVIG to prevent organ rejection (23). Controversies, however, remain regarding the significance of conventional cytotoxic lymphocyte crossmatch in liver transplantation (24,25). The single beads method has also been used to identify quantitative changes of donor specific antibody (DSA) in a case of fatal AMR (26). Comprehensive strategies for identifying DSA quantitative changes have nearly been established in KT, but remain a challenge in liver transplantation. Determined attempts are underway to introduce innovative B-cell depleting regimens for ABO-I transplantation when DSA-positive combination cannot be avoided in LDLT. Efforts are also currently focused on clarifying the importance of DSA in long-term graft injuries in kidney and liver transplantations. Further developments in immunosuppressants, which have led to the approval of evelorimus only for heart transplantation, are also being initiated to prevent organ rejection.

Tolerance

Innovations to reduce immunosuppresant use have been spearheaded by the Kyoto group, which has attempted tacrolimus withdrawal in pediatric LDLT (27). The tacrolimus withdrawal based on hepatic chemistry values caused severe graft fibrosis, but liver functions remained normal. The Hiroshima group has, in turn, identified an immunoregulatory role of sinusoidal endothelial cells in mice and has developed a novel mixed lymphocyte reaction assay capable of indicating donor specific hyporesponsiveness in humans (28,29). The group's strategy has been to gradually reduce immunosuppression by confirming donor specific hyporesponsiveness, successfully improving tolerance in adult LDLT cases.

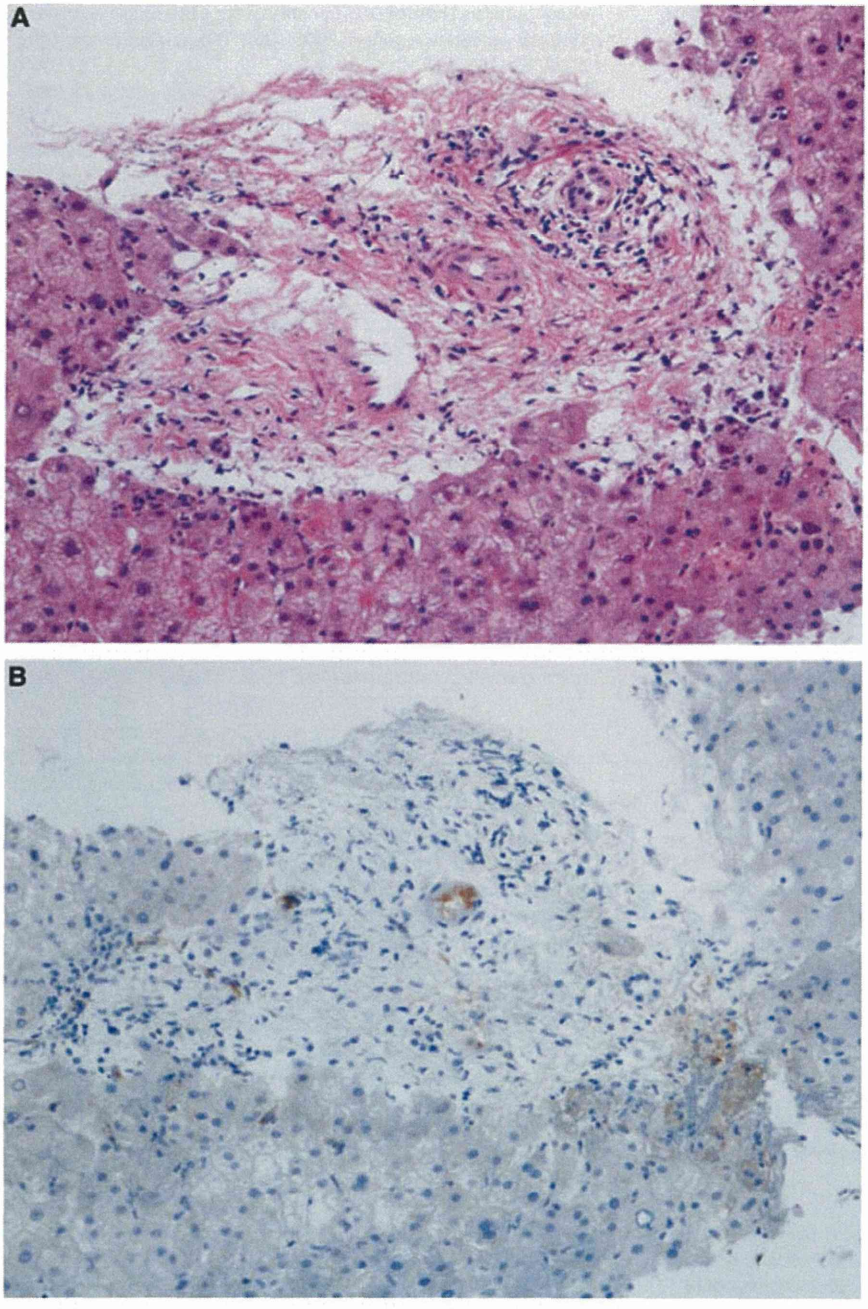

Figure 3: Early histopathological findings in antibody-mediated rejection after ABO-incompatible liver transplantation. The liver specimens were fixed in 10% buffered formalin, processed routinely, cut into 3-μm-thick paraffin sections and stained. (A) Edema in the portal tracts with portal hemorrhage and mild neutrophil infiltration (hematoxylin and eosin stain). Although periportal hepatocyte necrosis is occasionally observed, perivenular necroinflammation is usually minimal or absent in the early phase of antibody-mediated rejection. These histopathological findings can only be observed within several days after the onset of antibody-mediated rejection. (B) Diffuse C4d staining in portal capillaries and periportal areas in severe antibody-mediated rejection. A polyclonal antibody against C4d complement (BI-RC4D; Biomedia, Vienna, Austria) in the ratio 1:50 was used with an automated immunostainer (BENCHMARK XT, Ventana Medical Systems, Tucson, AZ, USA). For antigen recovery, deparaffinized and rehydrated sections were treated with protease I (Ventana Medical Systems, 0.5 U/mL) at 37°C for 20 min.

Tailor-made immunosuppression based on infectious immune status

Infectious complications have remained the primary cause of posttransplantation mortality. This has prompted the clarification of CD8 immunity features in LDLT (30). This has also led to the detailed elucidation of host immune regulation from the viewpoints of the $CD8^+CD45$ isoforms and the demonstration of the coupled regulation of interleukin-12 receptor beta-1 of $CD8^+$ central memory and CCR7-negative memory T cells in an early alloimmunity in liver transplant recipients (30). From this recent elucidation of immune molecular mechanisms, tailor-made immunosuppression seems promising and should receive greater attention.

Summary, Implications and Future Goals

The success of Japan in overcoming diseased donor shortage over the years lies in its strategy of maximizing organs transplanted per brain death donor, expanding the donor pool using living donors, using living and marginal organs to improve outcomes, steady improvements in living donor lung, liver, pancreas and KTs and advancing ABO blood

type incompatible liver transplantation. Moreover, the excellent outcomes of donor after cardiac death KT have inspired Western countries to follow Japan's example. Japan has also overcome the ABO blood type barrier in kidney and liver transplantations and is exerting sustained efforts in achieving this in pancreas transplantation. Immunosuppression reduction, leading to improved outcomes after organ transplantation, has been achieved by carefully monitoring donor-specific hyporesponsiveness and infectious immunostatus. This nonaggressive step has achieved tolerance, unlike aggressive strategies such as complete lymphocyte depletion or bone marrow transplantation.

Japan has currently achieved the maximum OTPD in brain death donors through the efforts of dedicated and experienced surgeons. The application of the Japanese strategies has enormous potential to increase the number of transplantations under the scarcity of diseased donors and the additional costs for intensive donor treatment may prove to be cost-effective.

Despite these innovations, the mortality rate of patients on the waiting list has remained at 30–40% for all organs. Therefore, the next issue that must be carefully addressed by Japan is how to institute amendments to the allocation systems. Moreover, Japan must intensify and orchestrate its efforts to decrease morbidity of living donors and to increase the number of brain death donors.

Acknowledgments

We greatly appreciate the following for providing important information regarding this mini-review: Japan Organ Transplant Network (JOTNW), Japan Transplant Society, Japanese Society of Lung and Heart-Lung Transplantation, Japanese Liver Transplantation Society, Japanese Registry of ABO Blood Type Incompatible Transplantation, Dr. Atsushi Aikawa (Toho University), Dr. Yuzawa Kenji (National Hospital Organization Mito Medical Center), Drs. Shiro Takahara and Toshinori Ito (Osaka University), Dr. Kenmochi Takashi (Chiba-East National Hospital), Drs. Kota Takahashi and Kazuhisa Saito (Niigata University) and Dr. Makiko Naka Mieno (Jichi Medical University).

We are also indebted to Assistant Professor Edward F. Barroga and Associate Professor Raoul Breugelmans of the Department of International Medical Communications at Tokyo Medical University for their editorial review of the English manuscript.

Disclosure

The authors of this manuscript have no conflicts of interest to disclose as defined by the *American Journal of Transplantation*.

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脳死ドナー評価・管理の現状と将来の展望

福 嶌 教 偉*

REVIEW ARTICLE

Current status and future aspect of evaluation and management of brain dead donor in Japan

As donor shortage is extremely severe in Japan because of very strict Organ Transplantation Law, special strategies for maximizing organ transplant opportunities should be established. Since November in 2002, special transplant management doctors were sent to donor hospitals in order to assess donor's organ function and to identify which organ could be transplanted. They also intensively cared the donor to stabilize hemodynamics and to improve cardiac and lung function by intravenously giving anti-diuretic hormone and pulmonary toileting by bronchofiberscopy. Organs procured from one donor increased from 4.5 to 5.6 after these strategies were applied. Patient survival rate at 10 years after each organ transplant was acceptable and comparable to that of other developed countries. Although the number of transplantation was still very small, the availability of organs has been very high and the outcomes of each organ transplantation were acceptable. These strategies may be useful to maximizing organ transplant opportunities.

*Norihide Fukushima**

key words : donor evaluation and management, organ transplantation, medical consultant, bronchofiberscopy

ドナー評価と管理を綿密に行うことにより，移植できる臓器を増加させ，移植後の臓器機能を向上させることは，移植を受ける患者にとっても，提供するドナーと家族にとっても重要である．

欧米では標準的なドナー適応基準に従ってドナーの適応が決められていることが多いため，日本に比較して胸部臓器の提供が少なく，1人のドナーから3,4臓器しか移植されていないが，わが国では5,6臓器が移植されている．同時に，わが国の移植後成績は欧米と遜色ない．

本稿では，このようなわが国の脳死ドナー評価・管理の現状と将来の展望について述べる．

脳死ドナーの臓器評価の流れ(表1)

1．第一次評価

まず，提供病院などからドナー情報があった時点で，日本臓器移植ネットワークコーディネーターは提供病院に赴き，本人および家族の臓器提供の意思の確認を行うとともに，ドナーの絶対的禁忌事項がないかどうかを確認する．

ドナーの絶対的禁忌事項とは，① 悪性腫瘍(原発性脳腫瘍などで完治したものは除く)，② 活動性の重症感染症(敗血症)，③ HIV抗体陽性，HB抗原陽性である．

また，厚生労働省は，Creutzfeldt-Jacob病，West Neil病を除外するために海外渡航歴を考慮した基準を独自につくっているので，たとえ医学的にその可能性が低いと考えられても，その基準に従わなくてはならない．

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表1 脳死下臓器提供におけるドナー評価の流れ

- ドナー情報
  - ↓ 第一次評価：ドナー適応基準
    ドナーとして妥当か？
- 家族の意思確認
- 第1回脳死判定
  - ↓ 第二次評価：各臓器機能評価
    どの臓器が移植可能？
- 第2回脳死判定
- レシピエント意思確認
  初期情報シート(第一次・第二次評価まとめ)
- 摘出チーム到着
  - ↓ 第三次評価：各移植施設が評価
- 摘出前ミーティング
  - ↓ 最終評価
- 臓器摘出

表2 ドナー評価のための検査

- 脳死完成時の血行動態(心肺蘇生の有無)
- 感染症などの禁忌事項のないことの確認
- 血行動態の解析
  使用カテコラミン，血圧，CVP，尿量など
- 胸部・腹部レントゲン写真
- 心電図
- 超音波検査(心臓・腹部)
- 気管支鏡検査
- 血清電解質・酵素など
- 感染症検査(喀痰，尿などの培養検査)
- できれば胸部・腹部CT検査

2．第二次評価

第1回の法的脳死判定が終了した時点で感染症検査，各臓器の機能検査，HLA検査を行い，メディカルコンサルタント(MC)の協力・指導を得ながらドナーとして適当であるか否かを確認する．

MCは，ドナー評価・管理担当のコーディネーターと連携しながら，各種検査データを確認したうえ，不足な検査をオーダーしたり，MC自身で心臓・腹部超音波検査を行ったり，移植施設へのレシピエント意思確認までに充分な評価を行うように努めている．ドナーの評価法の詳細を**表2**に示すが，MCは臓器ごとにドナーとして適当かどうかを各種検査結果から総合して評価する．

3．第三次評価

移植施設のスタッフが，摘出直前の臓器の状態を把握することは，移植後の臓器機能や問題点などを予測したり，ドナー臓器に応じて保存・摘出手技に工夫を加えたりすることができるので，移植後の成績を向上させていると考える．また，移植施設自らの責任で，移植するか否かを決定するので，臓器提供施設に評価(移植の可否の決定)の責任を転嫁することがないことも，提供施設の負担を減らすという意味で重要である．

メディカルコンサルタントの現状

2002年11月以降はMCが導入され，第1回の脳死判定以降に提供施設に派遣され，ドナーの評価を行い，第2回の脳死判定以降からドナー管理を行うようになっている．ドナー管理の基本が呼吸循環管理であるため，心臓移植医，ついで肺移植医がドナー管理を行っているが，必要に応じて臓器評価については臓器ごとのMCに評価を依頼することもある．2002年当初はMCの数も少なかったが，2011年1月末現在，心臓移植施設から各2名，肺移植施設から各3名，その他の臓器移植施設の移植医おのおの数名が日本臓器移植ネットワークからMCの委託を受けている．

MCは，ドナー家族による脳死臓器提供の承諾が得られて，第1回の脳死判定開始前に第一報を受け，多くの場合，第1回の脳死判定終了直後に提供施設に赴き，後述の業務を担当する．ドナーの血行動態が不安定な際には，それを安定させるために相談を受けたり，提供施設の希望がある場合には，無呼吸テストに立ち合い，循環動態管理の支援を行ったりすることもある．

拘束時間が長いため，ドナー評価，管理，臓器摘出手術の支援を複数のMCが分担することも多い．

1．ドナー評価

MCは臓器ごとの評価を行うとともに，ドナーチャートの記載内容を確認し，レシピエント候補が移植を受けるために必要な情報が記載されているかどうかを確認する．

まず，ドナーの脳死発生時の病態，血行動態の推移，各種検査(血液検査，画像検査など：**表2**)を確認する．そのうえで，検査の欠落をチェックし，脳死判定開始から摘出手術開始までの定期的検査

(末梢血, 生化学, 血液ガス, 胸部X線検査)をコーディネーターと相談して提供施設に依頼する(評価のためだけでなく, ドナー管理に必要な検査も必要に応じて依頼する). 血行動態の指標, 輸液量, カテコラミン・抗利尿ホルモン(ADH)の種類・投与量などのチェックも行い, 循環動態を正確に把握するように努める. 管理という意味では, 呼吸状態(人工呼吸器の条件, 画像, 喀痰の性状など)も評する.

心エコー, 腹部エコーをMC自身で行う. その際, 心機能および各臓器の形態を検査するとともに, 副病変(腫瘍など)の有無を確認する. できれば気管支鏡検査を行う(肺移植医の応援, 提供施設の医師に依頼することも多い).

評価終了後, ドナーチャートの記載内容をチェックし, 移植の可否がわかるような画像を選択し, レシピエントの意思確認の際に, 可能な限り電子ファイルにして移植施設に送るようにする. 移植施設でのレシピエントの意思確認の際に, 必要に応じて移植施設の担当者に情報を説明し, 移植を行うかどうかを決定する際の助言をする.

2. ドナー管理

MCは提供可能な臓器数を増加させるとともに, 移植後機能を良好にするための管理を行う. 基本的には, 呼吸循環管理を行い, 循環動態を安定させることが重要である. 本来は第2回の脳死判定以後の管理となるが, ADHの投与, 中枢ラインの確保(可能な限り頸静脈から), 人工呼吸器の条件の改善, 体位変換(ときにファーラー位), 気管支鏡などによる肺リハビリテーション, 感染症の管理(抗生剤の投与など)は, 提供施設の了解があれば, ドナー家族の脳死判定・臓器提供の承諾のとれた以後, 可能である.

ドナー臓器の機能を温存するための管理は, 第2回の脳死判定が行われ, かつ家族の臓器提供への同意が得られてから開始する. 心臓の場合には, 脳死完成時およびそれに引き続くショックのために心筋が障害されているので, 循環動態をうまく維持してやれば, 必ずしも早急に臓器摘出手術を開始する必要はない. むしろstunningが改善されてから摘出したほうがよい.

心機能の保全は, 前負荷および後負荷の調節によって行う. 尿量にかかわらず, ADHを中枢ルートから持続静脈内投与(0.5〜1 U/時間)して, カテコラミンの投与量を最低維持量(可能な限りドパミン10 μg/kg/min以下)にとどめる. 平均動脈圧を80 mmHg程度または収縮期血圧を90 mmHg以上(ただし120 mmHg以下), 中心動脈圧を5〜10 cmH_2Oに保つ. 低血圧に対しては原則的にドパミンを投与する. 状況に応じて輸血も行う(ヘマトクリットは30%以上に保つ). 脳死者は心臓や血管への神経反射が消失するため, 体位変換・気管内吸引(気道内圧の変動で, 肺の血液灌流が変動)などで血圧が変動しやすい[1]. このような状態で, ADHの投与により, 尿量を1〜2 mL/kgくらいにコントロールすると, 水分バランスの出納が安定し, 血行動態が安定することが多い[1,2]. ノルアドレナリンは腹部臓器の血流を低下させるので, なるべく使用しない. アドレナリンも投与量が増加すると, 心筋のアドレナリン受容体密度が減少するので, なるべく使用しない[3,4].

呼吸の管理は, PaO_2を70〜100 mmHg以上(SaO_2で95%以上), $PaCO_2$を40 mmHg前後, pHを7.35〜7.45に保つ. 気道への神経反射(咳嗽反射など)が消失するので, 定期的な体位変換と気道内吸引は肺感染症・無気肺の予防で重要である. 脳死状態では咳嗽反射が消失し, 無気肺から肺炎に進行しやすいため, 評価のみならず管理のためにも, 気管支鏡検査は重要である. 脳死下で充分な呼吸管理を行うためにも, ADHの投与は有用である. 脳死状態では, 低体温, 低カリウム血症になりやすいので, 体温, 電解質の補正も重要である. 褥瘡予防の体位変換, 感染予防のためのカテーテル, 気道系, 創部, 褥瘡のケアも大切である. 感染が疑われるときには, 可能であれば検査を依頼する.

3. 臓器摘出手術における呼吸循環管理の支援

MCは提供可能な臓器数を増加させるとともに, 移植後機能を良好にするための管理を行う(ドナー管理と同じくらい重要な役割である).

ドナー入室前には, 手術室内の準備を支援する. 摘出前ミーティングで, 臓器摘出法, 呼吸循環管理などについて必要に応じてコメントする. ドナー入室時に手術部内への搬送, 手術台への移動

(ときには病棟からの移送)を支援する．執刀前のドナーの状態把握，除細動パッド等の装着などの支援を行う．基本的に麻酔科医が呼吸循環管理を行うが，摘出手術の進行に応じて，輸血，輸液，呼吸管理などの支援を行う．可能であれば，摘出医のリーダー(多くは心臓摘出医)と連携して，摘出手術が円滑に行えるように支援する．

基本的には，吸入麻酔薬などは使用せず，極力カテコラミン(特にアドレナリン，ノルアドレナリンなど)を使用せず，血圧低下には輸血，アルブミン製剤の補填で対応する．こうすることで，各臓器の血流が維持され，保存液の灌流が良好となり，移植後の臓器機能が保たれる．

わが国の脳死臓器移植の成績

1999年2月の脳死臓器移植開始後，2011年末までに159件の脳死臓器提供があった．ドナーの平均年齢は45.1歳，男性91名，女性68名であった．脳死の原因は，くも膜下出血74名，脳梗塞7名，脳出血15名，頭部外傷28名，窒息25名，蘇生後脳症8名，その他2名であり，脳血管障害が多い．55歳以上45名，心肺蘇生の既往55名，ドパミン換算で10 μg/kg/min以上のカテコラミン持続点滴を要するドナー61名などの，マージナルドナーからの臓器移植が行われた．

上記の脳死ドナーから，120件の心臓，124件の肺，1件の心肺同時，136件の肝臓，20件の膵臓，99件の膵腎同時，196件の腎臓，12件の小腸移植が実施された．

臓器提供率(全ドナーに対するその臓器が提供された比率)は，心臓76.1%，肺62.9%，肝臓78.6%，膵臓74.2%，腎臓91.8%と高い水準を示していた．臓器提供率を米国と比較すると，日本では腎臓は同程度で，肝臓は低かった(脂肪肝，ショック肝が多いため)が，心臓，膵臓，肺は3〜5倍の提供率であった．臓器提供率を増加させた結果，ドナー1人当たりの提供臓器数，移植患者数も米国に比して高かった．この数値は漸増し，MC導入以前の1〜10例目の平均はおのおの3.8臓器，3.7名であったのに対し，脳死臓器提供の141〜160例目はおのおの5.6臓器，4.9名であった(**図1**)．

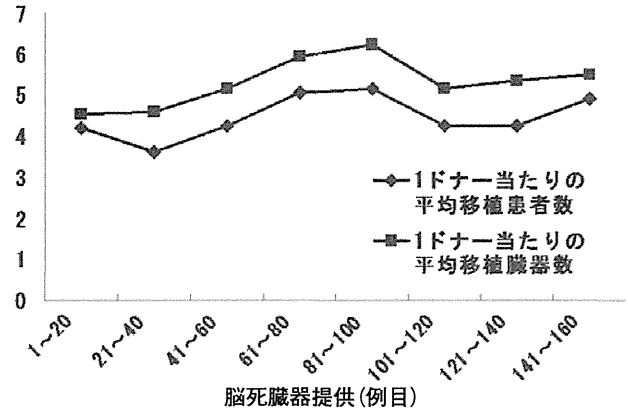

図1 わが国の脳死ドナー1人当たりの移植臓器数の推移(2011年12月31日)
米国：ドナー1人当たりの平均移植臓器数3.05

臓器提供率の増加に伴い，移植後成績が低下すれば問題となるが，各臓器の5年生着率は，心臓95.2%，肺72.7%，肝臓78.6%，膵臓76.0%であり(日本臓器移植ネットワーク調査，2010年12月末現在)，各臓器の移植後成績は遜色のないものである[4]．心臓については，70%以上がいわゆるextended criteria donorであるが，primary graft failureで死亡した症例はない．

2008年11月に，米国や他国の臓器提供施設を視察した際，わが国の臓器提供率と成績を紹介したところ，非常に高い評価を得，現地でもわが国の制度を導入したいという評価をもらっている．

臓器移植法改正後の課題

2010年7月に改正臓器移植法が施行され，脳死臓器提供数は飛躍的に増加し，2011年末までの半年弱で63件であった．心臓移植施設を中心に多くのMCが現地に派遣されることにより，提供可能と判断されるほとんどの臓器が提供に至り(**図1**)，移植後成績も維持されている．

現在，心臓・肺移植施設の協力を得て，緊急の連絡にもかかわらず，MCが提供病院に赴き，ドナー評価・管理を行っているが，今後脳死臓器提供数がさらに増加すると対応できない可能性もある．実際，同日に3,4件のドナー情報がある場合もあり，MCが到着するまでに，ある程度ドナー評価･管理ができるようにすることも重要である．

2008年度から，厚生労働科学研究費補助金　免疫アレルギー疾患等予防・治療研究事業「脳死並