Estimation of Expected Life-Years Saved From Successful Prevention of End-Stage Renal Disease in Elderly Patients With Diabetes

A nationwide study from Taiwan

Deng-Chi Yang, md[1,2]
Lukas Jyuhn-Hsiarn Lee, md, phd[3,4]
Chih-Cheng Hsu, md, drph[5]
Yu-Yin Chang, msc[3]

Ming-Cheng Wang, md[6]
Wei-Hung Lin, md[6,7]
Chia-Ming Chang, md[1,2]
Jung-Der Wang, md, scd[4,6,8]

OBJECTIVE—Because of the increasing incidence and prevalence of diabetes as a leading cause of end-stage renal disease (ESRD) in the aging population, we estimated the expected life-years (LYs) saved from successful prevention of ESRD in elderly patients with diabetes.

RESEARCH DESIGN AND METHODS—We conducted a population-based cohort study using the National Health Insurance Research Database. We identified all incidences of ESRD in the individuals >65 years of age who were receiving maintenance hemodialysis (N = 24,243) from the registry files of catastrophic illnesses in Taiwan from 1 July 1997 to 31 December 2005. We then retrospectively searched the database to determine whether there had been a diagnosis of diabetes in these cases. After the exclusion of individuals with malignancy (n = 3,423), we extrapolated the survival rates through the end of 2006 using the Monte Carlo method. Using the data of preventable ESRD cases due to diabetes and expected years of life lost (EYLL) in each age stratum, we further estimated the expected LYs saved from successful prevention of ESRD in elderly patients with diabetes.

RESULTS—The estimated average EYLL was 10.6–5.8 and 12.3–7.3 years for diabetic males and females, respectively, aged 65–79 years. In total, 5,430.1 LYs and 10,177 LYs could be saved by the successful prevention of ESRD in male and female elderly patients with diabetes, respectively, in a single year.

CONCLUSIONS—The LYs saved by successful prevention of ESRD in elderly patients with diabetes in a single year are substantial and deserve special attention, especially in elderly females.

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The incidence and prevalence of diabetes keeps rising worldwide (1). The combined effects of an aging population, increased obesity and inactivity, and improved survival among diabetic individuals all contribute to this emerging pandemic. Diabetes is a disease highly prevalent in older individuals (2,3), and approximately one-third of adults >65 years have diabetes (4), which presents a great burden to individuals, society, and healthcare services.

Chronic kidney disease (CKD) is one of the most common long-term complications related to diabetes, and diabetic nephropathy is the leading cause of end-stage renal disease (ESRD) in many countries (5). In developed countries, approximately half of the new ESRD cases are related to diabetes, and the prevalence of diabetes generally increases as the population ages (5,6). The U.S., Japan, Mexico, and Taiwan have the highest incidence and prevalence of ESRD in the world (5). In Taiwan, ~6.33% of all healthcare expenditures covered by the National Health Insurance were allocated to individuals with ESRD for dialysis in 2009, although these individuals accounted for only 0.24% of the total population (5). ESRD not only produces a financial burden but also impairs quality of life for the elderly and their families (7,8).

The standardized mortality ratios of elderly patients with ESRD are significantly higher in patients with diabetes than in nondiabetic subjects (9). Although life expectancy (LE) has been reported for elderly patients undergoing maintenance dialysis (9–12), research on the effects of diabetes among different age groups within the elderly population seems lacking (9,10). Moreover, the expected years of life lost (EYLL) for elderly patients with ESRD undergoing maintenance dialysis has not yet been investigated. We hypothesize that optimal control of blood glucose and blood pressure in elderly

patients with diabetes is a worthwhile prevention strategy to reduce the incidence of ESRD, even in the oldest populations. Using the National Health Insurance Research Database (NHIRD), we conducted a population-based cohort study to determine the impact of diabetes, sex, and age on LE in elderly patients undergoing maintenance hemodialysis. We also examined the EYLL and estimated life-years (LYs) gained by the successful prevention of ESRD in elderly patients with diabetes from different age strata to evaluate the potential gain of health benefits from the effective prevention of ESRD.

RESEARCH DESIGN AND METHODS

Study population and data collection

The current study was conducted following the approval of the Institutional Review Board of the National Cheng Kung University Hospital. Taiwan launched a single-payer National Health Insurance Program on 1 March 1995. In 2011, >99% of the people in Taiwan were enrolled in this program (13). The database of this program contains registration files and original claim data for reimbursement. The National Health Research Institutes transformed these datasets into a research database, entitled NHIRD. Because the identification number of each insured individual was transformed and encrypted, privacy was fully protected. These files provided detailed information on each individual's health care services, including all payments for outpatient visits, hospitalizations, and prescriptions.

We identified all incidences of ESRD in the individuals undergoing maintenance dialysis from the registry files of catastrophic illnesses in the NHIRD. Because each individual registered in the database of catastrophic illnesses is exempt from any copayment for dialysis therapy, the registry is comprehensive. Furthermore, the validity of the registry is assured by the careful monitoring of the National Health Insurance to prevent any abuse. A nephrologist typically makes the diagnosis of ESRD. The registry ESRD criteria are as follows: a diagnosis of CKD with an irreversible creatinine level of >8 mg/dL or a level of >6 mg/dL with diabetes as a comorbid condition. We allowed 6 months of duration (between 1 January and 30 June 1997) to exclude all prevalent cases. We also excluded cases undergoing maintenance peritoneal dialysis

because of the small number of these cases ($n = 769$). We defined dialysis of >90 days as maintenance (long-term) dialysis. From 1 July 1997 to 31 December 2005, there were 52,756 incident cases of ESRD under maintenance hemodialysis for >90 days. Among them, 24,243 cases were >65 years. To estimate the incidence rates of ESRD in elderly patients with and without diabetes, we retrospectively searched the database to determine if such a diagnosis had been reported in the discharge summary or outpatient claim for diabetes (ICD-9-CM code 250) before the diagnosis of ESRD. The diagnosis of diabetes was confirmed if it had been included as one of the diagnoses at discharge or if there had been more than three outpatient claims for diabetes. The proportions of patients with diabetes stratified by age and sex were estimated based on interpolation of data from the following three national surveys conducted in Taiwan: the 1999–2000 Elderly Nutrition and Health Survey (14) and the Taiwanese Surveys on Blood Sugar, Blood Lipids and Blood Pressure conducted during 2002 and 2007 (15–17). The 5-year age-specific incidence rates of ESRD in elderly patients with diabetes and nondiabetic subjects undergoing maintenance hemodialysis were then calculated with the national population of Taiwan as the denominator. Cumulative incidence rates between 65 and 84 years of age ($CIR_{65–84}$) were also calculated to estimate the occurrence of ESRD in elderly patients with diabetes and nondiabetic subjects undergoing maintenance hemodialysis using the following formula:

$$CIR_{65-84} = 1 - e^{-\sum_i (IR_i)(t_i)}$$

(18,19). To prevent confounding, we further excluded 3,423 cases with malignancy. Therefore, a total of 20,820 cases were included in the final analysis. Subsequently, the LE and EYLL in the elderly were estimated after stratification by age, sex, and the presence of diabetes, and LYs gained by successful prevention of ESRD in elderly patients with diabetes were calculated.

Survival in the ESRD population under maintenance hemodialysis

All incident cases were followed through the end of 2006 or death. The NHIRD indicates whether an individual is living, and therefore, most deceased cases of ESRD can be identified. For cases with missing information on this item, we

defined the date of death as 1 month after the date of the last medical visit. Because individuals undergoing dialysis typically die within 1 month if no renal replacement therapy is provided, the above assumption seems acceptable. We used the Kaplan-Meier method to estimate the survival function based on follow-up data from 1 July 1997 to 31 December 2006. All incident cases were further divided into patients with diabetes and nondiabetic subjects, and LE and EYLL were analyzed in the 5-year age stratification.

Extrapolation of long-term survival for the ESRD population under maintenance hemodialysis

Because many cohorts with chronic diseases may not have been followed for a sufficient amount of time, we used a semiparametric method for extrapolation (20) to estimate survival analysis up to 50 years. The extrapolation was mathematically proven to be valid if constant excess hazard can be assumed (21). It was composed of three processes (20). For every individual of the ESRD cohort, we first created an age- and sex-matched referent from the life tables of the general population using the Monte Carlo method. The life tables for the general population were obtained directly from the national vital statistics published by the Department of Statistics, Ministry of the Interior, Executive Yuan, Taiwan. The survival curve of the cohort of age- and sex-matched referents was obtained by applying the Kaplan-Meier method. Second, we fitted a simple linear regression line to the logit of the ratio of survival functions between the ESRD and referent cohorts to the end of follow-up. Finally, the regression line and survival curve of the cohort of referents were used to predict a long-term survival curve beyond the follow-up for the ESRD population. To facilitate the computation, we used an iSQoL (integration of Survival and Quality of Life) software program in the R statistical package. This software can be freely downloaded from http://www.stat.sinica.edu.tw/jshwang.

Estimation of EYLL

The average EYLL of an ESRD cohort was estimated as the difference in the area between the mean survival curves of the ESRD cohort and reference population. This calculation provides a measure of the burden of ESRD on an individual. It additionally demonstrates the amount of an individual's life that is likely to be saved by a preventive program targeted

at those with elevated risk for developing ESRD.

Expected LYs gained by diabetes care in the elderly due to successful prevention of ESRD

We first calculated the prevalence of patients with diabetes in 2010 by multiplying the proportion of patients with diabetes from the 2007 Taiwanese Survey on Blood Sugar, Blood Lipids and Blood Pressure with the 2010 national population of Taiwan. Then, the number of preventable new ESRD cases was estimated from the proportion of patients with diabetes in 2010 by multiplying this number with the excess incidence rate, (= incidence rate of ESRD [patients with diabetes] − incidence rate of ESRD [nondiabetic subjects]), which was then multiplied with the EYLL per case of ESRD due to diabetes. Finally, we summed up the expected LYs gained in each age stratum and obtained the total LYs that could be saved by successful prevention of ESRD in elderly patients with diabetes between 65 and 84 years of age in a single year.

RESULTS—The LE and EYLL of elderly patients undergoing maintenance hemodialysis are summarized in Table 1. The estimated average EYLL of an ESRD cohort is the difference between the areas of estimated survival curves for the reference population and the ESRD cohort, as shown in Fig. 1A and B, respectively. Elderly patients with ESRD exhibited the longest LE for those aged 65–69 years among both patients with diabetes (4.4 ± 0.1 years in males and 4.8 ± 0.2 years in females) and nondiabetic subjects (7.1 ± 0.3 years in males and 7.9 ± 0.3 years in females). Elderly patients with diabetes generally showed a significantly shorter LE than elderly nondiabetic subjects in both sexes. For example, in males aged 65–69 years, the average ESRD diagnosis age was 66.9 ± 1.5 years among patients with diabetes compared with 67.1 ± 1.4 years among nondiabetic subjects. Furthermore, the LEs were 4.4 ± 0.1 and 7.1 ± 0.3 years ($P < 0.001$) for patients with diabetes and nondiabetic subjects, respectively.

The estimated average EYLL was greater in elderly patients with diabetes than in elderly nondiabetic subjects after stratification by sex. For example, Table 1 showed that the estimated average EYLL for males aged 65–69 years was 10.6 ± 0.1 and 7.7 ± 0.3 years ($P < 0.001$) for patients with diabetes and nondiabetic subjects, respectively. For females aged 65–69 years, the estimated average EYLL was 12.3 ± 0.2 and 9 ± 0.3 years ($P < 0.001$) for patients with diabetes and nondiabetic subjects, respectively.

We further analyzed the incidence of ESRD ($1/10^6$ person-year) in elderly patients with diabetes and nondiabetic subjects, as summarized in Table 2. Table 2 shows that the incidence rates of ESRD undergoing maintenance hemodialysis were approximately three to five times higher in elderly patients with diabetes than in elderly nondiabetic subjects. CIR_{65-84} in elderly patients undergoing maintenance hemodialysis during 2002–2005 was 0.07472 and 0.09282 for diabetic males and females, respectively, but CIR_{65-84} was 0.01572 for and 0.01995 for nondiabetic males and females, respectively. In other words, 1 in 14 diabetic males and 1 in 11 diabetic females

Table 1—Comparison of LE and EYLL between elderly patients with diabetes and nondiabetic subjects undergoing maintenance hemodialysis

	Male		Female	
	Patients with diabetes	Nondiabetic subjects	Patients with diabetes	Nondiabetic subjects
Aged 65–69 years				
n	1,662	1,303	2,285	1,503
Age beginning dialysis (years)	66.9 ± 1.5	67.1 ± 1.4	67.0 ± 1.4	67.0 ± 1.4
LE (years)	4.4 ± 0.1*	7.1 ± 0.3	4.8 ± 0.2*	7.9 ± 0.3
EYLL	10.6 ± 0.1*	7.7 ± 0.3	12.3 ± 0.2*	9 ± 0.3
Aged 70–74 years				
n	1,386	1,332	1,984	1,446
Age beginning dialysis (years)	71.9 ± 1.4	72.0 ± 1.4	71.9 ± 1.4	72.0 ± 1.5
LE (years)	3.8 ± 0.2*	5.4 ± 0.2	4 ± 0.2*	6.8 ± 0.3
EYLL	8.1 ± 0.2*	6.4 ± 0.2	9.6 ± 0.2*	6.6 ± 0.3
Aged 75–79 years				
n	879	1,116	1,253	1,153
Age beginning dialysis (years)	76.8 ± 1.4	76.7 ± 1.4	76.8 ± 1.4	76.9 ± 1.4
LE (years)	3.5 ± 0.2†	4.3 ± 0.1	3.1 ± 0.1*	4.6 ± 0.1
EYLL	5.8 ± 0.2*	4.9 ± 0.1	7.3 ± 0.1*	5.5 ± 0.1
Aged 80–84 years				
n	369	600	601	769
Age beginning dialysis (years)	81.5 ± 1.4	81.7 ± 1.4	81.6 ± 1.3	81.7 ± 1.4
LE (years)	2.7 ± 0.1†	3.2 ± 0.2	3 ± 0.3*	4.1 ± 0.2
EYLL	4.3 ± 0.1†	3.6 ± 0.2	4.6 ± 0.3*	3.3 ± 0.2
Aged >85 years				
n	154	342	250	433
Age beginning dialysis (years)	88.0 ± 2.8	87.8 ± 3.1	88.3 ± 3.4	88.0 ± 3.0
LE (years)	3 ± 0.3	2.8 ± 0.2	2.5 ± 0.3	3.1 ± 0.2
EYLL	1.5 ± 0.3	1.7 ± 0.2	2.1 ± 0.3†	1.4 ± 0.2

*$P < 0.001$ and †$P < 0.05$ for comparison between elderly patients with diabetes and nondiabetic subjects.
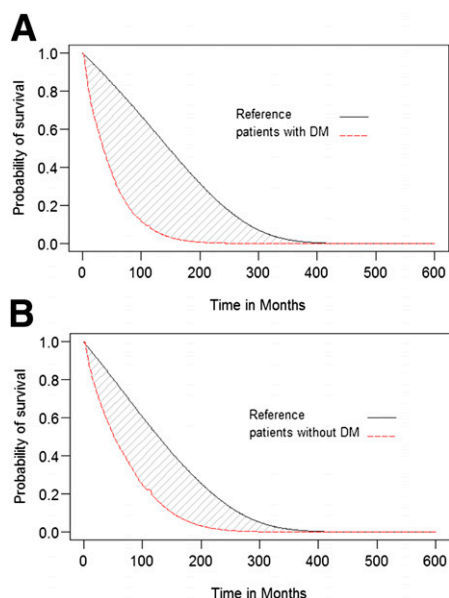
Figure 1—*Mean survival difference between elderly patients with ESRD under maintenance hemodialysis and age- and sex-matched reference population after 50 years of extrapolation. A: Elderly patients with diabetes. B: Elderly nondiabetic subjects. (A high-quality color representation of this figure is available in the online issue.)*

aged 65 years would develop ESRD and be treated with hemodialysis in the next 20 years if he/she did not die of other illnesses.

Table 3 displays the number of preventable ESRD cases due to diabetes and LYs gained by the successful prevention of ESRD in elderly patients with diabetes. The estimated prevalence of patients with diabetes in the year 2010 was 215,994 males and 266,991 females between 65 and 84 years of age. There were 676 and 1,080 preventable ESRD cases in males and females, respectively, due to diabetes in a year; thus, there would be 5,430.1 LYs and 10,177 LYs saved by the successful prevention of ESRD in elderly

diabetic males and females, respectively, in a year.

CONCLUSIONS—Although previous studies have investigated the impact of diabetes on elderly patients undergoing dialysis (9), the current study is the first to estimate the LE and EYLL (22) in elderly patients with ESRD stratified by age, sex, and the presence of diabetes. We found that the average EYLL for the young-old (between 65 and 75 years of age) patients with diabetes is quite substantial (Table 1). Therefore, attention should be paid to preventive care of ESRD in the patients with diabetes. For example, in elderly patients with diabetes who are 70–74 years

old, the average EYLL was 8.1 ± 0.2 and 9.6 ± 0.2 for males and females, respectively, indicating that for this age-group, successfully preventing development of ESRD in elderly patients with diabetes would save 8.1 and 9.6 LYs for society. Thus, the total number of LYs gained by successful prevention of ESRD in elderly patients with diabetes within a single year would be 5,430.1 and 10,177 LYs for males and females, respectively (Table 3). Because we did not count the potential LYs saved by sound diabetes care in elderly patients with ESRD undergoing maintenance dialysis, the above conclusion may be an underestimation. Moreover, the above calculation did not include the loss of utility from reduced quality of life or the additional financial burden related to the development of ESRD. These facts further stress the value of diabetes care in the elderly and prevention of diabetes-related complications, including ESRD.

According to a previous report (23), the cumulative lifetime risks for ESRD were 0.073–0.078 and 0.018–0.025 for 20-year-old black and white Americans, respectively. In the current study, we also calculated the CIR_{65-84} in elderly developing ESRD that requires maintenance hemodialysis. The results showed that the likelihood of developing ESRD for elderly patients with diabetes aged 65 years would be ~1 in 14 for males and 1 in 11 for females in the next 20 years, which would be nearly five times the risk for elderly nondiabetic subjects. Thus, careful screening and follow-up of renal function accompanied with optimal control of blood glucose, serum lipids, and blood pressure must be considered when treating this population (24–29). Prevention of diabetes-related ESRD could possibly be accomplished

Table 2—*Incidence rates of ESRD ($1/10^6$ person-year) and incident case numbers (in parentheses) in elderly patients with diabetes and nondiabetic subjects undergoing maintenance hemodialysis*

Age (years)	Calendar years	Male		Female	
		Patients with diabetes	Nondiabetic subjects	Patients with diabetes	Nondiabetic subjects
65–69	1998–2001	2,587 (790)	700 (758)	4,222 (1,123)	852 (853)
	2002–2005	4,013 (1,034)	597 (627)	4,453 (1,373)	712 (788)
70–74	1998–2001	2,295 (639)	745 (735)	4,613 (858)	972 (771)
	2002–2005	3,842 (946)	733 (726)	5,765 (1,347)	912 (812)
75–79	1998–2001	4,708 (362)	896 (620)	3,299 (496)	1,182 (627)
	2002–2005	3,416 (666)	857 (663)	5,240 (920)	1,024 (638)
80–84	1998–2001	4,443 (143)	977 (318)	5,252 (207)	1,192 (380)
	2002–2005	4,260 (295)	981 (415)	4,025 (486)	1,382 (481)
CIR_{65-84} (2002–2005)*		0.07472	0.01572	0.09282	0.01995

*Cumulative incidence rates of ESRD in individuals between 65 and 84 years of age undergoing maintenance hemodialysis during 2002–2005.

Table 3—The number of preventable incident ESRD cases due to diabetes and LYs gained by successful prevention of ESRD in elderly patients with diabetes between 65 and 84 years of age in a single year

Age (years)	Male			Female		
	Number of prevalent DM	Number of preventable ESRD	LYs gained by DM care	Number of prevalent DM	Number of preventable ESRD	LYs gained by DM care
65–69	78,046	267	2,830.2	89,087	333	4,095.9
70–74	55,865	174	1,409.4	77,096	374	3,590.4
75–79	47,001	120	696	68,121	287	2,095.1
80–84	35,082	115	494.5	32,687	86	395.6
Total	215,994	676	5,430.1	266,991	1,080	10,177

DM, diabetes mellitus.

through comprehensive diabetes care, and efforts to improve public awareness regarding prevention of CKD should also be strengthened (30,31).

Diabetes was reported to be associated with a higher risk of death in individuals with ESRD (9), which was corroborated in this study. We have further quantified magnitudes of differences in EYLL for different age strata (Table 1). However, differences between elderly patients with diabetes and nondiabetic subjects narrowed as the age advanced, and the effects of diabetes seemed to be greater in the young-old individuals. Our finding is consistent with a previous report (2), which showed that the young-old individuals have a higher risk of mortality, and the oldest old individuals (>85 years of age) have a lower rate of complications. Although Table 1 shows that the LE was better in females than in males, as was reported previously (6,32), the EYLL was greater in females than in males, which may result from a general longer life expectancy in females (33). Thus, both male and female elderly patients with diabetes should be paid attention for prevention of ESRD (24,34).

According to the Neal "thrifty gene" hypothesis (35), the diabetogenic genes persisted at a high level in times of nutritional deprivation because they contributed to a survival advantage, which might be good for survival of human species. However, as the food shortage is no longer a major threat nowadays, the sedentary lifestyles of modern times aggravate the occurrence of diabetes (36). Both factors contribute to the development of hyperlipidemia, metabolic syndrome, and diabetes, which further result in an increased premature mortality of cardio- and cerebrovascular diseases, especially among the ESRD cohort (9). Because Taiwan has the highest incidence

and prevalence of treated ESRD (5), it is crucial that we identify preventable factors as early as possible in life and control them. As mentioned in the position statement (24), all practitioners must emphasize lifestyle modifications on dietary intake and exercise to optimize glucose, lipids, and blood pressure control plus regular screening of urine albumin excretion and serum creatinine for early detection and control of CKD. With the standard of medical care and the CKD prevention program in elderly patients with diabetes with CKD (24–29), we hoped that diabetes-related ESRD could be decreased gradually in the future. Moreover, such a control program would generally produce spillover effects on reducing cardio- and cerebrovascular morbidities and mortalities, especially among the elderly (37,38). Future studies are needed to quantify the magnitudes of effects on different causes of death.

Although we analyzed the most comprehensive national data currently available in Taiwan, there are potential limitations that must be addressed. First, our estimation of LE and EYLL was dependent upon the assumption of constant excess hazard and premature mortality of ESRD. We checked the assumption by fitting the logit transform of the survival ratio between cohorts with ESRD and the age- and sex-matched general population, which showed a straight line and fulfilled the assumption. Second, the lifetime extrapolation was based on current and prior experiences of survival, including the life tables of the current population. As the dialysis technology and control for comorbidities may improve in the coming years, our results might underestimate the LE and overestimate the EYLL of elderly patients with diabetes and nondiabetic subjects with ESRD. However, because the improved survival of ESRD cohorts generally accompanies an increased

cost for treatment, the overall saving from prevention is still a worthwhile investment. Third, this study did not include elderly patients undergoing maintenance peritoneal dialysis and cannot make a general inference for this population. Although the Bureau of National Health Insurance has promoted peritoneal dialysis during the last 5 years, hemodialysis seems to be the predominant modality of dialysis therapy in the elderly in Taiwan because of a lower requirement for education and learning. Because no significant differences on survival for peritoneal dialysis and hemodialysis were found in the previous study (22), the current estimates of LE and EYLL might be a close approximation for peritoneal dialysis among elderly patients with diabetes and nondiabetic subjects. Fourth, we did not begin following these subjects when they had been first diagnosed with diabetes. Thus, we may underestimate the latency period and overestimate the incidence rate of ESRD for elderly patients with diabetes. However, the current study stratified the population at risk into 5-year age groups, which reduces the above effect to some extent. Finally, because the NHIRD does not contain any information related to quality of life, we were not able to calculate the quality-adjusted life expectancy. Future studies need to address these issues.

In conclusion, we found that successful prevention of ESRD in the elderly is worthwhile, especially among elderly patients with diabetes, and may save up to a decade of LYs for each diabetic individual. As the incidence of diabetes has increased continually, the LYs saved by comprehensive diabetes care in our society would be substantial, and diabetes care deserves special attention, especially in elderly females. Future studies should take into account quality of life and cost of active prevention and dialysis to evaluate cost-effectiveness of

prevention programs for elderly patients with diabetes.

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