

台灣移植醫學學會

2021 教育訓練暨移植年會



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Challenge the Past, A New Clinical Practice, A New Standard of care

Introduction: The TRANSFORM study demonstrated that an immunosuppression based on a combination of calcineurin inhibitors and de-novo mTOR inhibitors (mTORi) is safe and effective in kidney transplant recipients. However, data that validate this approach in clinical practice are currently missing.

Materials and methods: Analysis of 401 kidney transplant recipients transplanted from June 2013 to December 2016. All patients received tacrolimus with prednisone in combination with either mycophenolate (n = 186) or mTORi (either everolimus or sirolimus, n = 215). A propensity score to receive mTORi was calculated based on the inverse probability of treatment weighting (IPTW) from the following parameters: age and sex of donor and recipient, BMI, previous transplants, diabetes, cPRA, dialysis before transplantation, dialysis vintage, type of donor, ABO-incompatibility, HLA-mismatches, induction and ischemia time. Median follow-up was 2.6 [1.9; 3.7] years.

Results: Cox-regression analysis suggests good results for mTORi versus MPA in terms of 1-year biopsy-proven acute rejection (BPAR, P = 0.063), 1-year graft loss (P = 0.025) and patient survival (P < 0.001). Results observed for BPAR and graft failure were largely attributed to those patients that would have been excluded by the TRANSFORM because of some exclusion criteria (52.9% of the population, P = 0.003 for 1-year BPAR and P = 0.040 for graft loss). In patients who met selection criteria for TRANSFORM, no effect of treatment for BPAR or graft failure was observed, while the beneficial effect on overall survival persisted.

Conclusions: In a real-life setting, a protocol based on de-novo mTORi with tacrolimus and prednisone could be employed as a standard immunosuppressive regimen and was associated with good outcomes.

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Liver transplantation for hepatocellular carcinoma: concern and perspective

Nowadays, liver transplantation (LT) has been a routine work in numerous transplantation centers worldwide. Specifically, LT for hepatocellular carcinoma (HCC) has the potential to eliminate both the tumor as well as the underlying cirrhosis. Although LT is the ideal treatment for HCC in cirrhotic liver, there are still numerous unmet needs for improving long-term outcome of LT for HCC. First, limitations in organ availability, necessitate stringent selection of patients who would likely to derive most benefit. However, a number of selection criteria have been proposed but were found to be excessively restrictive. Moreover, modest expansion in criteria has also been shown to be associated with equivalent survival that had been reported by numerous transplantation centers. Meanwhile, down-staging of tumors to prevent progression while waiting for an organ or for reduction in size to allow enrolment for transplantation has met with variable success. Particularly, the evolution of systemic therapy including multi-kinase inhibitor, monoclonal antibody and novel immune check point inhibitor have emerged as a promising therapeutic option for advanced HCC. Somehow, advanced HCC could be down-staged to eligible for LT through these novels regimens. However, a bunch of unknown between LT and immunotherapeutic regimens remains to be explored.

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Organ care system in heart transplantation

Cardiac transplantation is the gold standard for treatment for select patients with end-stage heart failure, but the supply of viable donor organs is limited. New technology known as machine perfusion is now capable of preserving donor hearts outside the body and can be used to assess the donor organ as well as allow transport over longer distances. The TransMedics® Organ Care System is an investigational device that maintains the heart in a warm, beating state rather than transporting the heart on ice. The use of Organ Care System allows opportunities to assess viability in organs that may previously have been discarded, travel to distant sites to retrieve hearts, and provide more time to preserve the heart while preparing the recipient for surgery. In the future, it may also be possible to treat or improve the donor heart on the device prior to implantation.

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心臟移植者接受阿斯利康COVID-19疫苗後產生移植後
淋巴組織增生性疾病個案報告

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**Post-transplant lymphoproliferative disorder following AstraZeneca
COVID-19 vaccine in a heart transplant recipient**

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We report a case of a heart transplant recipient who presented with a rapidly growing Epstein-Barr virus (EBV)-positive, diffuse large B-cell lymphoma seven days after receiving the first dose of the ChAdOx1 nCoV-19 vaccine.

Because of the atypical radiological presentation, the initial tentative diagnosis was a mediastinal abscess. This observation indicates a potential risk of EBV reactivation after COVID-19 vaccination, which might lead to or aggravate the presentation of post-transplant lymphoproliferative disorder in transplantation patients.

Transplant surgeons should be aware of the potential immunomodulatory effects of COVID-19 vaccination.

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腸引流的胰臟移植:台北榮民總醫院之經驗

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Pancreas Transplant with Enteric Drainage:

Experience of Taipei Veterans General Hospital

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Purpose

This study is to assess immunological and graft survival outcomes after pancreas transplant at a single institute in Asia.

Methods

Patients undergoing pancreas transplant with enteric drainage were included. Clinical data and outcomes were evaluated and compared between each subgroup.

Results

There were 165 cases of pancreas transplant, including 38 (23%) simultaneous pancreas-kidney transplant (SPK), 24 (15%) pancreas after kidney transplant (PAK), 75 (46%) pancreas transplant alone (PTA), and 28 (17%) pancreas before kidney transplant (PBK). The overall surgical complication rate was 46.1%, with highest (62.5%) in PAK and lowest (32.0%) in PTA, $P = 0.008$. The late complications included 32.7% infection and 3.6% malignancy. Overall rejection of pancreas graft was 24.8% including 18.2% acute and 9.7% chronic rejection. Rejection was highest in PTA group (36.0%) and lowest in PBK (3.6%). There were 56 cases (33.9%) with graft loss in total, with highest graft loss rate in PTA (38.7%). The 1-year, 5-year and 10-year pancreas graft survivals for total patients were 98.0%, 87.7% and 70.9% respectively.

Conclusions

Enteric drainage in pancreas transplant could be applied safely not only in SPK but also in other subgroups. Enteric drainage itself would not compromise the immunological and graft survival outcomes.

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器官捐贈之性別差異

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Gender differences in organ transplantation

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人們對器官捐贈的態度和人口學變項之間是有關係的。本文主在討論2005-2019年器官捐贈登錄中心完成大愛器官捐贈者中性別上的差異探討性別因子在器官捐贈過程中之影響。

目的(Purpose)

本研究以財團法人器官捐贈移植登錄中心於西元2005至2019年的器官捐贈資料作為探討各項人口變項的分配差異和相關情況，省思目前器官捐贈政策之形象及未來展望。

方法(Material and Methods)：

研究方法主要為回溯性研究，以器官捐贈移植登錄中心取得之捐贈者資料3,839人次，進行描述性統計如次數分配、卡方檢定。

結果(Results)：

資料顯示器官捐贈者中女性有1,135人，占全部資料庫的29.60%、男性有2,704人，占全部資料庫的70.40%。有簽屬器官捐贈卡只占約18%。捐贈者年齡以45-64歲居多占48.80%、血型以O型居多占44.0%、已婚者為多數占42.40%、國高中學歷為多數占58.40%、產業別以初級產業為多數占42.00%。

結論(Conclusion)：

資料庫中捐贈者男性居多，但是性別與器官捐贈成功並無顯著差異。資料中也沒有顯示簽屬器官捐贈同意書與捐贈者之間是有關係存在。器官捐贈流程中，當急重症加護病房有合適的捐贈者出現時，醫護團隊會收集個案資料、評估生前是否填寫器官捐贈卡，並於病人末期生命之際，會在病情解釋家庭會議由主治醫師適時提出器官捐贈的要求，最後經由最近親屬簽屬器官捐贈同意書後會進入器官捐贈流程，將捐贈者將可以繼續使用之器官與組織留在人間為生命延續的最高境界。

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Severe herpes zoster infection in patients with solid organ transplantation: a nationwide population-based cohort study with propensity score matching analysis

Running title: Herpes zoster infection in SOT

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Abbreviations:

SOT: solid organ transplantation; NHIRD, National Health Insurance Research Database; aHR: adjusted hazard ratio; CI: confidence interval; VZV: Varicella-zoster virus; HZ: herpes zoster; ICD-9-CM: International Classification of Diseases, Ninth Revision, Clinical Modification

Background: Solid organ recipient is suggested to be likely associated with various infections including virus infection. We conducted a nationwide population-based cohort study to investigate the risk of herpes virus infection in this population.

Methods: From the Taiwan National Health Insurance Research Database (NHIRD) records, individuals hospitalized as solid organ recipients were defined as a case group of solid organ transplantation (SOT) patients and matched with a non-SOT cohort.

Results: We included 9374 SOT patients and 9374 non-SOT patients. The competing risk analysis disclosed that patients in the case group had an 8.41-fold higher risk (aSHR = 8.41, 95% CI = 6.44–11.00). The time frame analysis showed that patients with SOT had a 20.62-fold, 9.10-fold, and 4.98-fold increased risk of developing herpes zoster within 1 year, after 1–3 year(s), and after 3 years, respectively. The risk of recurrence of herpes zoster among patients receiving SOT was not significantly different while compared with that among non-SOT patients.

Conclusion: To our knowledge, this study is the first to disclose that a high herpes zoster infection risk was observed in solid organ transplant recipients including heart, lung, liver as well as kidney. Moreover, HZ risk is remarkably high at the first year post-transplantation. For clinical practice, professionals should maintain high index of suspicion in patients with solid organ transplantation.

Keywords: Solid organ recipient; herpes virus; anti-varicella-zoster virus; lymphocyte cell; cohort study

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病友手冊與個案管理電子化之整合性平台

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Innovative System of Health Care for Patients and Digital Health Technologies for Case Management

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目的(Purpose)

為改善現行器官移植個案管理以人工及紙本作業，造成效率低下、資訊無法即時查詢及更新等缺點，發展整合登錄、檢查及治療計畫之個案資訊管理系統，搭配「心肝寶貝雲APP」使用，未來將藉由居家健康資訊(EHR)與在院醫療資料(EMR)的整合分析、串聯院外健保雲端醫療數據，發展智慧應用，讓醫院到家居的照顧流程無縫接軌。

材料與方法(Material and Methods)

個案資訊管理系統可綜整和查詢待贈者、捐贈者及受贈者之相關病歷紀錄，具備將整體評估、治療結果等資料介接、建立、自動追蹤及備份之功能；還能依器官捐贈移植登錄中心要求的資料介接上傳，自動進行校正比對，建立完善且專業的權限及災難備援機制，以維護資料安全。「心肝寶貝雲APP」則為國內第一個針對器官移植病人的互動式管理平台，整合病友手冊與自主管理，內容由跨團隊專業人員合作編撰，勾稽院內系統方便查詢抽血報告，系統化自我量測表單強化病友自我監測能力、利於醫護進行分析，達到有效傳遞與更新資訊的效果。

結果(Results)

個案資訊管理系統已進入線上測試階段，「心肝寶貝雲APP」已於2021年6月正式上線，將申請步驟製成簡易圖文說明，使病友及其家屬完成下載，針對操作困難者，予以面對面教學，使各年齡層使用時都能得心應手，早日達成完全電子化、脫離傳統紙本作業的目標。經實測，平均每位病人看診時間縮短約5分鐘，但實際上是將看診期間之每秒鐘皆利用於醫病互動，增加看診效率，圖像化顯示臨床表現與賦權病人，此APP確實可在各方面幫助病友，是值得推廣的智慧醫療照護模式。

結論(Conclusion)

隨著應用程式漸趨成熟，將針對各方意見進行優化與開發APP的功能模組，使各式資料圖表化，持續與器官移植個案管理平台進行資料介接、功能導入，讓病友及醫護人員能無縫串聯在院及居家期間的身體狀態、趨勢變化，強化醫病合作互動與結構化資料共創共編。針對此特殊族群，突破場域限制與不間斷的照護網絡勢在必行，未來將持續整合IoT終端資料，與符合國際標準的HL7/FHIR資料格式接軌，期許發展聯邦式學習(federated learning)模式，壯大國內移植研究量能，以智慧化分析提升照護水平，創造醫療端及病人端雙贏的局面。

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利用大隱靜脈植體之活體親屬腎臟移植：個案報告

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Living Related Kidney Transplantation Using Great Saphenous Vein Graft : A Case Report

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Introduction:

Living related kidney transplantation is gaining popularity in recent years in Taiwan. Left kidney in kidney transplantation is anatomically preferred than right kidney due to the length of renal vein is longer. However, when both kidneys are capable candidate of donation, we preserve the one with better renal function to the donor. The other one, either by inferior but acceptable renal function, or the one with minor abnormality, we give it to the recipient. Right kidney transplantation could be challenging in venous anastomosis due to shorter length of renal vein. In these case, we mobilize the recipient external iliac vein and common iliac vein, or adopt a vein graft to extend the donor renal vein. Here we provide a case using great saphenous vein graft.

Case Report:

A 68-year-old man(blood type A, Rh+), has history of gouty arthritis and bilateral renal stones with repeat recurrence and received extracorporeal shock wave lithotomy for many times. However, deteriorated renal function was noted during follow up and finally progressed to end stage renal disease and started hemodialysis since August 2020. He received ABO compatible living related kidney transplantation from his 38-year-old son (blood type A, Rh-) in April 2021. The donor has left kidney with renal function superior to right kidney, and there was a small hypoechoic nodule over right kidney about 3.1cm, favored angiomyolipoma. The comprehensive renal function test with Tc-99m MAG3 showed split renal function total of left kidney 361 ml/ minute (63.2%) and right kidney 211 ml/ minute (36.8%). The donor's right kidney was harvested laparoscopically with intraperitoneal approach. There was one renal artery and two major renal vein with early bifurcation. Warm ischemia time of graft kidney was 14 minutes and 37 seconds. Cold ischemia time was 1 hour and 53 minutes. We tried direct anastomosis first with graft renal veins to external iliac vein in 23 minutes and 16 seconds, and graft renal artery to external iliac artery in 29 minutes and 29 seconds.

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利用大隱靜脈植體之活體親屬腎臟移植：個案報告

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Living Related Kidney Transplantation Using Great Saphenous Vein Graft : A Case Report

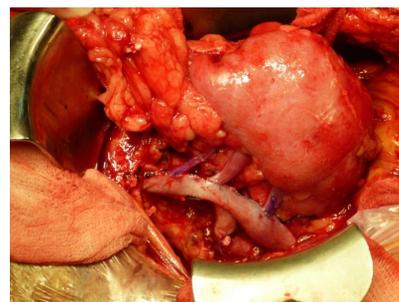
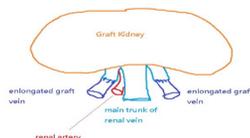
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However, graft congestion was noted. We table consulted the cardiovascular surgeon and performed great saphenous vein graft harvest and graft renal vein elongation (7-0 Prolene, end-to-end). Second anastomosis cost vein anastomosis 19 minutes (7-0 Prolene, end-to-side), and artery anastomosis 25 minutes and 21 seconds (6-0 Prolene, end-to-side). The graft kidney perfusion was good and doppler sonography showed good blood flow immediately and after surgery. Immunosuppressive induction was arranged using Tacrolimus, Mycophenolate mofetil and Basiliximab, and kept maintenance immunosuppression with Tacrolimus, Mycophenolate mofetil and Methylprednisolone. The patient's creatinine level decreased from 10.54 mg/dl before surgery, 6.73 mg/dl at postoperative care unit, and reached its nadir of 1.78 mg/dl on postoperative day 8 when he was discharged.

Conclusions:

Great saphenous vein graft is easy-harvesting and effective for elongation of graft renal vein when a right kidney is used.



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小兒雙側腎臟捐贈

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Pediatric Dual kidney transplantation

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Background:

Expanding the kidney donor pool has always been challenging. Pediatric dual kidney transplantation (DKT), the transplantation of two kidneys from the same pediatric donor into a single recipient, is one potential strategy to reduce organ wastage and recipient waiting time. However, there are only a few transplant centers that incorporate pediatric donors (PD). The major concerns of PD for adults are increased surgical complications, inadequate nephron mass, hyperfiltration injury, and the relative sensitivity of pediatric kidneys to rejection episodes. Currently, there is no consensus on the selection criteria and optimal techniques for DKT. We reported four cases of pediatric dual kidney transplants performed in an en bloc graft fashion. A literature review was performed on different DKT aspects, techniques, and results to address the direction for future study.

Material and Methods:

From 1990 to 2021, 4 cases of dual kidneys transplantation were performed in our hospital. Donors and Recipients characteristics, surgical techniques were retrospectively collected through chart review. All 4 recipients underwent dual en-bloc (DEB) kidney transplantation with a similar surgical technique. The kidneys were harvested with a segment of IVC, aorta, and bilateral ureter as en block graft (Fig.1A). The proximal end of the donor IVC and aorta was closed using prolene sutures (Fig.1b). Polar vessels were preserved whenever identified. The graft was placed into the iliac fossa and the graft vessels were anastomosed to the external iliac vessels in an end to side fashion (Fig.1c). The ureteroneocystostomy was made with a common channel ureter, which was sutured on the back table or with separate ureters over the dome of the urinary bladder. We performed daily bedside sonography and blood tests to detect peri-graft fluid accumulation, acute rejection, vascular thrombosis and delayed graft function. Systolic blood pressure was controlled below 150mmHg to prevent hyperfiltration injury.



Fig1A. The bilateral kidneys, aorta, IVC, and bilateral ureters are harvested as an en bloc graft.

Fig1B. The proximal end of the great vessel was sutured on the back table

Fig1C. The graft was placed into the iliac fossa and anastomosed to the external iliac vessels

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Pediatric Dual kidney transplantation

Han-Chung Yang¹, Jia-Wen Lu¹, Sheng-Chun Hung¹, Chuan-Shu Chen¹,
Cheng-Kuang Yang¹ and Kun-Yuan Chiu¹ Taichung Veterans General Hospital

Result:

A total of three female and one male donor were examined. The baseline characteristics are listed below in Table 1. Two were small pediatric donors (< 4-year-old and <20Kg) and the other two were pediatric donors. The cause of death was all traumatic brain injury. Donor No.1 suffered a massive cerebral infarction after the initial injury. The donors' age ranged from 14-month-old to 5-year-old, and their body weight ranged from 10.5 to 17kg. The recipients' age ranged from 17 to 59-year-old and weighed from 42.8 to 54 kg. The mean body weight discrepancy was 34 kilograms (32.8, 35.6, 25.8, 43.5 Kg). No delayed graft function, thromboembolic complications, or acute rejection was noticed in all four cases. During the follow-up period of a minimum of 6 months, patient and graft survival were both 100%. The mean calculated creatinine clearance at 6 months using Cockcroft Gault's formula was 59.1mL/min.

Table 1. Baseline characteristics of donors(D) and recipients(R)

Case	D COD	D/R GENDER	D/R age (y/o)	D/R BW (kg)	D/R BSA (m ²)	UNOS KDPI	DGF	Complication	Recipient sCr at 6m (mg/dL)	eGFR at 6m (ml/min)	f/u(year)
1	TBI/Stroke	F/F	1.9/17	11/43.8	0.501/1.4	71%/1.24	No	No	8.3->1.4	70	0.5
2	TBI	F/F	4/59	16/51.4	0.66/1.5	49%/0.98	No	No	6.58->1.1	51.1	1
3	TBI	F/F	5/56	17/42.8	0.71/1.43	51%/1.01	No	No	3.6->0.7	62	3
4	TBI	M/F	1.2/45	10.5/54	0.45/1.5	66%/1.1	No	No	7.3->0.67	70.5	15

COD: Cause Of Death, BW: Body Weight, BSA: Body Surface Area, UNOS: United Network for Organ Sharing, KDPI: kidney donor profile index, DGF: Delayed Graft Function, sCr: Serum Creatinine, f/u: follow-up, eGFR: Estimated Glomerular Filtration Rate, TBI: Traumatic Brain Injury

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1 台中榮民總醫院外科部泌尿科

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Cheng-Kuang Yang¹ and Kun-Yuan Chiu¹ Taichung Veterans General Hospital

Discussion:

The idea of pediatric dual en bloc (PDEB) kidney transplant(KT) was first proposed by Carrel and colleagues in 1908. The first successful PDEB KT to an adult recipient was reported in 1972. Despite its long history, such practice is decreasing because of the belief that technical complications, decreased functional nephron reserve, increased severity in rejection reaction, hyperfiltration injury, and the claims of a diminished patient and graft survival are more common compared with adult deceased donors transplant. In the early experience of PDEB transplant, Hayes and colleagues reported a higher incidence of ureteral, bladder complication, and renal artery stenosis despite comparable graft functional outcomes compared to adult cadaveric transplantation.[1] There's also an increased risk of vascular thrombosis as well as graft renal artery stenosis requiring intervention in the PDEB KT cases compared with an adult donor.[2]

As surgical techniques improve and equipment innovates, recent studies have pointed out that the complication rate and graft survival between pediatric and adult donors are comparable. In the study by Maluf and colleagues[3], the utilization of the pediatric donor, regardless of split KT or PDEB KT, has equivalent outcomes compared to adult living kidney donation if performed by an experienced center. Several similar studies also reached the same conclusion.[4]

Currently, there's no effective scoring system that predicts the possibility of graft failure for a PDEB KT. The UNOS Kidney Donor Profile Index (KDPI) had the tendency to overestimate the risk of graft failure for PDEB KT. The original Kidney Donor Risk Index (KDRI) created by Dr.Rao contains four extra variables, that is, coefficients for HLA match, cold ischemic time, en-bloc (EB), and dual kidney in addition to the 10 variables adopted by the UNOS KDPI. In the study by Preczewski and colleagues, 74 PDEB transplants had a median UNOS KDPI of 82.5. When re-calculated with KDRI and taking EB into account, the median score was 50.5.[5] The mean decrease in score was 30.5. The fact that KDPI may overestimate the risk of graft failure in PDEB means that these donors are subjected to inappropriate allocation.

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There's considerable heterogeneity between transplant surgeons as to an acceptable age and bodyweight limit in pediatric kidney donation. To maximize functional glomerular reserve, we generally refuse donors with a bodyweight lower than 10 Kg because they carry a high risk for delayed graft function and graft failure. Balanchandaran and colleagues found a significantly increased likelihood of delayed graft function and a trend towards more graft loss from donors weighing less than 10 Kg. On the other hand, a study using Scientific Registry of Transplant Recipients (SRTR) data demonstrated that patient and death-censored graft survival were similar among standard criteria adult donor, PDEB donor and, and split pediatric donor and were all superior to an extended criteria donor. [6] The author concluded that a significant fraction of kidneys from pediatric donors >10 kg who have had other organs used for a transplant could potentially become a split kidney donor. In our study, the two small pediatric donors are the ones with the best GFR at 6 months after transplant, implying that after careful donor selection and accurate graft allocation, even the smallest graft can provide adequate nephron mass for an adult.

There are several different techniques for dual kidney transplantation. Bilateral placement, unilateral placement with separate anastomoses, and unilateral placement with patch angioplasty are all feasible techniques for graft inset apart from DEB graft. In the systemic review by Cocco and colleagues,[7] the graft survival, total operative time, incidence of delayed graft function, and renal vein thrombosis were equivalent in all three techniques. In pediatric donors such as our cases, bilateral insets are usually not required and reduce cold ischemia time compared to a separate anastomosis.

Conclusion:

The result herein and the listed study demonstrate that the use of pediatric dual kidney en bloc grafts, transplant into selected adult recipients, provides long-term graft survival and function that is comparable to the standard adult donors. Future study is needed to investigate the accurate graft failure risk, allocation, potential risk factors for urologic complications, and their prevention. A more aggressive utilization of pediatric dual en-bloc kidney donation could help expand the donor pool without comprising recipient outcomes.

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單一醫學中心高齡活體捐贈者腎臟移植之安全性與受贈者預後經驗

郭芳成¹ 陳正彥¹ 吳采虹² 林釀呈¹ 鍾孟軒¹ 龍藉泉¹

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Single-center experience of the patient safety and the long-term prognosis with aged kidney donation in living kidney donors and recipients

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Purpose:

Recent researches have suggested that the use of kidneys from older live donors has acceptable outcomes in the recipient and is considered safe in the donor. This present study aims to examine the long-term real-time changes of estimated glomerular filtration rate (eGFR) after aged kidney donation in both living donors and recipients.

Materials and Methods:

From 2005 to 2019, we collected follow-up data of 156 pairs of living kidney donors and recipients in our institution. Donors and recipients were both separated into old and young groups based on age ≥ 50 and < 50 . We monitored eGFR changes after transplantation at multiple time points in five years for donors and three years for recipients. An adjusted linear regression model evaluated the recovery of recipient eGFR by four relations between the donor and recipient (group 1: old donor-old recipient; group 2: old donor-young recipient; group 3 young donor-old recipient; group 4 young donor-young recipient).

Results:

During donor follow-up of 5 years, all donors eGFR recovered with time. The young donors had higher eGFR than old donors, but the percentile decline in eGFR became similar after three years. For recipient follow-up of 3 years, we excluded four recipients due to early graft loss within one month. The rest of 152 participants all had preserved graft function for three years after transplantation or at the end of study. As regards the recipient recovery, group 1 had the lowest eGFR with median eGFRs of 49.9, 50.6, and 48.3 ml/min/1.73m² at 1-year, 2-year, and 3-year. Compared to group 1, group 2 had similar results; group 4 had the highest eGFRs at every time points; the group 3 had improving eGFR after two years.

Conclusion:

From our experience, we consider live aged kidney donation is safe in old donors due to a similar percentile decline in eGFR compared with young donors. In addition, although the young kidney has a higher eGFR, the aged kidney still provides preserved and stable renal function.

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單一醫學中心使用腦死小兒捐贈者腎臟移植之經驗

廖麗鳳^{1,2} 陳正彥² 黃雅琳^{1,2} 林姿妤^{1,2} 蔡昕霖³ 吳采虹⁴

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Single-center experience of utilizing brain death pediatric donor kidney in kidney transplantation

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目的：

行政院衛生署衛署2004年08月09日發布腦死判定準則後，2011年12月17日修正並放寬腦死小兒器官捐贈條件，但是小兒捐贈者因體重、年齡分布差異大，還有器官發育的成熟性考量，所以在受贈者選擇上與預後也充滿了不確定性。本篇研究主要在探討單一醫學中心使用腦死小兒腎臟捐贈與移植術後的追蹤結果。

方法：

針對本院2003年至2020年期間使用腦死小兒腎臟捐贈之受贈者進行回顧性研究，分析捐贈者年齡，體重，腎臟大小與受贈者選擇的關聯性，同時追蹤受贈者預後。

結果：

研究期間共有7名受贈者接受小兒腎臟捐贈，其中有3位成人受贈者接受雙腎同時移植，2位成人受贈者接受單側腎臟移植，2位幼兒受贈者接受單側腎臟移植。其中1位幼兒受贈者因術後合併症導致腎衰竭，兩年後再次接受小兒腎臟移植。7位受贈者目前皆腎功能良好。另外本研究發現若小兒捐贈者體重大於15公斤同時腎臟大小大於6公分可以考慮單一腎臟移植給適合的成人受贈者，否則建議雙腎同時移植。若有幼兒等待者時，在捐贈者體重大於15公斤或腎臟大小大於6公分的情況下，可以依受贈者體型考量進行單腎移植。

結論：

依本院經驗，使用腦死小兒腎臟是可行的，而且也有良好的預後。在適當的捐贈者與受贈者選擇條件下，腦死小兒腎臟捐贈可以緩解台灣大愛捐贈腎臟短缺的困境，同時給予幼兒腎臟等待者腎臟移植的機會



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運用肝臟移植治療晚期肝癌的曙光乍現：以免疫療法做為移植前降期治療的策略

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Dawn of downstaging therapy for advanced hepatocellular carcinoma before liver transplantation: Is Immunotherapy the light?

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Purpose: Immune checkpoint inhibitor (ICI) or immunotherapy has gained wide recognition in the treatment of hepatocellular carcinoma (HCC). While liver transplantation (LT) offers the best option of cure for patients with HCC, use of ICI in the setting of solid organ transplantation poses a concerning risk of allograft rejection. Nonetheless, several reports have shown promising results on the use of ICI in intermediate to advanced HCC, as downstaging therapy prior to LT.

Material and Methods: We report two successful cases of patients with advanced HCC who received ICI as the downstaging therapy prior to LT.

Results: One case received ICI treatment as last resort for persistent disease progression, while the other case received ICI with intention to treat as bridging therapy for LT. Partial to complete remission of tumor was achieved making these patients eligible for LT. To date, no evidence of severe allograft rejection or tumor recurrence has been observed for both patients at least one year after transplantation.

Conclusion: Although recent studies suggest high incidence of allograft rejection with the use of ICI in the setting of solid organ transplantation including LT, these two cases illustrate the feasibility and efficacy of ICI for advanced stage HCC as a downstaging strategy for eventually curative-intent LT.

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右肝活肝移植使用人工血管重建靜脈的術後併發症：單一醫學中心病例系列報告

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Complications after using artificial graft for venous reconstruction in right lobe living donor liver transplantation: case series in single center

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Purpose:

Due to shortage of cryopreserved and autologous vascular graft, artificial vascular graft (AVG) was commonly used in reconstruction of middle hepatic vein (MHV) for right lobe living donor liver transplantation (LDLT). The aim of this study was to report single-center experience in AVG migration into hollow viscus after LDLT and experience in prevention strategy.

Material and Methods:

A total 424 adult patients who underwent artificial vascular graft for reconstruction of MHV tributaries in right lobe LDLT between July 2005 and June 2021 were included in this study. Of these, patients who occurred AVG migration were further investigated.

Results:

There are 7 patients who had migration of artificial venous graft into hollow viscus between 30 and 72 years of age (median, 53 y; mean \pm SD, 50 \pm 13.4 y). AVG migration occurred median 7.8 months after LT (range, 1.8 to 81.5 months; mean \pm SD, 19.5 \pm 28.1 months). Three of the patients who are asymptomatic and accidentally found during follow-up by CT, panendoscopy, or ERCP. The remaining cases presented with fever (n=3), anemia (n=1), or bloody stool (n=1). There are 5 patients (5/7, 71.4%) who received interventions for biliary complications included ERCP, PTCO or percutaneous drainage before AVG migration. All of AVG thrombosis (n=7) were confirmed by CT, between 0.6 and 9.4 months (median, 2 months; mean \pm SD, 3.5 \pm 3.2 months) postoperatively. 7 of them received operation with either removal of AVG, primary closure of erosion site. AV graft migration site included stomach antrum(n=3), duodenal 1st portion(n=1), bile duct(n=2), transverse colon (n=1). Postoperative bile leakage (n=3), septic shock (n=1), pulmonary complication (n=2) were observed in 4 cases during follow-up. Only one patient died due to lung cancer and tongue cancer which occurred 4 years postoperatively.

Conclusion:

The incidence rate of AVG migration in our hospital was 1.65%. Potential risk factors related to AVG migration included biliary complications and early occlusion of AVG. To increase patency of AVG, several modifications of surgical technique such as preventing unnecessary anastomosis, redundant AVG, axis of AVG, retro-hepatic space widening were made. A further study is needed to evaluate outcome of such modifications.

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腎移植患者感染新冠病毒後的死亡率，急性腎損傷及失去移植腎功能：
縱論與統合分析研究

吳欣旭

林口長庚腎臟科

Incidence of Mortality, Acute Kidney Injury and Graft Loss in Adult Kidney Transplant Recipients with Coronavirus Disease 2019: Systematic Review and Meta-Analysis

Purpose

The adverse impact of Coronavirus disease 2019 (COVID-19) on kidney function has been reported since the global pandemic. The burden of COVID-19 on kidney transplant recipients, however, has not been systematically analyzed. A systematic review and meta-analysis with a random-effect model was conducted to explore the rate of mortality, intensive care unit admission, invasive mechanical ventilation, acute kidney injury, kidney replacement therapy and graft loss in the adult kidney transplant population with COVID-19.

Material and methods

Two independent reviewers comprehensively searched for studies published before June 2021 on PubMed, Medline, the Cochrane Library and Embase. The search strategy targeted published clinical trials, cohort studies, case series, letters to the editor and commentaries. The keyword and Mesh term used on PubMed were: (COVID-19, or SARS-CoV-2, or coronavirus) and (Kidney Transplantation, or Kidney transplant, or Renal transplantation, or Renal transplant) with the following filters: Humans, Adult: 19+ years. English-language articles that were published from 2019–2021 were screened.

Results

A pooled mortality rate of 21% (95% CI: 19–23%), an intensive care unit admission rate of 26% (95% CI: 22–31%), an invasive ventilation rate among those who required intensive care unit care of 72% (95% CI: 62–81%), an acute kidney injury rate of 44% (95% CI: 39–49%), a kidney replacement therapy rate of 12% (95% CI: 9–15%), and a graft loss rate of 8% (95% CI: 5–15%) in kidney transplant recipients with COVID-19. The meta-regression indicated that advancing age is associated with higher mortality; every increase in age by 10 years was associated with an increased mortality rate of 3.7%.

Conclusions

Renal transplant recipients carried high mortality rate and high comorbidities compared to general population. Specific care and attention in these patients may be warranted.

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心死捐贈之腎臟移植結果報告：台中榮總經驗分享

張家程 楊晨洸 賀昊中

高雄榮民總醫院屏東分院外科部泌尿科, 台中榮民總醫院外科部泌尿科, 彰濱秀傳外科部泌尿科

Results of Donation after Cardiac Death in Kidney transplant: the TCVGH single-center experience
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Objective:

It is extremely shortage of kidney donor sources compared with the ESRD patients on the waiting list worldwide. Donation after cardiac death (DCD), formerly non-heart-beating donation had become an important solution to organ shortage in American, Australia and some European countries. The DCD concepts and techniques were in the developing stage in Taiwan. We would like to share our DCD experiences of kidney transplant in Taichung Veteran General Hospital.

Method:

Our institute kidney transplant team started the DCD program in January 2008. Kidney organs was harvested for both controlled and uncontrolled donors in the pioneering period. The Ministry of Health and Welfare announced the DCD guideline on 2017.12.26 as standard to follow up. After the milestone time point, a 5-minutes stand-off period was observed before declaring the death and performing the in situ cold perfusion. Procurement retrograde perfusion was performed over the aorta above the iliac bifurcation level. Kidney cold ischemia was completed as liver or mesentery organ cold ischemia appearance.

Result:

From January 2008 to December 2020, our renal transplant team performed 16 kidney transplant from 9 controlled and uncontrolled DCD donors, which accounted for 11.8% (9/76) of the cadaveric donors. There were 8 UNOS criteria standard donors and 1 extended criteria donor, ranging from Maastricht Category II to IV. Mean recipient age was 46.4(27~62) years old. Male/female ratio was 7/7. We had 1 case of primary non-function (PNF) and 81.3%(13/16) of delayed graft function (DGF). Patient and graft survival were 100% and 87.5%(14/16), respectively, at 1 year; 93%(13/14) and 86%(12/14), respectively, at 5 years; 93.8%(15/16) and 75%(12/16) at least follow-up. The estimated glomerular filtration rate was 37.68 mL/min/1.73m² at 1 year, 36.11 mL/min/1.73m² at 5 year, 30.04 mL/min/1.73m² at last follow-up

Conclusion:

Our institute results showed encouraging graft survival result that DCD kidney donors could be solution sources for kidney organ transplantation. Even though low risk of primary non-function, however, recipient selection should be cautious due to high prevalence of delay graft function. More tolerable recipients, non-highly sensitized, without high immune risk, with shorter graft survival necessity, were preferable choices.

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Transplantation of kidneys from hepatitis C-infected circulation death donors to hepatitis C-negative recipients

C 肝捐贈者心臟停止後死亡的腎臟捐贈

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According to statistics from Taiwan's 2020 Kidney Annual Report, the number of kidney transplants was between 282 and 319 each year from 2014 to 2018. However, the number of people on the waiting list for kidney transplantation reached 7364 in 2018. The shortage of transplant donors is still a dilemma in Taiwan. In order to expanding the donor pool to increase public health benefit, the Ministry of Health and Welfare (MoHW) issued a reference guide for Donation after Circulatory Death (DCD) since 2017 in Taiwan. In the past, Hepatitis C virus (HCV)-infected donor kidney were only transplanted into HCV-infected recipients. The transmission of HCV from donor to recipient was associated with graft failure and inferior survival outcome. However, the landscape for HCV treatment had been a revolution with the introduction of direct-acting antiviral (DAA) agents since 2013. DAA is well tolerated and has relatively high cure rates, even in kidney transplant recipients. Here we report our experience of transplantation of kidneys from one hepatitis C-infected circulation death donor to two hepatitis C-negative recipients in Shuang Ho hospital on 2020.

Donor is an HCV-infected circulation death 44-year-old male and recipients were all HCV-negative, one is a 40-year-old female with IgA nephropathy in ESKD under hemodialysis and the other one is a 50-year-old male with focal segmental glomerular sclerosis in ESKD under peritoneal dialysis. Both of the recipients had detectable HCV-RNA of 2995 IU/ml and 723 IU/ml respectively post kidney transplantation. They started on pan-genotypic DAA with sofosbuvir/velpatasvir (400mg/100mg) once a day within 1 week after kidney transplantation and continue for 12 weeks treatment course without significant treatment-related adverse events. Both recipients achieved sustained virologic response 12 weeks after therapy (SVR12). Otherwise, because of the kidney from donation after circulatory death (DCD), both recipients encountered delayed graft function (5-day and 16-day respectively) but reached stable creatinine level within one month after kidney transplantation.

To solve the shortage of transplanted kidneys, in addition to continuing to promote living donor organ transplants from relatives, the establishment of management methods for living kidney transplantation and donation after circulation death has also increased the chances of transplantation. Furthermore, in the Era of DAA with high HCV curative rate, kidney transplantation from HCV-positive donors into HCV-negative recipients appears to be a safe and efficacy measure to expand the donor pool and decrease organ discard.

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多瘤病毒腎病變患者泌尿道腫瘤的高發生率及早期發生的現象

田亞中

林口長庚醫院腎臟科及腎臟研究中心

High incidence and early onset of urinary tract cancers in patients with polyomavirus BK-associated nephropathy

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Background Over-immunosuppressed kidney transplant recipients are susceptible to malignancies and polyomavirus nephropathy (BKVAN). This study aimed to verify the association between BK polyomavirus (BKPyV) infection and urinary tract cancers (UTC).

Methods A total of 244 kidney transplant recipients were enrolled at Chang Gung Memorial Hospital from June 2000 to February 2020.

Results Biopsy-proven BKVAN patients ($n=17$) had worse kidney function ($eGFR: 26 \pm 13.7$ vs. 47.8 ± 31.0 mL/min/1.73 m²). The 5-year allograft survival rates for patients with and without BKVAN were 67% and 93%, respectively ($p=0.0002$), while the 10-year patient survival was not different between the two groups. BKVAN patients had a significantly higher incidence of UTC compared to the non-BKVAN group (29.4% vs. 6.6%). Kaplan–Meier analysis showed that the UTC-free survival rate was significantly lower in BKVAN patients, and the onset of UTC was significantly shorter in BKVAN patients (53.4 vs. 108.9 months). The multivariate logistic regression analysis demonstrated that age ($RR=1.062$) and BKVAN ($RR=6.459$) were the most significant risk factors for the development of UTC.

Conclusions Our study demonstrates that BKVAN patients have greater allograft losses, higher incidence, a lower cancer-free survival rate, and an earlier onset with a higher relative risk of developing UTC compared to non-BKVAN patients.

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腎移植病人BK病毒感染與腎病變的案例系列報告分享

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BK virus Infection and BK nephropathy in kidney transplant recipients: case series

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Kidney transplantation is the treatment option with better survival rate and quality of life for patients with end-stage renal disease. However, the risk of infection or malignancy also increases after kidney transplantation. The reactivation of BK polyomavirus (BKV) is an important cause of graft loss resulted from over immunosuppression in renal transplant recipients.

The 2009 KDIGO guideline of kidney transplant suggests screening all kidney transplant recipients (KTRs) for BKV with quantitative plasma nucleic acid testing (NAT) at least monthly for the first 3 to 6 months after transplantation then every 3 months until the end of the first post-transplant year or whenever there is an unexplained rise in serum creatinine or after treatment for acute rejection. If BKV plasma NAT is persistently greater than 10,000 copies/mL, further reduction of immunosuppressive medications is indicated.

The American Society of Transplantation Infectious Diseases Community of Practice (AST-IDCOP) also released updated information about BKV of solid organ transplantation in 2019. The AST-IDCOP recommended screen all KTRs for BKPyV-DNAemia monthly until month 9, and then every 3 months until 2 years post-transplant. Kidney transplant recipients should be screened for BKPyV-DNAemia when undergoing renal allograft biopsy or allograft dysfunction. The mainstay of therapy for BKPyV-DNAemia or BK nephropathy in KTRs is reducing maintenance immunosuppression. As of October 2021, sixteen patients (11 males and 5 females) from Shuang-Ho Hospital with BKPyV-DNAemia or high urine BKpyV were analyzed. The average age was 54.6 years old. Six patients were found BKV from urine or blood test within one year of kidney transplant and five patients were undergoing renal biopsy. Since there is no consensus for the timing of screening, diagnosis or treatment strategy for BKV infection in Taiwan, we usually initially reduce the dosage of mycophenolate and add leflunomide. If the following BK virus load was not decreased, further reduction of tacrolimus concentration or add mTOR inhibitor may be the choice. We reviewed the BKV patients and there is a continuing need for conducting the ideal management for BKV infection and nephropathy.

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Monoclonal antibody use in kidney transplantation patient with Critical COVID 19 infection.

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SARS-COV2 has become pandemic in the past two years, causing more than 200 million confirmed cases, 5% of the case is critical (eg, respiratory failure, shock, multiorgan failure), and case fatality rate is around 2% worldwide according to most recent CDC data.

Underlying diseases such as T2DM, coronary artery disease, immunosuppression agents, and age greater than 60 are considered to be a major risk of confirmed infected cases becoming critical cases.

Therefore, monoclonal antibody, and steroid are listed as CDC guideline to prevent high risk patient from progressing to critical case.

Limited data are available for the use of Monoclonal antibody in kidney transplantation patient for COVID-19.

Today I am going to present a 65 years old male with diabetic nephropathy in chronic kidney stage 5 under dialysis, and received renal transplantation in 2008.

He was admitted in January due to watery diarrhea for one month, and elevated Creatinine level from 1.85mg/dl to 3.93mg/dl.

During hospitalization BK viruria, and viremia were detected with adjustment of his immunosuppression agents. Renal echo was performed showing RI index is 0.723, and patient received DFPP, IVIG, Pulse therapy for suspicious acute antibody mediated rejection.

Between February, and May, patient was treated for Hospital-acquired pneumonia with respiratory failure, difficult weaning with tracheostomy, and bedsores infection.

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On June 13, patient was confirmed COVID-19 PCR positive with CT value 29.

His condition deteriorated within the next few days along with progressed CT value to 17, and increased right lung infiltration on June 17 with the use of ventilator PCV mode.

Remdesivir was used On June 17 with significant improvement shown from improved CXR, CT value 25, and ventilator mode to T-piece in the following one week. His immunosuppressant agents at this time were tacrolimus 1mg BID, Leflunomide 5mg QD.

However, on July 1, follow up CT value progressed from stationary 19 to 14 along with CXR change, and increased oxygen demand. Previous co-infection with fungemia, bacteremia were treated properly with follow up blood culture showing negative result.

As for his decreased urine output under the concern of acute antibody mediated rejection due to tapering immunosuppressant agents for BK virus, we arranged plasma exchange, titrated his immunosuppressant agents on July 1, which urine output improved afterwards. Bamlanivimab, Etesevimab, Remdesivir were combined use for reactivation of COVID-19 infection. In the following one week, both clinical, and CXR improved gradually, then after two weeks, he was successfully weaned from ventilator, and transferred to general ward under high flow system use with CT value 27.

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