Available online at www.sciencedirect.com

ScienceDirect

Journal of the Chinese Medical Association 81 (2018) 766–771

www.jcma-online.com

Original Article

Renal transplantation delays major adverse cardiac events (MACEs) in patients with end-stage renal disease: A nationwide population-based study

Hsien-Tzung Liao [a,b,c], Ming-Chin Lin [d,e,f], Chang-Youh Tsai [a,c], Chien-Yeh Hsu [g,h], Tsai-Hung Wu [c,i,*]

[a] *Division of Allergy, Immunology and Rheumatology, Department of Medicine, Taipei Veterans General Hospital, Taipei, Taiwan, ROC*
[b] *Division of Allergy, Immunology and Rheumatology, Department of Internal Medicine, School of Medicine, College of Medicine, Taipei Medical University, Taipei, Taiwan, ROC*
[c] *Faculty of Medicine, National Yang-Ming University School of Medicine, Taipei, Taiwan, ROC*
[d] *Graduate Institute of Biomedical Informatics, College of Medicine Science and Technology, Taipei Medical University, Taipei, Taiwan, ROC*
[e] *Division of Neurosurgery, Department of Surgery, Shuang-Ho Hospital, Taipei, Taiwan, ROC*
[f] *International Center for Health Information Technology (ICHIT), Taipei Medical University, Taipei, Taiwan, ROC*
[g] *Master Program in Global Health and Development, College of Public Health, Taipei Medical University, Taipei, Taiwan, ROC*
[h] *Department of Information Management, National Taipei University of Nursing and Health Sciences, Taipei, Taiwan, ROC*
[i] *Division of Nephrology, Department of Medicine, Taipei Veterans General Hospital, Taipei, Taiwan, ROC*

Received December 15, 2017; accepted April 24, 2018

Abstract

Background: Whether renal transplantation (RT) influences the risk of cardiovascular events remains controversial.
Methods: This nationwide population-based study investigated the risk of major adverse cardiac events (MACEs) and stroke after RT in patients with end-stage renal disease (ESRD), using data obtained from the National Health Insurance Research Database in Taiwan. A total of 164 ESRD patients who underwent RT formed the study cohort, and an age- and sex-matched control group comprised 164 patients without RT selected from 6976 ESRD patients. All patients were enrolled between January 1, 2000 and December 31, 2009. Those who developed MACEs and/or stroke during the study period were identified according to the International Classification of Diseases, Ninth Revision, Clinical Modification. A Kaplan–Meier MACEs-free curve was used to compare MACEs episodes between the study and control groups.
Results: The mean age was similar between RT and non-RT patients, with most between 30 and 50 years old. In this age range, MACEs developed in 47.5% of the RT group and in 52.5% of the non-RT group ($p = 0.0882$). The survival rate among all ESRD patients was significant higher in the RT group than in non-RT group ($p < 0.001$). The MACEs-free, stroke-free and MACEs-or-stroke-free rates were significantly higher in the RT group than in the non-RT group ($p = 0.0134$, 0.035 and 0.005, respectively) as demonstrated by Kaplan–Meier curves.
Conclusion: RT seemed not to reduce the risk of MACEs directly, but it could have dramatically delayed MACEs and stroke episodes in the ESRD patients. Furthermore, a lower mortality rate was observed in the ESRD patients who received RT than in those undergoing chronic dialysis. Further in-depth investigation is necessary to identify other protective factors against MACEs or stroke in ESRD.

Keywords: End-stage renal disease (ESRD); Major adverse cardia events (MACEs); Renal transplantation (RT); Stroke

Conflicts of interest: The authors declare that they have no conflicts of interest related to the subject matter or materials discussed in this article.

* Corresponding author. Dr. Tsai-Hung Wu, Division of Nephrology, Department of Medicine, Taipei Veterans General Hospital, 201, Section 2, Shi-Pai Road, Taipei 112, Taiwan, ROC.
E-mail address: thwu@vghtpe.gov.tw (T.-H. Wu).

https://doi.org/10.1016/j.jcma.2018.04.003

1. Introduction

End-stage renal disease (ESRD) increases the incidence of variable comorbidities and mortality.[1] In addition to the increasing incidence of ESRD with age, various burdens of ESRD on other organs also increase with age.[2] Renal transplantation (RT) is one of the renal replacement therapies (RRTs) for patients with ESRD that can change the survival rate, decrease the complications and improve the quality of life.[3–5] ESRD patients have an increased risk of mortality compared with the general population, with cardiovascular disease as the most common cause of death.[6,7] Furthermore, cardiovascular morbidity, major adverse cardiovascular events (MACEs) and stroke are commonly observed in these patients. The prevalence of MACEs in patients with ESRD receiving dialysis varies by country.[8] ESRD is highly prevalent, particularly in Taiwan, which has the highest dialysis rate for ESRD patients worldwide.[9–11] However, the data regarding outcomes of RRTs including dialysis or RT in this country are lacking. Information regarding the individual catastrophic sequelae, such as MACEs and/or stroke, in patients undergoing either dialysis or RT is also insufficient. The outcomes of RT vary according to socio-economical, ethnic, and/or health insurance coverage factors. However, in RT patients, chronic use of immunosuppressive agents and/or steroid may induce hypertension, osteoporosis, hyperglycemia and increased infection rates,[12–15] which could affect rates of MACEs, stroke and mortality. Therefore, surveys of adverse events such as MACEs and stroke as well as survival status in these populations are critical, particularly in countries with high dialysis rates, such as Taiwan.

In the present investigation, nation-wide population-based cohort study was conducted using Taiwan's National Health Insurance Research Database (NHIRD).[16] The NHIRD is a complete enumerated and encrypted database of almost the entire population of Taiwan because citizens are compulsorily (>99%) covered by the government-initiated National Health Insurance (NHI) system in Taiwan; therefore, this cohort is representative of the real-world situation in Taiwan.

In this study, we aimed to investigate the incidence of MACEs and stroke in ESRD patients and to estimate the MACEs-free, stroke-free and MACEs-or-stroke-free rates in those receiving RT and those instead continuing to receive dialysis in Taiwan. These data help to answer the clinical concerns about MACEs and stroke outcomes in maintenance dialysis and RT in Taiwanese patients with ESRD.

2. Methods

2.1. Study design and cohort

The present retrospective population-based cohort investigation consisted of a survey of a cohort of patients with ESRD undergoing regular hemodialysis/peritoneal dialysis (HD/PD) or received RT, selected from 2 million NHI beneficiaries, randomly sampled from Taiwan's population of 23 million people. Data were obtained from the NHIRD,[16] which includes information on disease diagnoses coded according to the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM), treatment procedures, date of service, prescribed medications that can be classified into the Anatomical Therapeutic Chemical (ATC) system of medications, reimbursement amounts, patient demographic information, and patient- and provider-encrypted identifiers. The present study used NHIRD data collected from 2000 to 2009. It was approved by the Institutional Review Board of Taipei Veteran General Hospital (approval number: 2013-07-020A).

2.2. Study patients

The ESRD patients who received HD/PD were identified based on ICD-9-CM diagnosis codes (HD: ICD-9-CM code: 58001C, 58027C, 58029C; PD: ICD-9-CM code: 58002C, 58002CB, 58011A, 58011AB, 58011B, 58011C, 58017B, 58017C, 58028C) in the NHIRD from 2000 to 2009. Those who received RT were identified based on ICD-9-CM coding with 76020A, 76020B and 76020C. MACEs were identified as the following: death from cardiovascular diseases (ICD-9-CM codes 390.x-459.x), coronary heart disease (ICD-9-CM codes 410.x-414.x), heart failure (ICD-9-CM codes 428.x), acute ischemic stroke (AIS, ICD-9-CM codes 433.xx or 434.xx), transient ischemic attack (TIA, ICD-9-CM codes 435.x) and intracerebral hemorrhage (ICH, ICD-9-CM codes 431). The administration of immunosuppressive medication in renal transplant patients, such as tacrolimus (ATC code L04AD02), everolimus (ATC code L01XE10 and L04AA18), sirolimus (ATC code L04AA10), cyclosporin (ATC code L04AA01) and mycophenolate mofetil (ATC code L04AA06) were identified by the prescription.

2.3. Statistical analysis

RT and non-RT groups were followed from the index date (diagnosis) until December 31, 2009. The tracing time-point was the first HD or PD session that the patient received. These data were washed-out for the first year (2000 AD) to confirm that these patients had new-onset ESRD and had never undergone HD or PD before the start date of this study. Furthermore, the appearance of the ICD-9-CM codes for MACEs or stroke was later than either RT in RT group or the first HD/PD session in non-RT group. The standardized differences among all covariates were used to evaluate the differences between matched pairs. The chi-squared test was used to calculate the difference between the RT and non-RT groups. Kaplan–Meier MACEs-free, stroke-free and MACEs-or-stroke-free curves were used to compare the time of MACE or stroke occurrence in the RT and non-RT patients

with ESRD. All analyses were performed using SAS/STAT 9.2 software (SAS Institute Inc., Cary, NC, USA) and STATA 12 software (Stata Corp LP, College Station, TX, USA). A p value < 0.05 was considered significant.

3. Results

3.1. Demographic data

The demographic and clinical characteristics of 164 ESRD patients who underwent RT (study group) and 164 ESRD patients who received HD/PD (non-RT, control group) are shown in Table 1. The mean ages of the study and control groups were 38.0 ± 11.4 and 39.4 ± 10.9 years ($p = 0.286$). Most of their ages were between 30 and 50 years. The percentage of sex difference was the same in the two groups. No significant global differences were observed in MACEs, stroke, diabetes mellitus, hypertension or hyperlipidemia between these two groups. Nevertheless, a lower percentage of MACEs was observed in the RT group than in the non-RT group, although it was not statistically significant ($p > 0.05$). Immunosuppressive medications were used more commonly in the RT group ($p < 0.001$). The survival rate among ESRD patients was significant better in RT group than in non-RT group ($p < 0.001$).

Table 1
Summary of the differences between patients with end-stage renal disease who underwent renal transplantation and those who underwent hemodialysis and/or peritoneal dialysis.

	ESRD with RT (n = 164)		ESRD with HD/PD (n = 164)		p
Age (mean ± SD, yrs old)	38.0 ± 11.4		39.4 ± 10.9		0.286
Age Group					0.608
<30 yr (pt No. and %)	37	54.4%	31	45.6%	
30–40 yr	55	51.9%	51	48.1%	
40–50 yr	47	44.8%	58	55.2%	
50–60 yr	23	53.5%	20	46.5%	
>60 yr	2	33.3%	4	66.7%	
Gender (No. and %)					≒1.000
Male	87	50.0%	87	50.0%	
Female	77	50.0%	77	50.0%	
MACE-total patients (No. and %)					0.550
No MACE	116	51.1%	111	48.9%	
MACE	48	47.5%	53	52.5%	
MACE-30–50 yr (No. and %)					0.882
Non-MACE	73	48.7%	77	51.3%	
MACE	29	47.5%	32	52.5%	
Stroke-total patients (No. and %)					0.250
No Stroke	152	51.0%	146	49.0%	
Stroke	12	40.0%	18	60.0%	
Stroke-30–50 yr (No. and %)*					0.775
No Stroke	92	48.7%	97	51.3%	
Stroke	10	45.5%	12	54.5%	
MACE or Stroke-total patients (No. and %)					0.490
No MACE & No Stroke	108	51.4%	102	48.6%	
MACE or Stroke	56	47.5%	62	52.5%	
MACE or Stroke-30–50 yr (No. and %)					0.948
No MACE & No Stroke	66	48.2%	71	51.8%	
MACE or Stroke	36	48.6%	38	51.4%	
Diabetes mellitus (No. and %)					≒1.000
absent	143	50.0%	143	50.0%	
present	21	50.0%	21	50.0%	
Hypertension (No. and %)					≒1.000
absent	56	50.0%	56	50.0%	
present	108	50.0%	108	50.0%	
Hyperlipidemia (No. and %)					≒1.000
absent	146	50.0%	146	50.0%	
present	18	50.0%	18	50.0%	
Immunosuppressive medications (No. and %)					<0.001*
absent	11	6.6%	156	93.4%	
present	153	95.0%	8	5.0%	
Survival or death (No. and %)					<0.001*
Alive	149	56.0%	117	44.0%	
Dead	15	24.2%	47	75.8%	

ESRD = end-stage renal disease; RT = renal transplantation; HD = hemodialysis; PD = peritoneal dialysis; SD = standard deviation; no. = number; MACEs = major adverse cardiac events; *$p < 0.05$, significant difference.

3.2. Time from indexing of ESRD (first HD or PD session) to MACEs, stroke and MACEs or stroke in RT group and in dialysis group

We calculated the time period from ESRD being indexed (the first HD or PD session) to the initial development of MACE, stoke, and MACLE or stroke in these two patient groups, stratified by age. As shown in Table 2A, 2B and 2C, the times until the occurrence of MACE, stroke, and MACE or stroke were all longer in the RT group than in non-RT group, particularly at younger ages (30–50 yr, $p = 0.038$) (Table 2C).

Table 2A
Comparison of the time from indexing of end-stage renal disease (first hemodialysis or peritoneal dialysis session) to major adverse cardiac event between patients with and without renal transplantation.

	RT group with MACE	Regular HD/PD with MACE	*p*
All patients, time period (mean ± SD, yrs)	n = 48, 2.49 ± 2.24	n = 53, 1.75 ± 1.82	0.075
30–50 (yrs of age), time period (mean ± SD, yrs)	n = 29, 2.38 ± 2.24	n = 32, 1.43 ± 1.76 yrs	0.070

ESRD = end-stage renal disease; MACE = major adverse cardiac event; RT = renal transplantation; HD = hemodialysis; PD = peritoneal dialysis; SD = standard deviation; no. = number.

Table 2B
Comparison of the time from indexing of end-stage renal disease (first hemodialysis or peritoneal dialysis session) to stroke between patients with and without renal transplantation.

	RT group with Stroke	Regular HD/PD with Stroke	*p*
All patients, time period (mean ± SD, yrs)	n = 12, 4.08 ± 2.40	n = 18, 2.92 ± 3.03	0.273
30–50 (yrs of age), time period (mean ± SD, yrs)	n = 10, 4.17 ± 2.59	n = 12, 2.16 ± 2.56 yrs	0.084

ESRD = end-stage renal disease; RT = renal transplantation; HD = hemodialysis; PD = peritoneal dialysis; SD = standard deviation; no. = number.

Table 2C
Comparison of the time from indexing of end-stage renal disease (first hemodialysis or peritoneal dialysis session) to major adverse cardiac event or stroke between patients with and without renal transplantation.

	RT group with MACE or Stroke	Regular HD/PD with MACE or Stroke	*p*
All patients, time period (mean ± SD, yrs)	n = 56, 2.69 ± 2.35	n = 62, 1.99 ± 2.19	0.096
30–50 (yrs of age), time period (mean ± SD, yrs)	n = 36, 2.72 ± 2.44	n = 38, 1.61 ± 2.05 yrs	0.038*

ESRD = end-stage renal disease; MACE = major adverse cardiac event; RT = renal transplantation; HD = hemodialysis; PD = peritoneal dialysis; SD = standard deviation; no. = number; *$p < 0.05$, significant difference.

3.3. Kaplan–Meier MACE-free curve analysis in evaluation of the cumulative risk of MACEs, stroke, and MACEs or stroke in RT and non-RT patients with ESRD

To evaluate whether RT can influence or delay the MACEs and stroke, we used Log-rank tests and Kaplan–Meier survival curves to analyze the cumulative risk of MACEs and stoke in the RT and non-RT patients. As shown in Fig. 1A, B and 1C, significant lower cumulative risks of MACEs, stroke, and MACEs or stroke were observed in ESRD patients who received RT than in those who received dialysis ($p = 0.0134$, 0.0350 and 0.0047, respectively).

4. Discussion

The present retrospective investigation demonstrated an associated between RT and a reduced risk of MACEs or stroke in ESRD patients, although the association was non-significant ($p > 0.05$). This might imply the cardiovascular-protective effect of RT for ESRD patients. Besides, the time to occurrence of MACE and stroke was longer in RT group than in non-RT group, particularly for patients in the RT group who suffered from MACEs or stroke later ($p = 0.038$, Table 2C). These evidences indicated that RT might decrease vascular inflammation or damage for ESRD patients, thus delaying the onset of cardiovascular accidents or stroke events. Furthermore, we observed a significantly lower mortality rate in the RT group than in the non-RT group ($p < 0.001$).

Most of the non-RT ESRD patients received regular HD via vascular shunt. These artificial vascular accesses might also increase the risk of MACEs or stroke for the following reasons: (a) An unstable blood flow induces micro-thrombi and a higher blood flow velocity of shunt is compensated by high cardiac output which then result in heart failure[17]; (b) in long-term HD patients, impaired vascular shunt or vascular endothelial thickness lead to under-dialysis, which has been proven as a cause of high morbidity and mortality[18,19]; (c) repeated hemodialytic needle/catheter insertions into the vascular shunt can induce chronic trauma and increase inflammatory reaction in vascular wall[20]; (d) chronic colonization by microbes on the synthetic catheter in HD/PD can increase infective endocarditis/peritonitis or even sepsis[21,22]; and (e) ESRD patients undergoing chronic dialysis may present with calcium-phosphate imbalance and increase vascular calcification.[23] As reported by Schlieper et al.,[24] calcification of the arteriovenous fistula or synthetic catheter is an independent risk factor for cardiovascular mortality. Conversely, RT can correct uremia and improve the glomerular infiltration rate in patients with ESRD.[25] Therefore, it is conceivable that dialysis, rather than RT, increases the risk of MACEs and stroke as well as the mortality rate in ESRD patients, and the results of this study are compatible with previous reports.[26,27]

The Kaplan–Meier curves for the occurrence of MACEs or stroke in patients with ESRD showed that RT could also reduce MACEs or stroke in ESRD patients over time ($p < 0.05$). These also implied that the lower mortality rate in RT group than in non-RT ESRD patients as shown in the Table 1 is reasonable.

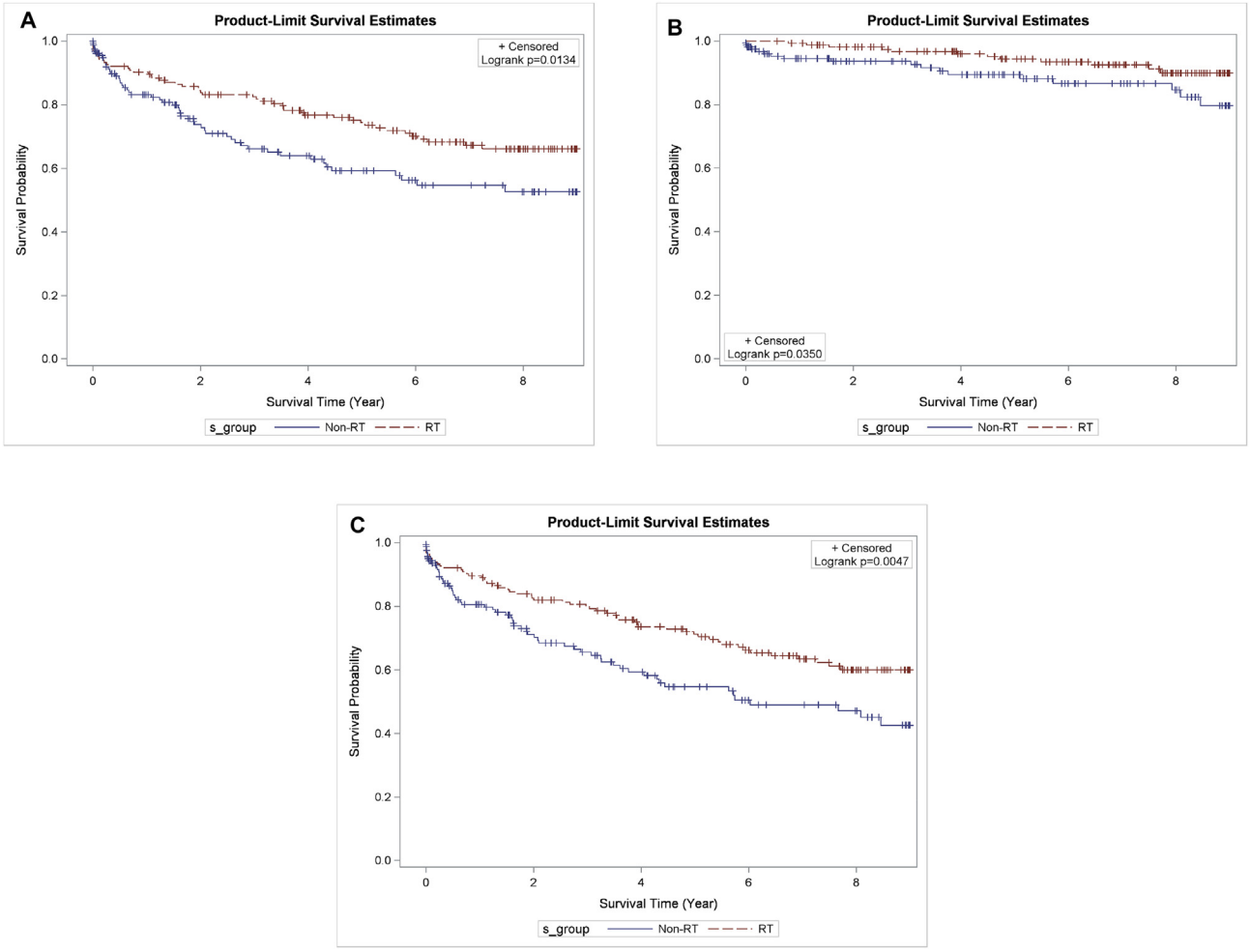

Fig. 1. Kaplan–Meier curve for major adverse cardiac events (MACEs)-free periods (A), stroke-free periods (B), and MACEs-or-stroke-free periods between the groups with and without renal transplantation (RT). These curves show a significantly higher cumulative probability of MACEs-free, stroke-free, and MACEs-or-stroke-free periods in ESRD patients who received RT than in those that never underwent RT (p = 0.0134, 0.035 and 0.0047, respectively).

We also found that the ESRD patients who underwent RT received more immunosuppressive medications than the patients in the non-RT group ($p < 0.001$, Table 1). This was expected because immunosuppressive medications can protect RT patients from graft rejection, although these drugs might also play a role in suppression and control of inflammatory reactions in the vascular system.

The present study had some limitations. First, the NHIRD lacks information on lifestyle-related risk factors such as smoking and alcohol or coffee consumption; the influence of social-economic status on ability to undergo RT; serial laboratory manifestations such as lipid profiles, complete blood count, electrolytes, and inflammation indices such as erythrocyte sedimentation rate or C-reactive protein; physical manifestations such as body habitus, height or body mass indices, which are crucial contributors to MACEs or stroke but unfortunately are exactly the intrinsic defects of claimed data in general. Second, these data did not provide the age, sex, medical history, human leukocyte antigen typing and/or mismatch of the donors as well as donors' willingness to donate the graft. Third, the database could not be used to determine the definitive causes of chronic kidney diseases and the consequent ESRD (e.g., Chinese herbs, alternative therapies, nephrotoxic drugs or food, or other comorbidities such as taking contraceptive, bed-ridden status or trauma), which might also be confounding factors for MACEs or stroke.

In conclusion, the present investigation has demonstrated that Taiwanese ESRD patients who received RT had a higher survival rate and delayed occurrence of MACEs or stroke. To identify the exact factors for MACEs or stroke in patients with ESRD that receive or do not receive RT, a global, prospective and multi-ethnic survey may be necessary in the future.

Acknowledgments

This is supported by Ministry of Science and Technology (NSC102-2314-B075-067-MY3) and Taipei Veterans General Hospital (V105C-114).

References

1. Locatelli F, Del Vecchio L, Manzoni C. Morbidity and mortality on maintenance haemodialysis. *Nephron* 1998;**80**:380−400.
2. Stevens LA, Viswanathan G, Weiner DE. Chronic kidney disease and end-stage renal disease in the elderly population: current prevalence, future projections, and clinical significance. *Adv Chron Kidney Dis* 2010;**17**: 293−301.
3. Laupacis A, Keown P, Pus N, Krueger H, Ferguson B, Wong C, et al. A study of the quality of life and cost−utility of renal transplantation. *Kidney Int* 1996;**50**:235−42.
4. Wolfe RA, Ashby VB, Milford EL, Ojo AO, Ettenger RE, Agodoa LY, et al. Comparison of mortality in all patients on dialysis, patients on dialysis awaiting transplantation, and recipients of a first cadaveric transplant. *N Engl J Med* 1999;**341**:1725−30.
5. Loubeau PR, Loubeau JM, Jantzen R. The economics of kidney transplantation versus hemodialysis. *Prog Transplant* 2001;**11**:291−7.
6. Foley RN, Parfrey PS. Cardiovascular disease and mortality in ESRD. *J Nephrol* 1998;**11**:239−45.
7. Collins AJ, Foley RN, Herzog C, Chavers B, Gilbertson D, Herzog C, et al. US renal data system 2012 annual data report. *Am J Kidney Dis* 2013;**61**(Suppl 1). A7.e1−476.
8. Goodkin DA, Bragg-Gresham JL, Koenig KG, Wolfe RA, Akiba T, Andreucci VE, et al. Association of comorbid conditions and mortality in hemodialysis patients in europe, Japan, and the United States: the dialysis outcomes and practice patterns study (DOPPS). *J Am Soc Nephrol* 2003; **14**:3270−7.
9. Levey AS, Coresh J. Chronic kidney disease. *Lancet* 2012;**379**:165−80.
10. Lin YC, Hsu CY, Kao CC, Chen TW, Chen HH, Hsu CC, et al. Incidence and prevalence of ESRD in Taiwan renal registry data system (TWRDS) 2005-2012. *Acta Nephrologica Taiwan* 2014;**28**:65−8.
11. Yang WC, Hwang SJ. Incidence, prevalence and mortality trends of dialysis end-stage renal disease in Taiwan from 1990 to 2001: the impact of national health insurance. *Nephrol Dial Transplant* 2008;**23**:3977−82.
12. Halloran PF. Immunosuppressive drugs for kidney transplantation. *N Engl J Med* 2004;**351**:2715−29.
13. Seibel MJ, Cooper MS, Zhou H. Glucocorticoid-induced osteoporosis: mechanisms, management, and future perspectives. *Lancet Diabetes Endocrinol* 2013;**1**:59−70.
14. Ha Y, Lee KH, Jung S, Lee SW, Lee SK, Park YB, et al. Glucocorticoid-induced diabetes mellitus in patients with systemic lupus erythematous treated with high-dose glucocorticoid therapy. *Lupus* 2011;**20**:1027−34.
15. Lionakis MS, Kontoyiannis DP. Glucocorticoids and invasive fungal infections. *Lancet* 2003;**362**:1828−38.
16. (NHIRD) NHIRD. *Introduction to the national health insurance Research database (NHIRD), taiwan*. 2010. Available from: http://w3.nhri.org.tw/nhird//date_01.html.
17. Engelberts I, Tordoir JH, Boon ES, Schreij G. High-output cardiac failure due to excessive shunting in a hemodialysis access fistula: an easily overlooked diagnosis. *Am J Nephrol* 1995;**15**:323−6.
18. Plantinga LC, Fink NE, Jaar BG, Sadler JH, Levin NW, Coresh J, et al. Attainment of clinical performance targets and improvement in clinical outcomes and resource use in hemodialysis care: a prospective cohort study. *BMC Health Serv Res* 2007;**7**:5.
19. Wolfe RA, Hulbert-Shearon TE, Ashby VB, Mahadevan S, Port FK, et al. Improvements in dialysis patient mortality are associated with improvements in urea reduction ratio and hematocrit, 1999 to 2002. *Am J Kidney Dis* 2005;**45**:127−35.
20. Dikow R, Schwenger V, Zeier M, Ritz E. Do AV fistulas contribute to cardiac mortality in hemodialysis patients? *Semin Dial* 2002;**15**: 14−7.
21. Dhingra RK, Young EW, Hulbert-Shearon TE, Leavey SF, Port FK. Type of vascular access and mortality in U.S. hemodialysis patients. *Kidney Int* 2001;**60**:1443−51.
22. Jones SM, Ravani P, Hemmelgarn BR, Muruve D, Macrae JM, et al. Morphometric and biological characterization of biofilm in tunneled hemodialysis catheters. *Am J Kidney Dis* 2011;**57**:449−55.
23. London GM, Guerin AP, Marchais SJ, Métivier F, Pannier B, Adda H. Arterial media calcification in end-stage renal disease: impact on all-cause and cardiovascular mortality. *Nephrol Dial Transplant* 2003;**18**: 1731−40.
24. Schlieper G, Kruger T, Djuric Z, Damjanovic T, Markovic N, Schurgers LJ, et al. Vascular access calcification predicts mortality in hemodialysis patients. *Kidney Int* 2008;**74**:1582−7.
25. Glicklich D, Vohra P. Cardiovascular risk assessment before and after kidney transplantation. *Cardiol Rev* 2014;**22**:153−62.
26. Yoo KD, Kim CT, Kim MH, Noh J, Kim G, Kim H, et al. Superior outcomes of kidney transplantation compared with dialysis: an optimal matched analysis of a national population-based cohort study between 2005 and 2008 in Korea. *Medicine (Baltimore)* 2016;**95**:e4352.
27. Tonelli M, Wiebe N, Knoll G, Bello A, Browne S, Jadhav D, et al. Systematic review: kidney transplantation compared with dialysis in clinically relevant outcomes. *Am J Transplant* 2011;**11**:2093−109.