Epidemiology and Mortality of New-Onset Diabetes After Dialysis

Taiwan national cohort study

KAI-JEN TIENT, MD1,2
ZHE-ZHONG LINT, MD3
CHUNG-CHING CHIO, MD4
JHI-JOUNG WANG, MD, PHD5

CHIN-CHEN CHU, MD, PHD6
YIH-MIN SUnt, PHD6
WEI-CHIH KANT, MD7,8
CHIH-CHIANG CHIEN, MD7,9

OBJECTIVE—We examined the predictors and risks associated with pre-existing versus new-onset diabetes mellitus (DM) after initiation of chronic dialysis therapy in end-stage renal disease (ESRD) patients.

RESEARCH DESIGN AND METHODS—In the Taiwan National Health Insurance Research Database, we examined records of ESRD patients who initiated dialysis between 1999 and 2005. Patients were followed until death, transplant, dialysis withdrawal, or 31 December 2008. Predictors of new-onset DM and mortality were calculated using Cox models.

RESULTS—A total of 51,487 incident dialysis patients were examined in this study, including 25,321 patients with pre-existing DM, 3,346 with new-onset DM, and 22,820 without DM at any time. Patients’ age (mean ± SD) was 61.8 ± 11.5, 61.6 ± 13.7, and 56.5 ± 16.6 years in pre-existing, new-onset DM, and without DM groups, respectively. The cumulative incidence rate of new-onset DM was 4% at 1 year and 21% at 9 years. Dialysis modality was not a risk factor for new-onset DM (peritoneal dialysis to hemodialysis hazard ratio [HR] of new-onset DM, 0.94 [95% CI 0.83–1.06]). Pre-existing DM was associated with 80% higher death risk (HR 1.81 [95% CI 1.75–1.87]), whereas the new-onset DM was associated with 10% increased death risk (HR 1.10 [95% CI 1.03–1.17]).

CONCLUSIONS—Whereas dialysis modality does not appear to associate with new-onset DM, both pre-existing and new-onset DM are related to higher long-term mortality in maintenance dialysis patients.

Diabetes Care 36:3027–3032, 2013

The increasing prevalence of diabetes mellitus (DM) is a global health issue in the obese and aging (1). Chronic kidney disease is an important complication of DM. Diabetic nephropathy, the leading cause of end-stage renal disease (ESRD) (2), accounts for ~40% of patients on maintenance dialysis (3).

Many studies (2, 4) report an association between pre-existing DM at the initiation of dialysis and a poor outcome in ESRD patients undergoing dialysis. However, few published studies have focused on postdialysis new-onset DM (4–7). Glucose is one of the contents of hemodialysates (8) and peritoneal dialysates (9). Peritoneal dialysis (PD) patients, who received 24-h continuous high-glucose-concentration peritoneal dialysates, can develop hyperglycemia and transient hyperinsulinism (10). Woodward et al. (6), examining the U.S. Renal Data System, showed the incidence of new-onset DM to be ~6% per year in dialysis patients. In Asia, Chinese patients in Hong Kong have been observed to have a high prevalence of hyperglycemia with a daily exchange of 1.5% glucose dialysate (7). Some epidemiological studies of glycemic load in relation to incident DM report inconsistent results. For example, although high intake of foods with high glycemic load has been found to increase the risk of type 2 DM in Chinese (11), Mosdøl et al. (12) did not find such an association in the Whitehall II study. Nevertheless, one meta-analysis of prospective cohort studies enrolling 13 trials concluded that there was a positive association between glycemetic load and type 2 DM (13). Pure glucose has the highest glycemic index, but few long-term follow-up studies have investigated the glucose load and the risk of DM, especially in patients with ESRD. In addition, it has been demonstrated that increased plasma glucose levels are an independent risk factor for mortality among dialysis patients, even a minor degree of hyperglycemia (7). It has also been reported that the cumulative advanced atherosclerotic change in DM could be responsible for the increased further cardiovascular mortality thereafter.

The worldwide number of ESRD patients undergoing dialysis has grown significantly in recent decades. The incidence and prevalence rates of ESRD are high in Taiwan (14). However, studies on new-onset DM are scarce, especially studies with epidemiological data from a national cohort of Asians with ESRD on maintenance dialysis. Therefore, this study investigates whether there is an association between dialysis modality and new-onset DM and whether new-onset DM is a risk factor for long-term mortality. To find out, we used a large dataset from the Taiwan National Health Insurance Research Database (NHIRD) from
with DM diagnosed before the initiation of dialysis (pre-existing DM group, \( n = 25,321 \)). Next, we identified the patients with new-onset DM during the follow-up period from a subset of patients who did not have pre-existing DM (\( n = 26,166 \)).

### Table 1—Patient characteristics and association with pre-existing DM (\( n = 25,321 \)), new-onset DM (\( n = 3,346 \), and non-DM (\( n = 22,820 \)) in ESRD dialysis patients

|                         | Pre-existing DM | New-onset DM | Non-DM | \( \text{P value} \) |
|-------------------------|-----------------|--------------|--------|----------------------|
| **Sex**                 |                 |              |        | <0.001               |
| Female                  | 12,828 (47.8)   | 1,948 (7.3)  | 12,036 (44.9) |
| Male                    | 12,493 (50.6)   | 1,398 (5.7)  | 10,784 (39.7) |
| **Age at start of dialysis (years)** | <0.001 |        |        |                      |
| <45                     | 1,779 (22.4)    | 407 (5.1)    | 5,744 (72.4) |
| 45–64                   | 12,450 (55.6)   | 1,376 (6.1)  | 8,688 (38.6) |
| 65                      | 11,092 (52.7)   | 1,563 (7.4)  | 8,386 (39.9) |
| **Diagnosis**           | <0.001          |              |        |                      |
| HTN                     |                 |              |        |                      |
| No                      | 2,759 (25.2)    | 908 (8.3)    | 7,369 (66.5) |
| Yes                     | 22,562 (55.6)   | 2,438 (6.0)  | 15,551 (38.3) |
| CHF                     | <0.001          |              |        |                      |
| No                      | 16,572 (42.6)   | 2,737 (7.0)  | 19,626 (50.4) |
| Yes                     | 8,749 (69.7)    | 609 (4.9)    | 3,194 (25.4) |
| CAD                     | <0.001          |              |        |                      |
| No                      | 19,543 (43.8)   | 2,730 (6.8)  | 19,784 (49.3) |
| Yes                     | 7,778 (67.8)    | 616 (5.4)    | 3,072 (26.8) |
| **Peripheral vascular disease** | <0.001 |        |        |                      |
| No                      | 24,096 (48.8)   | 3,227 (6.5)  | 22,016 (46.4) |
| Yes                     | 1,225 (57)      | 119 (5.5)    | 804 (37.4) |
| Other cardiac\(^a\)     | <0.001          |              |        |                      |
| No                      | 22,842 (48.7)   | 3,031 (6.5)  | 21,051 (44.9) |
| Yes                     | 2,479 (54.3)    | 315 (6.9)    | 1,769 (38.8) |
| Dysrhythmia             | <0.001          |              |        |                      |
| No                      | 23,612 (48.9)   | 3,133 (6.5)  | 21,519 (44.6) |
| Yes                     | 1,709 (53)      | 213 (6.6)    | 1,301 (40.4) |
| COPD                    | <0.001          |              |        |                      |
| No                      | 22,702 (48.7)   | 2,996 (6.4)  | 20,942 (44.9) |
| Yes                     | 2,619 (54)      | 350 (7.2)    | 1,878 (38.7) |
| Gastrointestinal bleeding | <0.001         |              |        |                      |
| No                      | 19,452 (48.5)   | 2,569 (6.4)  | 18,077 (45.1) |
| Yes                     | 5,869 (51.5)    | 777 (6.8)    | 4,743 (41.6) |
| Liver disease           | 0.002           |              |        |                      |
| No                      | 22,997 (48.9)   | 3,068 (6.5)  | 20,925 (44.5) |
| Yes                     | 2,324 (51.7)    | 278 (6.2)    | 1,893 (42.1) |
| Cancer                  | <0.001          |              |        |                      |
| No                      | 24,124 (49.8)   | 3,154 (6.5)  | 21,193 (43.7) |
| Yes                     | 1,197 (39.7)    | 192 (6.4)    | 1,629 (54) |
| Hyperuricemia           | <0.001          |              |        |                      |
| No                      | 22,540 (50.5)   | 2,773 (6.2)  | 19,344 (43.3) |
| Yes                     | 2,781 (40.7)    | 573 (8.4)    | 3,476 (50.9) |
| Dyslipidemia            | <0.001          |              |        |                      |
| No                      | 19,499 (44.6)   | 3,042 (7.0)  | 21,204 (48.5) |
| Yes                     | 5,822 (75.2)    | 304 (3.9)    | 1,616 (20.9) |

Data are \( \% \) unless otherwise indicated. *Includes pericarditis, endocarditis, myocarditis, other complications of heart disease, heart transplant, heart valve replacement, and cardiac devices.
New-onset DM after the initiation of dialysis was defined as DM diagnosed at least 3 months after dialysis began (new-onset DM group, n = 3,346). The remaining members of the no pre-existing DM, those without new-onset DM during follow-up period, were assigned to the non-DM group (n = 22,820).

Ascertaining the demographic and comorbid variables

We linked to the diagnostic codes through the inpatient and outpatient claims databases of the NHIRD. Cases of DM and those with comorbidities were identified according to one of the following definitions: 1) diagnostic codes in outpatient visits if the patient had an initial diagnosis at any time the year leading up to beginning of dialysis and then experienced one or more additional diagnoses within the subsequent 12 months, and the first and last outpatient visit within 1 year must have had to be >30 days apart to avoid accidental inclusion of miscoded patients; or 2) diagnostic codes in hospitalization databases at least one time within the year leading up to start of dialysis. This method of identifying these comorbidities has been used extensively in various studies of Taiwan NHIRD, and many articles have been published (15–18). This study included not only the cumulative incidence of new-onset DM, but also date of death, patient demographics, and baseline comorbidities. ICD codes are provided in Supplementary Table 1.

Statistical analyses

Baseline characteristics between groups (pre-existing DM, new-onset DM, and without DM) were compared. Age was entered as a categorical variable (<45, 45–64, and ≥65 years). Significance was set at P < 0.05. The cumulative proportion of patients with new-onset DM and of survivors after the initiation of dialysis was calculated using the Kaplan-Meier method. The log-rank test was used to analyze significance. Cox proportional hazards models were used to identify the risk factors of new-onset DM and mortality after the initiation of dialysis. Hazard ratios (HRs) and 95% CIs were derived from Cox proportional hazards models. Cox models met the assumption of proportionality of risks. The purposeful selection process begins by a univariate analysis of each variable. Any variable having a significant univariate test was selected as a candidate for the multivariate analysis. The independent associations were examined using multivariate analysis. All statistical operations were performed using the Statistical Package for Social Sciences for Windows 17.0 (SPSS Inc., Chicago, IL).

RESULTS

Demographics and clinical characteristics

A total of 51,487 incident dialysis patients were enrolled in this study. Of these patients, 25,321 had pre-existing DM, 3,346 had new-onset DM, and the other patients did not have DM throughout the study period (Table 1). There were 147 cases of type 1 DM among 25,321 pre-existing DM patients, but no type 1 DM among 3,346 new-onset DM patients. A total of 7% of female and 6% of male patients had new-onset DM (P < 0.001). Only 5% of those <45 years old had new-onset DM, but 7% of those ≥65 years old did (P < 0.001). In Taiwan dialysis patients, 93% patients received hemodialysis (HD), and only 7% patients received PD. A total of 51 and 6% of the HD patients had pre-existing DM and new-onset DM, respectively, whereas only 32 and 8% of the PD patients had pre-existing DM had new-onset DM, respectively (P < 0.001).

Table 2—Risk factors for new-onset DM after initiation of dialysis in ESRD non-pre-existing DM dialysis patients (n = 26,166)

| Covariate                        | Univariate analysis | Multivariate analysis |
|----------------------------------|---------------------|-----------------------|
| Sex (male vs. female)            | 0.88 (0.82–0.84)*   | 0.84 (0.78–0.91)*     |
| Age at start of dialysis (years) |                     |                       |
| <45                              | 1                   | 1                     |
| 45–64                            | 2.24 (2.01–2.51)*   | 2.15 (1.92–2.40)*     |
| ≥65                              | 3.44 (3.09–3.84)*   | 3.00 (2.68–3.36)*     |
| Dialysis modality (PD vs. HD)    | 0.94 (0.83–1.06)    | —                     |
| HTN (yes vs. no)                 | 1.27 (1.18–1.38)*   | 1.08 (1.00–1.17)*     |
| CHF (yes vs. no)                 | 1.57 (1.44–1.72)*   | 1.26 (1.14–1.38)*     |
| CAD (yes vs. no)                 | 1.67 (1.53–1.82)*   | 1.19 (1.08–1.31)*     |
| CVD (yes vs. no)                 | 1.77 (1.58–1.99)*   | 1.39 (1.24–1.57)*     |
| Peripherial vascular disease (yes vs. no) | 1.13 (0.94–1.36)   | —                     |
| Other cardiac* (yes vs. no)      | 1.33 (1.19–1.50)*   | 1.13 (1.01–1.28)*     |
| Dysrhythmia (yes vs. no)         | 1.33 (1.16–1.53)*   | 0.93 (0.80–1.07)      |
| COPD (yes vs. no)                | 1.59 (1.42–1.78)*   | 1.20 (1.07–1.35)*     |
| Gastrointestinal bleeding (yes vs. no) | 1.28 (1.18–1.39)* | 1.10 (1.01–1.19)*     |
| Liver disease (yes vs. no)       | 1.10 (0.97–1.24)    | —                     |
| Cancer (yes vs. no)              | 1.03 (0.89–1.19)    | —                     |
| Hyperuricemia (yes vs. no)       | 1.22 (1.11–1.33)*   | 1.07 (0.97–1.18)      |
| Dyslipidemia (yes vs. no)        | 1.31 (1.16–1.47)*   | 1.21 (1.07–1.36)*     |

Data are HR (95% CI). *HR adjusted for sex, age, HTN, CHF, CAD, CVA, other cardiac disease, dysrhythmia, COPD, gastrointestinal bleeding, hyperuricemia, and dyslipidemia. *Includes pericarditis, endocarditis, myocarditis, other complications of heart disease, heart transplant, heart valve replacement, and cardiac devices.

Cumulative incidence and risk factors for new-onset DM

The cumulative incidence rate of new-onset DM were 4% at 1 year, 9% at 3 years, 14% at 5 years, and 21% at 9 years (Supplementary Fig. 2A). Being female, being older, and having baseline comorbidities were independent risk factors for new-onset DM in dialysis patients (Table 2). There was no significant difference between the modalities of HD and PD with regard to new-onset DM (Supplementary Fig. 2B). Patients ≥65 years old had nearly a threefold increase in new-onset DM compared with those <45 years old (HR 3.00 [95% CI 2.68–3.60]). Additionally, factors increasing the likelihood that new-onset DM would develop included hypertension (HTN) (HR 1.08, 95% CI 1.00–1.17), congestive heart failure (CHF) (HR 1.26, 95% CI 1.14–1.38), coronary artery disease (CAD) (HR 1.19 [95% CI 1.08–1.31]), cerebrovascular accident (CVA) (HR 1.39 [95% CI 1.24–1.57]), and chronic obstructive pulmonary disease (COPD) (HR 1.20 [95% CI 1.07–1.35]).

Cumulative survival rate and risk factors for all-cause mortality

The Kaplan-Meier survival curves for patients in the pre-existing DM, new-onset DM, and non-DM groups are shown in Fig. 2.
New-onset DM after dialysis

Fig. 1. The cumulative survival rate of the pre-existing DM group was 92% at 1 year, 51% at 5 years, and 26% at 9 years. The cumulative survival rate of the new-onset DM group was 96% at 1 year, 68% at 5 years, and 42% at 9 years. The cumulative survival rate of the non-DM group was 95% at 1 year, 74% at 5 years, and 58% at 9 years. The differences in survival among these three groups were significant (log-rank: \( P < 0.001 \)). We have further analyzed the survival rate after new-onset DM was diagnosed (Supplementary Fig. 3) and found the mean duration between new-onset DM diagnosed and death was 6.10 ± 1.01 years.

Pre-existing DM was associated with 80% higher death risk (HR 1.81 [95% CI 1.75–1.87]), whereas the new-onset DM was associated with 10% increased death risk (HR 1.10 [95% CI 1.03–1.17]) (Table 3). As can be seen in Supplementary Table 2, further analysis revealed individuals with pre-existing DM <45 years old were 2.99 (95% CI 2.65–3.39) times more likely to die than individuals of a similar age without DM, with the HR decreasing in elderly individuals with pre-existing DM. The trend was similar to those with new-onset DM compared with those without DM. Risk estimates for mortality tended to be higher in women than in men in both pre-existing DM and new-onset DM groups.

CONCLUSIONS—In this nationwide study of 51,487 incident dialysis patients, we found no significant association between dialysis modality and new-onset DM. However, new-onset DM was significantly associated with sex, age, and baseline comorbidity. It was a risk factor for long-term mortality in patients on maintenance dialysis.

The incidence of new-onset DM after dialysis varies. One study (5) reported that the incidence after HD was 20 per 1,000 patient-years, and the prevalence was 7.6% during only 3 years of follow-up. Our nearly 10-year follow-up study found a higher incidence (29 per 1,000 patient-years) and prevalence (12.8%) rate after HD. Another 6-year follow-up study (4) reported that 8.5% of dialysis patients, including HD and PD, who initiated dialysis developed new-onset DM within 6 years. In our study, 12.7% of dialysis patients, including HD and PD, developed new-onset DM within 10 years. This higher rate of new-onset DM may reflect the longer follow-up period in our study. Woodward et al. (6) also found that immunosuppressant agents had great impact on the new-onset DM and reported that new-onset DM over the first 2 years posttransplant had a very high incidence of almost 18–30% among patients receiving cyclosporine and tacrolimus.

We found no significant difference in percentage of new-onset DM after the initiation of dialysis between patients undergoing HD (12.80%) and patients undergoing PD (12.20%), even after adjustment. This finding differs from that for the wait-listed transplanted renal allograft recipients in Woodward et al. (6). This discrepancy may be because the results in Woodward et al. (6) were not adjusted.

Being female and being older were significant risk factors for the development of new-onset DM in our patients. Age not only affected the prevalence of new-onset DM, but also the mortality. The prevalence of DM increases with age (1), which is considered one parameter of diabetes risk scores (19). The pathogenesis of age-related DM is related to insulin resistance and decreased B-cell function (20). We also found that cardiovascular disease (CVD) to be a significant risk factor for the development of new-onset DM. This relationship might be explained by the fact that atherosclerosis contributes to most of the macrovascular disease. Dyslipidemia and vascular inflammation result in endothelial dysfunction and atherosclerosis (21). Elevated values of circulatory makers such as interleukin-6 and high-sensitivity C-reactive protein (CRP) commonly accompany CVD. Vascular inflammation and endothelial dysfunction may also be associated with an increased risk of developing type 2 DM. Hu et al. (22) conducted a prospective, case-control study of inflammatory markers as predictors of type 2 DM among 32,826 subjects. These data support the role of inflammation in the pathogenesis of type 2 DM. A 4-year follow-up study in a nationwide cohort of 27,628 subjects shows elevated levels of CRP and interleukin-6 predict the development of type 2 DM (23). A 7.2-year follow-up study also showed that subjects with elevated CRP had a higher risk of developing diabetes and concluded that inflammation could be one of the risk factors for developing DM (24). Meigs et al. (25) performed a prospective study that showed that endothelial dysfunction could predict type 2

![Cumulative survival rate](image-url)
Table 3—Risk factor for all-cause mortality in ESRD dialysis patients (n = 51,487)

| Covariate | Univariate analysis | Multivariate analysis |
|-----------|--------------------|-----------------------|
| Sex (male vs. female) | 1.18 (1.15–1.21)* | 1.19 (1.16–1.23)* |
| Age at start of dialysis (years) | | |
| <45 | 1 | |
| 45–64 | 2.63 (2.47–2.79)* | 2.01 (1.89–2.14)* |
| ≥65 | 5.89 (5.54–6.25)* | 4.25 (3.99–4.52)* |
| DM | | |
| Non-DM | 1 | 1 |
| New-onset DM | 1.35 (1.27–1.43)* | 1.10 (1.03–1.17)* |
| Pre-existing DM | 2.28 (2.21–2.35)* | 1.81 (1.75–1.87)* |
| Dialysis modality (PD vs. HD) | 0.71 (0.66–0.75)* | 1.19 (1.11–1.26)* |
| CHF (yes vs. no) | 1.88 (1.82–1.93)* | 1.32 (1.28–1.37)* |
| CAD (yes vs. no) | 1.83 (1.78–1.89)* | 1.13 (1.10–1.17)* |
| CVD (yes vs. no) | 1.92 (1.85–2.00)* | 1.37 (1.32–1.42)* |
| Peripheral vascular disease (yes vs. no) | 1.39 (1.30–1.48)* | 1.08 (1.02–1.15)* |
| Other cardiacc (yes vs. no) | 1.32 (1.26–1.38)* | 1.08 (1.03–1.13)* |
| Dysrhythmia (yes vs. no) | 1.81 (1.72–1.90)* | 1.21 (1.15–1.27)* |
| COPD (yes vs. no) | 1.78 (1.70–1.85)* | 1.21 (1.16–1.27)* |
| Gastrointestinal bleeding (yes vs. no) | 1.44 (1.40–1.49)* | 1.19 (1.16–1.23)* |
| Liver disease (yes vs. no) | 1.41 (1.34–1.47)* | 1.35 (1.29–1.41)* |
| Cancer (yes vs. no) | 1.74 (1.65–1.84)* | 1.55 (1.47–1.64)* |

Data are HR (95% CI). *HR adjusted for sex, age, type of diabetes, dialysis modalities, CHF, CAD, CVA, peripheral vascular disease, other cardiac disease, dysrhythmia, COPD, gastrointestinal bleeding, liver disease, and cancer. ‡Includes pericarditis, endocarditis, myocarditis, other complications of heart disease, heart transplant, heart valve replacement, and cardiac devices.

Acknowledgments—The study was supported by Grant CMFHR10124 from Chi-Mei Medical Center and Grant NHRI-NHIIRD-99182 from the National Health Research Institutes in Taiwan.

No potential conflicts of interest relevant to this article were reported.

K.-J.T. contributed to the discussion and reviewed and edited the manuscript. Z.-Z.L. contributed to the discussion. C.-C.Chien drafted the manuscript. J.-J.W. designed the study, researched data, and drafted the manuscript. Y.-M.S. drafted the manuscript. W.-C.K. and C.-C.Chien contributed to the discussion and reviewed and edited the manuscript. Z.-Z.L. is the guarantor of this work and, as such, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

References

1. Wild SH, Roglic G, Green A, Sicree R, King H. Global prevalence of diabetes: estimates for the year 2000 and projections for 2030. Diabetes Care 2004;27: 1047–1053
2. Hoffmann F, Haastert B, Koch M, Giani G, Glaeske G, Icks A. The effect of diabetes on incidence and mortality in end-stage renal disease in Germany. Nephrol Dial Transplant 2011;26:1634–1640
3. United States Renal Data System. USRDS 2011 Annual Data Report: Atlas of Chronic Kidney Disease and End-Stage Renal Disease.
New-onset DM after dialysis

in the United States. National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases, Bethesda, MD, 2011

4. Lok CE, Oliver MJ, Rothwell DM, Hux JE. The growing volume of diabetes-related dialysis: a population based study. Nephrol Dial Transplant 2004;19:3098–3103

5. Salifu MO, Abbott KC, Aytug S, et al. New-onset diabetes after hemodialysis initiation: impact on survival. Am J Nephrol 2010;31:239–246

6. Woodward RS, Schnitzler MA, Baty J, et al. Incidence and cost of new onset diabetes mellitus among U.S. wait-listed and transplanted renal allograft recipients. Am J Transplant 2003;3:590–598

7. Szeto CC, Chow KM, Kwan BC, Chung KY, Leung CB, Li PK. New-onset hyperglycemia in nondiabetic Chinese patients started on peritoneal dialysis. Am J Kidney Dis 2007;49:524–532

8. Raimann JG, Kruse A, Thijssen S, et al. Metabolic effects of dialyzate glucose in chronic hemodialysis: results from a prospective, randomized crossover trial. Nephrol Dial Transplant 2012;27:1559–1568

9. Wideroe TE, Smeby LC, Myking OL. Plasma concentrations and transperitoneal transport of native insulin and C-peptide in patients on continuous ambulatory peritoneal dialysis. Kidney Int 1984;25:82–87

10. Lindholm B, Karlander SG. Glucose tolerance in patients undergoing continuous ambulatory peritoneal dialysis. Acta Med Scand 1986;220:477–483

11. Villegas R, Liu S, Gao YT, et al. Prospective study of dietary carbohydrates, glycemic index, glycemic load, and incidence of type 2 diabetes mellitus in middle-aged Chinese women. Arch Intern Med 2007;167:2310–2316

12. Mosdøl A, Witte DR, Frost G, Marmot MG, Brunner EJ. Dietary glycemic index and glycemic load are associated with high-density-lipoprotein cholesterol at baseline but not with increased risk of diabetes in the Whitehall II study. Am J Clin Nutr 2007;86:988–994

13. Dong JY, Zhang L, Zhang YH, Qin LQ. Dietary glycaemic index and glycaemic load in relation to the risk of type 2 diabetes: a meta-analysis of prospective cohort studies. Br J Nutr 2011;106:1649–1654

14. Yang WC, Hwang SJ. Taiwan Society of Nephrology. 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;23:3977–3982

15. Chen HF, Ho CA, Li CY. Age and sex may significantly interact with diabetes on the risks of lower-extremity amputation and peripheral revascularization procedures: evidence from a cohort of a half-million diabetic patients. Diabetes Care 2006;29:2409–2414

16. Chen HF, Chen P, Li CY. Risk of malignant neoplasms of liver and biliary tract in diabetic patients with different age and sex stratifications. Hepatology 2010;52:155–163

17. Chen PC, Chan YT, Chen HF, Ko MC, Li CY. Population-Based Cohort Analyses of the Bidirectional Relationship Between Type 2 Diabetes and Depression. Diabetes Care 2012;36:376–382

18. Sun Y, Chang YH, Chen HF, Su YH, Su HF, Li CY. Risk of Parkinson disease onset in patients with diabetes: a 9-year population-based cohort study with age and sex stratifications. Diabetes Care 2012;35:1047–1049

19. Lindström J, Tuomilehto J. The diabetes risk score: a practical tool to predict type 2 diabetes risk. Diabetes Care 2003;26:725–731

20. Chen M, Bergman RN, Pacini G, Porte D Jr. Pathogenesis of age-related glucose intolerance in man: insulin resistance and decreased beta-cell function. J Clin Endocrinol Metab 1983;60:13–20

21. Libby P, Ridker PM, Maseri A. Inflammation and atherosclerosis. Circulation 2002;105:1135–1143

22. Hu FB, Meigs JB, Li TY, Rifai N, Manson JE. Inflammatory markers and risk of developing type 2 diabetes in women. Diabotes 2004;53:693–700

23. Pradhan AD, Manson JE, Rifai N, Buring JE, Ridker PM. C-reactive protein, interleukin 6, and risk of developing type 2 diabetes mellitus. JAMA 2001;286:327–334

24. Thorand B, Löwel H, Schneider A, et al. C-reactive protein as a predictor for incident diabetes mellitus among middle-aged men: results from the MONICA Augsburg cohort study, 1984-1998. Arch Intern Med 2003;163:93–99

25. Meigs JB, Hu FB, Rifai N, Manson JE. Biomarkers of endothelial dysfunction and risk of type 2 diabetes mellitus. JAMA 2004;291:1978–1986

26. Mozaffarian D, Marfiss R, Levantesi G, et al. Incidence of new-onset diabetes and impaired fasting glucose in patients with recent myocardial infarction and the effect of clinical and lifestyle risk factors. Lancet 2007;370:667–675

27. Culver AL, Ockene IS, Balasubramanian R, et al. Statin use and risk of diabetes mellitus in postmenopausal women in the Women’s Health Initiative. Arch Intern Med 2012;172:144–152

28. Preiss D, Seshasai SR, Welsh P, et al. Risk of incident diabetes with intensive-dose compared with moderate-dose statin therapy: a meta-analysis. JAMA 2011;305:2556–2564

29. Sattar N, Preiss D, Murray HM, et al. Statins and risk of incident diabetes: a collaborative meta-analysis of randomised statin trials. Lancet 2010;375:735–742

30. Cohen D, Ridker PM, Mora S, Buring JE, Glynn RJ. Blood pressure and risk of developing type 2 diabetes mellitus: the Women’s Health Study. Eur Heart J 2007;28:2937–2943