SAGL, and Zone C with high risk of SAGL. Graft volumes were calculated in a volumetric study, using pre-operative CT scans. LDLT recipients in Zone A had the prognosis of Group A, Zone B had the prognosis of Group B, and Zone C had the prognosis of Group C as described in Figure 2. Recipient-donor matches in Zone A are ideal, and matches in Zone C should be avoided.

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Table 1 Demographies and variables

	SAGL group	Control group	P
Number of patients	12	125	
Male/Female	6/6	65/60	0.895
Age (yr)	46.8±14.6	50.8±11.8	0.286
Etiology (n)			
HBV	3	26	
HCV	3	47	
Alcholic	0	2	0.563
PBC/PSC/AIH	1	17	
Fulminant	1	9	
others	4	16	
Pre-operative MELD score	32.1±11.0	19.7±7.0	<0.001
Donor age (yr)	46.9±14.4	39.1±13.1	0.054
Graft type (n)			
Left lobe	6	50	0.707
Right lobe	1	67	
Right lateral section	5	10	
ABO blood type incompatibility (n)	2	15	
Graft Weight (g)	483.1±158.4	563.1±131.7	0.05
Graft Weight/recipient esitmated SLV (%)	39.4±12.4	46.8±10.2	0.021
Graft Weight/recipient weight ratio	0.74±0.26	0.88±0.23	0.043
Operative time (min)	985±260	796±163	0.030
Warm ischemic time (min)	50.2±15.6	43.0±10.4	0.138
Cold ischemic time (min)	112.2±86.3	95.5±53.1	0.697
Operative blood loss (ml)	20199±18115	8412±9000	0.057
Highest serum bilirubin level 4-28 days after transplant (mg/d	35.5±11.4	13.0±9.5	<0.001
Post-operative surgical complications (n)	1 (8.3%)	17 (13.6%)	
Hepatic artery thrombosis	0	1 (0.8%)	0.606
Portal venous thrombosis/stenosis	1 (8.3%)	4 (3.2%)	
Bile duct stricture/leak	0	12 (9.6%)	

Table 2 Multivariate Logistic regression analyses

All pre- and post-operative variables

Variables	OR	95% CI		P
Pre-operative MELD score	0.802	0.670	0.961	0.021
Donor age (yr)	-			0.802
Graft Weight/recipient esitmated SLV (%)	1.221	1.017	1.466	0.032
Operative time (min)	-			0.065
Operative blood loss (ml)	-			0.428
Highest serum bilirubin level 4-28 days after transplant (mg/dl)	0.829	0.725	0.949	0.006

Pre-operative variables

Variables	OR	95% CI		P
Pre-operative MELD score	0.783	0.689	0.891	<0.001
Donor age (yr)	-			0.599
Graft Weight/recipient esitmated SLV (%)	1.163	1.039	1.301	0.008

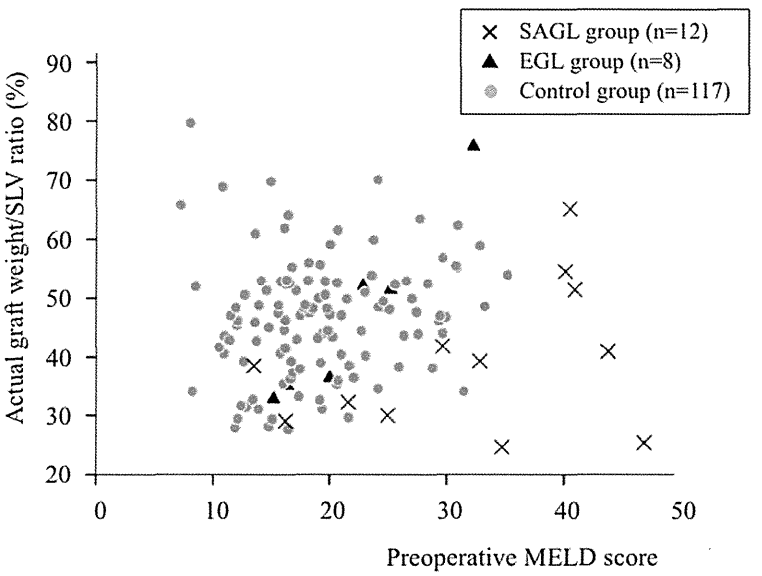

Figure 1. Scattered plots with actual graft weight/SLV ratio and preoperative MELD score in LDLT recipients (n=137)

Figure 1. Scatter plots of the actual graft weight/SLV ratios and pre-operative MELD scores in LDLT recipients (n=137).
SAGL, small-for-size associated graft loss (n=12); EGL, early graft loss (n=8); Control, the rest of the recipients (n=117).

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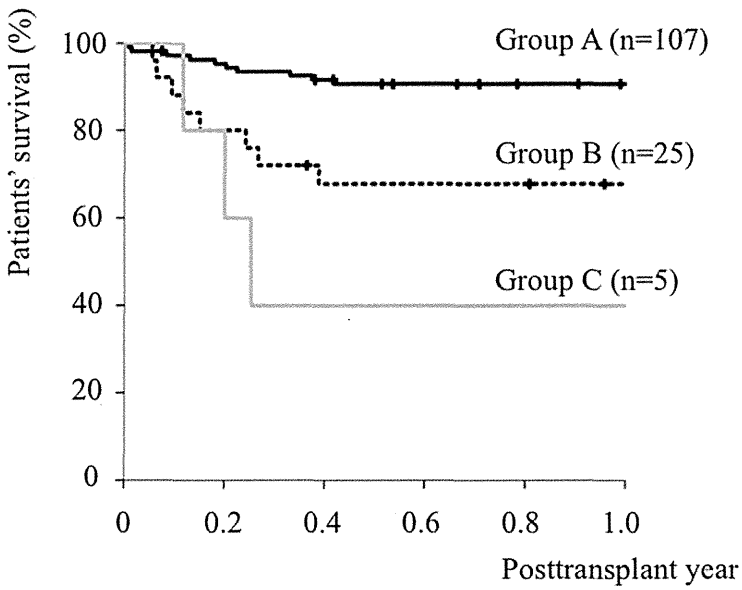

Figure 2. Patients' survival after LDLT in Group A, B, and C

Figure 2. Patient survival after LDLT in Groups A, B, and C.
Recipient-donor matches were categorized into three groups according to risk score: Group A (n= 107), risk score > 2.187; Group B (n=25), risk score > 0 and ≤ 2.187; Group C (n= 5), risk score ≤ 0. The risk score was calculated based on the logistic regression model. The graft survival curve for the recipients showed excellent stratification of these three groups (P=0.003, log rank test). The graft survival rate 6 months after LDLT was 90.6% in Group A, 67.8% in Group B, and 40.0% in Group C.

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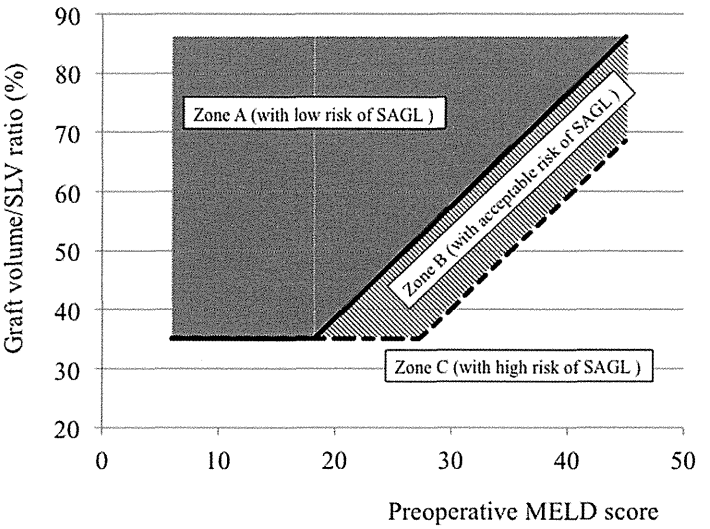

Figure 3. Zone A, B, and C according to Graft volume and MELD score matches

Figure 3. Zones A, B, and C according to graft volume and MELD score matches.
Zone A includes cases with low risk of SAGL, Zone B with acceptable risk of SAGL, and Zone C with high risk of SAGL. Graft volumes were calculated in a volumetric study, using pre-operative CT scans. LDLT recipients in Zone A had the prognosis of Group A, Zone B had the prognosis of Group B, and Zone C had the prognosis of Group C as described in Figure 2. Recipient-donor matches in Zone A are ideal, and matches in Zone C should be avoided.

254x190mm (72 x 72 DPI)

De Novo Malignancy After Pancreas Transplantation in Japan

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ABSTRACT

Background. Long-term immunosuppression is associated with an increased risk of cancer. Especially, the immunosuppression in pancreas transplantation is more intensive than that in other organ transplantation because of its strong immunogenicity. Therefore, it suggests that the risk of post-transplant de novo malignancy might increase in pancreas transplantation. However, there have been few studies of de novo malignancy after pancreas transplantation. The aim of this study was to analyze the incidence of de novo malignancy after pancreas transplantation in Japan.

Methods. Post-transplant patients with de novo malignancy were surveyed and characterized in Japan.

Results. Among 107 cases receiving pancreas transplantation in Japan between 2001 and 2010, de novo malignancy developed in 9 cases (8.4%): post-transplant lymphoproliferative disorders in 6 cases, colon cancer in 1 case, renal cancer in 1 case, and brain tumor in 1 case.

Conclusions. We clarified the incidence of de novo malignancy after pancreas transplantation in Japan.

RECENTLY, prognosis after organ transplantation has been much improved because of development in immunosuppressive methods, surgical techniques, and perioperative management, resulting in increases in post-operative long-term survival cases. With the improved prognosis, an increased risk of de novo malignancy becomes one of the problems after transplantation because of long-term immunosuppression [1,2]. Especially, the immunosuppression in pancreas transplantation (PTx) is more intensive than that in other organ transplantation because of its strong immunogenicity, which suggests a possibility of increased incidence of de novo malignancy after PTx. Thus far, however, there have been few studies of de novo malignancy after PTx [3–6]. Moreover, these limited studies are all from Europe and the United States, and no studies are reported regarding the incidence of post-PTx de novo malignancy in Japan. In the present study, we aimed to analyze the incidence of de novo malignancy after PTx and to characterize the malignancy in the PTx patients in Japan.

PATIENTS AND METHODS

Between 2001 and 2010, 107 PTx from deceased donors were performed for type 1 diabetes in Japan. PTx of these cases were performed in 14 of 17 institutions approved in Japan. Among them, 9 cases (8.4%) developed de novo malignancy after PTx. Nine patients with post-transplant de novo malignancy were surveyed and characterized. Clinical backgrounds of the 9 patients with post-PTx de novo malignancy are shown in Table 1; they included 7 men and 2 women, with a median age of 37 years (range, 30–54 years). The pancreas grafts included 6 from deceased donors and 3 from living donors. The 9 cases included 8 simultaneous pancreas-kidney transplantations and 1 pancreas-after-kidney transplantation. Regarding immunosuppression, basiliximab was used for induction therapy in 8 of 9 cases. As maintenance, all the patients received calcineurin inhibitors (CNI) (tacrolimus in 7 cases, cyclosporine A in 2 cases), mycophenolate mofetil (MMF), and steroids. Rejection of the transplanted pancreas graft occurred in 1 case.

RESULTS

In Table 1, the clinical backgrounds are summarized for the 9 patients who developed de novo malignancy after PTx:

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Table 1. Clinical Backgrounds of Cases With De Novo Malignancy After PTx

Factors	
Sex (M/F)	7/2
Age at PTx (years)	37 (30–54)
Age at diagnosis of malignancy (years)	47 (37–62)
Interval between PTx and diagnosis of malignancy (months)	23 (5–106)
History of malignancy before PTx (–/+)	9/0
PTx category (SPK/PAK)	8/1
Donor (deceased/living)	6/3
Immunosuppressant	
Induction; basiliximab (–/+)	1/8
Maintenance; CNI, steroids, MMF (–/+)	0/9 (CNI; TAC in 7, CsA in 2)
History of rejection (–/+)	8/1
De novo malignancy	
PTLD	6
Colon cancer	1
Renal cancer	1
Brain tumor	1

Data are expressed as number of patients or median (range).
Abbreviations: PTx, pancreas transplantation; SPK, simultaneous pancreas-kidney transplantation; PAK, pancreas-after-kidney transplantation; CNI, *calcineurin inhibitor*; MMF, *mycophenolate mofetil*; TAC, *tacrolimus*; CsA, cyclosporine A; PTLD, post-transplant lymphoproliferative disorder.

post-transplant lymphoproliferative disorders (PTLD) in 6 cases, colon cancer in 1 case, renal cancer (renal cell carcinoma) in 1 case, and brain tumor (glioblastoma) in 1 case. Clinical characteristics of the 9 patients with de novo malignancy are shown in Table 2. In terms of the 6 cases with PTLD (Nos. 1–6), PTLD was found in the lymph nodes (3 cases; Nos. 1, 3, and 5), brain (2 cases; Nos. 2 and 6), and liver (1 case; No. 4). The median interval between PTx and diagnosis of de novo malignancy was 23 months (range, 5–106 months). None of the 9 patients had a history of malignant diseases, and the developed malignancies were not detected at the pre-PTx examination. For treatments against the malignancy, dosage of MMF and CNI was reduced in all the patients, and everolimus, an mTOR inhibitor, was added in 2 patients of the 9 patients. Chemotherapy was performed in 5 patients with PTLD (Nos. 1–5), and the remaining 1 patient with PTLD received whole-brain radiotherapy (No. 6); chemotherapy included a single agent with anti-CD20 monoclonal antibody (rituximab) in 4 patients (Nos. 1, 2, 4, and 5) and cyclophosphamide, doxorubicin, vincristine, and prednisone plus rituximab in 1 patient (No. 3). The patient with colon cancer was treated with endoscopic mucosal resection (No. 7), and the patients with renal cancer and brain tumor received surgical resection (Nos. 8 and 9, respectively).

In response to these treatments, 5 patients (Nos. 1, 3, and 4–6) showed complete response to the treatments, and they remain alive without recurrence after the treatment. On the other hand, in the remaining 1 patient with brain PTLD, the effect of the chemotherapy was not enough, resulting in death from the malignancy (No. 2). The

Table 2. Clinical Characteristics of De Novo Malignancy After PTx

No.	Sex	Age (Years)	Donor	PTx Category	Immunosuppressant	Type of Malignancy	Interval Between PTx and Diagnosis of Malignancy (Months)	Treatment for Malignancy	Survival After Diagnosis of Malignancy (Months)	Prognosis
1	M	30	Living	SPK	Basiliximab, TAC, steroids, MMF	PTLD (LN)	5	Rituximab	75	Alive w/o recurrence
2	M	36	Living	SPK	Basiliximab, CsA, steroids, MMF	PTLD (brain)	99	Rituximab	5	Dead of the malignancy
3	M	37	Deceased	SPK	Basiliximab, TAC, steroids, MMF	PTLD (LN)	6	R-CHOP	46	Alive w/o recurrence
4	M	40	Living	SPK	Basiliximab, TAC, steroids, MMF	PTLD (liver)	43	Rituximab	45	Alive w/o recurrence
5	M	54	Deceased	SPK	Basiliximab, TAC, steroids, MMF, everolimus	PTLD (LN)	19	Rituximab	90	Alive w/o recurrence
6	F	43	Deceased	SPK	Basiliximab, TAC, steroids, MMF	PTLD (brain)	18	Radiotherapy	78	Alive w/o recurrence
7	F	37	Deceased	SPK	Basiliximab, TAC, steroids, MMF, everolimus	Colon cancer	106	Endoscopic mucosal resection	13	Alive w/o recurrence
8	M	36	Deceased	SPK	Basiliximab, TAC, steroids, MMF	Renal cancer	23	Surgical resection	49	Alive w/o recurrence
9	M	36	Deceased	PAK	Basiliximab, CsA, steroids, MMF	Brain tumor	48	Surgical resection	31	Alive w/o recurrence

Abbreviations: PTx, pancreas transplantation; SPK, simultaneous pancreas-kidney transplantation; PAK, pancreas-after-kidney transplantation; TAC, tacrolimus; CsA, cyclosporine A; MMF, mycophenolate mofetil; PTLD, post-transplant lymphoproliferative disorder; LN, lymph node; R-CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone.

Table 3. Previous Reports of Post-PTx De Novo Malignancy

No.	Year	Country	PTx Category	Incidence Rate	Details of De Novo Malignancy
1	1997	Italy	SPK	9.6% (7/73)	PTLD (n = 2), skin (n = 1), breast (n = 1), lung (n = 1), liver (n = 1), vagina (n = 1)
2	2004	United States	SPK (n = 515), PAK (n = 422), PTA (n = 235)	3.8% (44/1172)	PTLD (n = 15), skin (n = 15), breast (n = 5), GI (n = 2), uterus (n = 2), CNS (n = 1), oral (n = 1), parotid (n = 1), lung (n = 1), testis (n = 1)
3	2004	Germany	SPK	6.4% (5/78)	PTLD (n = 1), PTLD + pancreas (n = 1), skin (n = 1), breast (n = 1), colorectal (n = 1)
4	2011	Czech Republic	SPK	6.9% (25/360)	skin (n = 8), PTLD (n = 5), lung (n = 2), bladder (n = 2), peritoneum (n = 2), thyroid (n = 1), stomach (n = 1), kidney (n = 1), unknown (n = 3)
5	2014	Japan (current study)	SPK (n = 8), PAK (n = 1)	8.4% (9/107)	PTLD (n = 6), brain (n = 1), kidney (n = 1), colon (n = 1)

Abbreviations: PTx, pancreas transplantation; SPK, simultaneous pancreas-kidney transplantation; PAK, pancreas-after-kidney transplantation; PTA, pancreas transplant alone; PTLD, post-transplant lymphoproliferative disorder; GI, gastroenterological; CNS, central nervous system.

remaining 3 patients, in whom the tumor was resected, also remain alive without recurrence after the treatment (Nos. 7–9). The median survival after the diagnosis of de novo malignancy in all the cases was 46 months (range, 5–90 months).

DISCUSSION

The present study analyzed the incidence of de novo malignancy after PTx in Japan. To our knowledge, this is the first report to show the incidence of de novo malignancy after PTx in Japan, which led us to consider that the present study is worth reporting. To date, there have been only 4 studies from Europe and the United States to report the incidence of de novo malignancy after PTx [3–6] (Table 3). In these reports, the incidence rate of de novo malignancy is reported as 3.8% to 9.6%, and the rate calculated in the present study was compatible with these reports. To determine the epidemiological significance of this finding in comparison with the normal Japanese population, we used data of cancer incidence reported from the National Cancer Center [7]. The incidence rate calculated in the current study was approximately 5 times higher than that in the normal Japanese population, according to the database. Although there remains the possibility that the calculated incidence rate is at least partly affected not only by underlying diseases such as diabetes and renal dysfunction but also by kidney transplantation, the result was comparable to the previous studies reporting increased risk of malignancy after organ transplantation [1,2].

Furthermore, in the present study, we investigated details of de novo malignancy and compared them with the previous reports mentioned above. Our results showed that PTLD is the most common, which was consistent with the previous reports. On the other hand, skin cancer was also prevalent in the previous reports from Western countries, whereas there were no cases with skin cancer in the current investigation. Similar discrepancies were observed also in the field of other organ transplantation [8]. Furthermore, the incidence rate of skin cancer is different between Western countries and Japan even in the normal populations [9,10]. Taken together, the difference of the incidence rate of skin cancer after PTx between Western countries and Japan was considered to be due to the difference of race.

Thus far, no registry systems have been established for de novo malignancy of post-transplant patients in Japan. Considering the possibility that difference of race may affect development of the malignancy, such a registry is necessary for characterization of the malignancy in each race, which will in turn help to establish post-transplant screening programs for de novo malignancy.

In summary, the current study demonstrated the incidence rate of de novo malignancy after PTx in Japan. The results of the current study would play an important role not only in the characterization but also in the establishment of screening programs for post-transplant de novo malignancy.

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■ 症例報告

胆嚢管を用いて胆道再建を施行した生体肝移植の1例

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A case of living-donor liver transplantation using the cystic duct for biliary tract reconstruction

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【Summary】

We report a case of right-lobe living-donor liver transplantation using the cystic duct for biliary tract reconstruction. The patient was a 49-year-old woman who underwent the transplantation for fulminant hepatitis. The donor was her husband, and his preoperative DIC-CT examination showed that the right posterior segmental bile duct spontaneously merged into the common bile duct and was widely separated from the right anterior segmental bile duct. During the operation, it was impossible to transform the anterior duct and posterior duct into a single orifice because the orifices of the ducts were widely separated. Therefore the posterior duct and the anterior duct were separately anastomosed with the cystic duct and the common hepatic duct. Cholangiography and biliary scintigraphy three months after the transplantation and MRCP three years later showed no leakage or stricture at the anastomotic sites. The case suggested the feasibility of usage of cystic duct for biliary tract reconstruction during living-donor liver transplantation.

Keywords: living-donor liver transplantation, biliary tract reconstruction, cystic duct

I. 緒　言

肝移植の胆道再建において，以前は胆管空腸吻合が基本であったが，近年，乳頭機能の温存に伴う逆行性感染の少ない胆管胆管吻合が標準となっている。当科においても，以前は胆管空腸吻合による再建が中心であったが，2002年以降は胆管胆管吻合を基本術式としている[1]。胆管胆管吻合において，レシピエント側の胆管としては通常，総胆管，総肝管，左右胆管を使用するが，再建すべきグラフトの胆管が複数存在する場合，これらとレシピエント側の胆管との吻合が困難な場合がある。今回，われわれは合併症の多いとされる右葉グラフトを用いた生体部分肝移植において[2]，ドナー胆管に分岐異常を認めたため，レシピエントの胆嚢管を用いた胆道再建を施行し，良好な経過が得られた1例を経験したので報告する。

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II. 症　例

症例：49歳，女性
主訴：全身倦怠感，嘔気，褐色尿
現病歴：2011年11月に全身倦怠感，嘔気，褐色尿が出現し，近医を受診した。肝機能障害を指摘され入院となったが，肝性脳症（II度）が出現し，劇症肝炎と