Journal of Diabetes and Its Complications 33 (2019) 107400

Contents lists available at ScienceDirect

Journal of Diabetes and Its Complications

journal homepage: WWW.JDCJOURNAL.COM

Biologic and social factors predict incident kidney disease in type 1 diabetes: Results from the T1D exchange clinic network

Janet B. McGill [a], Mengdi Wu [b], Rodica Pop-Busui [c], Kara Mizokami-Stout [c], William V. Tamborlane [d], Grazia Aleppo [e], Rose A. Gubitosi-Klug [f], Michael J. Haller [g], Steven M. Willi [h,k], Nicole C. Foster [b,*], Chelsea Zimmerman [g], Ingrid Libman [i], Sarit Polsky [j], Michael R. Rickels [k]

[a] Washington University School of Medicine, St. Louis, MO, United States of America
[b] Jaeb Center for Health Research, Tampa, FL, United States of America
[c] University of Michigan, Department of Internal Medicine, Division of Metabolism, Endocrinology and Diabetes, Ann Arbor, MI, United States of America
[d] Yale University School of Medicine, New Haven, CT, United States of America
[e] Northwestern University, Chicago, IL, United States of America
[f] Univeristy Hospitals of Cleveland, Cleveland, OH, United States of America
[g] University of Florida, Gainesville, FL, United States of America
[h] Children's Hospital of Philadelphia, Philadelphia, PA, United States of America
[i] UPMC Children's Hospital of Pittsburgh, Pittsburgh, PA, United States of America
[j] Barbara Davis Center for Diabetes, Aurora, CO, United States of America
[k] University of Pennsylvania Perelman School of Medicine, Rodebaugh Diabetes Center, Philadelphia, PA, United States of America

ARTICLE INFO

Article history:
Received 4 April 2019
Received in revised form 19 June 2019
Accepted 19 June 2019
Available online 26 June 2019

Keywords:
Type 1 diabetes
Diabetic kidney disease
T1D exchange
Diabetes management
Glycemic management

ABSTRACT

Aims: Diabetic kidney disease (DKD) is a major complication of type 1 diabetes (T1D). To better understand the development of DKD in modern clinical practice, we evaluated risk factors in participants from the T1D Exchange Registry who completed 5-years of longitudinal follow-up.
Methods: Participants had T1D duration ≥ 1 year, age ≥ 10 years, eGFR ≥ 60 ml/min and no albuminuria at enrollment, and at least two serum creatinine and urine albumin measurements recorded during follow-up. Adverse kidney outcomes were defined as eGFR ≪ 60 ml/min and/or albuminuria (ALB) defined by as two consecutive albumin/creatinine ratios or two out of the past three measurements ≫ 30 μg/mg at any follow-up data collection. Associations of baseline characteristics with adverse kidney outcomes were assessed.
Results: Among 3940 participants (mean age 41 ± 15 yrs, T1D duration 21 ± 13 yrs), 653 (16.6%) experienced an adverse kidney outcome: 268 (6.8%) experienced incident ALB only, 322 (8.2%) had eGFR decline to ≪60 ml/min without ALB, and 63 (1.6%) experienced eGFR ≪ 60 ml/min with ALB. In a multivariable analysis, higher HbA1c, higher SBP, lower DBP, older age and lower education level were associated with the development of adverse kidney outcomes (all p values ≤ 0.03).
Conclusions: Improving modifiable risk factors, including glucose and blood pressure control, remain important to reduce the risk of DKD in T1D.

1. Introduction

Diabetic kidney disease (DKD) is a risk factor for both progression to end-stage renal disease (ESRD) and for mortality in persons with type 1 diabetes (T1D). While diabetic kidney disease was initially identified by the presence of albuminuria, more recent reports suggest that kidney function decline can occur without concurrent albuminuria in persons with T1D.[1,2] Kidney biopsies in T1D patients with evidence of kidney damage show similar glomerular lesions in those with and without albuminuria early in the disease process with variable pathology findings emerging over time.[3,4] Consequently, the definition of DKD has expanded to include the presence of albuminuria at any level of kidney function or renal function decline in the absence of detectable albuminuria.[5,6]

Despite recommendations for improvements in glucose control, blood pressure, and greater use of renin-angiotensin system (RAS) blockers over the past decades, persons with T1D continue to develop albuminuria and loss of kidney function.[7–9] Long-term follow-up of patients in the Diabetes Control and Complications Trial (DCCT) and the subsequent observational study, Epidemiology of Diabetes Interventions and Complications (EDIC), clearly demonstrates that early intensive therapy compared to conventional therapy reduces later

* Corresponding author: Jaeb Center for Health Research, 15310 Amberly Drive, Suite 350, Tampa, FL 33647, United States of America.
E-mail address: t1dstats3@jaeb.org (N.C. Foster).

https://doi.org/10.1016/j.jdiacomp.2019.06.005
1056-8727/

development of renal complications, including both the appearance of albuminuria and reduced kidney function.[2,10–12] Guidelines for blood pressure targets and treatment with angiotensin-converting enzyme inhibitors are based on studies that have demonstrated slowing of progression of kidney disease in persons with T1D and proteinuria.[5,13,14]

In the initial report of the T1D Exchange Clinic Network and Registry, the frequency of DKD was 8% of the entire cohort, and increased with the duration of T1D.[15] In persons with T1D duration ≫ 30 years, ≫20% had DKD. In persons with T1D duration ≫ 50 years, ≫29% had DKD.[15]

Here we report the rate of and risk factors for incident DKD in persons who were followed over 5 years in the T1D Exchange Clinic Network and who were without evidence of DKD at the baseline evaluation. This cohort reflects a broad spectrum of persons with T1D and current care practices across academic centers and private practice settings in the US.

2. Subjects, materials and methods

The T1D Exchange Clinic Network includes over 80 US-based pediatric and adult endocrinology practices that provide specialized diabetes care. Details on Registry participant eligibility criteria, the informed consent process, and data collection have been published previously.[15] Over 25,000 individuals with T1D were enrolled between September 2010 and August 2012. Core data were updated annually from medical record data extraction.

This report includes data from 3940 Registry participants who were at least 10 years old with at least 1 year diabetes duration, had absence of kidney damage as evident from an albumin/creatinine ratio ≪ 30 mg/g creatinine and normal kidney function (estimated glomerular filtration rate (eGFR) ≥ 60 ml/min) at a 2010–2012 baseline visit, and who completed 5 or more years of study follow-up. Demographic data on sex, race/ethnicity, annual household income, and education level were collected through comprehensive participant questionnaires at the initial visit. Information about age, diabetes duration, insulin modality (pump or multiple daily injections), use of a continuous glucose monitor (CGM), blood pressure, use of anti-hypertensive medications, height, albuminuria status, serum creatinine level, and HbA1c levels obtained as part of usual care were collected from clinic medical records. Albuminuria was defined as two consecutive albumin/creatinine ratios or two out of the past three measurements ≥ 30 μg/mg. Clinic sites were instructed to enter all serum urine albumin and serum creatinine measures not previously recorded on annual data collections.

2.1. Statistical methods

Calculation of eGFR was determined using the Schwartz equation for participants ≪19 years old and using the CKD-Epi equation for participants ≥ 19 years old.[16,17] Adverse renal outcome was defined as eGFR ≪ 60 ml/min and/or the presence of albuminuria (2 consecutive or 2 out of 3 measurements) reported on at least one data collection form after baseline. Renal outcome was further categorized as: 1) never experienced eGFR ≪60 ml/min or albuminuria, 2) experienced only albuminuria, 3) experienced only eGFR ≪60 ml/min, and 4) experienced both eGFR ≪ 60 ml/min and albuminuria.

The associations between binary adverse renal outcome and baseline demographic and clinical characteristics were assessed using chi-square tests for categorical characteristics and Wilcoxon Rank-Sum tests for continuous characteristics. The association also was assessed using a multivariable logistic regression model with a stepwise selection procedure. Data analyses were performed using SAS software version 9.4 (SAS Institute Inc., Cary, NC). In view of multiple comparisons, only *p*-values ≪ 0.01 were considered statistically significant. All p-values are two-sided.

3. Results

The 3940 participants ranged in age from 10 to 85 years at the 2010–12 baseline (mean 41 ± 15 years); 55% were female and 92% were non-Hispanic White. Median diabetes duration at baseline was 19 years (interquartile range (IQR) 11, 30 years). Additional participant and clinical characteristics at baseline are presented in Table 1.

Among the 3940 participants, 653 (17%) experienced an adverse renal outcome (eGFR ≪ 60 ml/min or new ALB or both); 268 (7%) experienced only ALB, 322 (8%) experienced only eGFR ≪ 60 ml/min, and 63 (2%) experienced both eGFR ≪ 60 ml/min and albuminuria. In adjusted analyses, the occurrence of an adverse renal outcome was associated with the following baseline characteristics (Table 2): older age (median 47 (30, 59) years versus 40 (30, 51) years in participants with adverse renal outcome vs participants without adverse renal outcome, respectively; $P = 0.01$); diagnosis of T1D as a child (59% vs 55%; $P \ll 0.001$); higher HbA1c level (8.0% ± 1.3% vs 7.6% ± 1.0%; $P \ll 0.001$); higher systolic blood pressure (124 ± 10 mmHg vs 122 ± 10 mmHg; $P \ll 0.001$); and lower diastolic blood pressure (71 ± 7 mmHg vs 73 ± 7 mmHg; $P \ll 0.001$). Compared with participants without an adverse renal outcome, there was a trend for individuals with adverse renal outcome to have lower education level (50% less than Bachelor degree vs 37%; $P = 0.03$) and lower CGM use (47% vs 56% CGM users; $P = 0.04$). Characteristics not meeting criteria for inclusion in the final adjusted model that had an indication of an association with an adverse renal outcome included (Table 2): longer diabetes duration (median 23 (11, 36) years vs 19[11,28] years; unadjusted $P \ll 0.001$) and lower annual household income (31% less than $50,000 vs 22%; unadjusted $P \ll 0.001$). We found no association between the occurrence of adverse renal outcome and race/ethnicity ($P = 0.57$) or use of an insulin pump ($P = 0.76$).

4. Discussion

Prevention of DKD is an important goal for persons with T1D and their health care providers. Attainment of HbA1c targets is problematic in children, for whom higher targets may be appropriate, in adolescents learning independent disease management and in adults who may not be diagnosed or treated appropriately early in the course of their

Table 1
Participant characteristics at baseline.

	N = 3940
Age (years) – *median* (*IQR*)	41 (30,53)
T1D duration (years) – *median* (*IQR*)	19 (11,30)
Female - *N*(%)	2159 (55%)
Race/ethnicity – *N*(%)	
Non-Hispanic White	3600 (92%)
Non-Hispanic Black	100 (3%)
Hispanic/Latino	116 (3%)
Other race/ethnicity	104 (3%)
Education level[a] – *N*(%)	
Less than bachelor degree	1657 (42%)
Bachelor degree	1393 (35%)
Master, professional, doctorate degree	890 (23%)
Annual household income[b] – *N*(%)	
Less than $50,000	749 (24%)
$50,000 to less than $75,000	598 (19%)
≥$75,000	1734 (56%)
CGM use – *N*(%)	616 (16%)
Pump use[b] – *N*(%)	2451 (63%)
HbA1c[b] – *mean* ± *std*	7.6% ± 1.2%
Systolic blood pressure[b] - *mean* ± *std*	121 ± 13
Diastolic blood pressure[b] - *mean* ± *std*	72 ± 9
Anti-hypertensive medication use – *N*(%)	2273 (58%)

[a] Highest education level for participants ≥ 18 years old; highest parental education level for participants ≪ 18 years old.

[b] Annual household income missing for 859 participants; information on use of an insulin pump missing for 23 participants; HbA1c information missing for 159 participants; systolic blood pressure information missing for 115 participants; diastolic blood pressure information missing for 115 participants.

Table 2
Association between renal status[a] and baseline participant/clinical characteristics.

	Never experienced e-GFR ≪ 60 or albuminuria	Experienced only albuminuria	Experienced only e-GFR ≪ 60	Experienced both e-GFR ≪ 60 and albuminuria	Unadjusted P-value[b]	Adjusted P-value[c]
Overall – *N*(%)	3287 (83%)	268 (7%)	322 (8%)	63 (2%)	–	–
Age – *median* (*IQR*)	40 (30,51)	40 (28,50)	53 (34,62)	55 (43,63)	≪0.001	0.01
Diabetes duration – *median* (*IQR*)	19 (11,28)	23 (14,33)	20 (8,37)	33 (18, 40)	≪0.001	–
Age at diabetes onset – *N*(%)					0.06	≪0.001
Pediatric (≪19 years old)	1815 (55%)	182 (68%)	173 (54%)	32 (51%)		
Adult (≥19 years old)	1472 (45%)	86 (32%)	149 (46%)	31 (49%)		
Female – *N*(%)	1781 (54%)	151 (56%)	193 (60%)	34 (54%)	0.08	–
Race/ethnicity – *N*(%)					0.57	–
Non-Hispanic White	3018 (92%)	240 (90%)	299 (93%)	55 (87%)		
Non-Hispanic Black	79 (2%)	14 (5%)	5 (2%)	2 (3%)		
Hispanic/Latino	98 (3%)	6 (2%)	8 (2%)	4 (6%)		
Other race/ethnicity	85 (3%)	8 (3%)	10 (3%)	2 (3%)		
Education level – *N*(%)					≪0.001	0.03
Less than Bachelor	1166 (37%)	124 (48%)	154 (50%)	31 (53%)		
Bachelor degree	1185 (38%)	90 (35%)	71 (23%)	17 (29%)		
Master/professional/doctorate	803 (25%)	43 (17%)	81 (26%)	10 (17%)		
Annual income – *N*(%)					≪0.001	–
Less than $50,000	579 (22%)	67 (31%)	68 (30%)	18 (42%)		
$50,000–≪$75,000	438 (17%)	33 (15%)	47 (20%)	8 (19%)		
≥$75,000	1633 (62%)	116 (54%)	115 (50%)	17 (40%)		
HbA1c - *mean* ± *std*	7.6% ± 1.0%	8.1% ± 1.4%	7.9% ± 1.2%	8.2% ± 1.3%	≪0.001	≪0.001
Systolic blood pressure - *mean* ± *std*	122 ± 10	125 ± 11	123 ± 10	129 ± 11	≪0.001	≪0.001
Diastolic blood pressure - *mean* ± *std*	73 ± 7	73 ± 7	70 ± 7	70 ± 8	≪0.001	≪0.001
Ever used pump – *n*(%)	2384 (73%)	193 (72%)	233 (72%)	43 (68%)	0.76	–
Ever used CGM – *n*(%)	1856 (56%)	130 (49%)	151 (47%)	24 (38%)	≪0.001	0.04

[a] eGFR calculated using the Schwartz equation for participants ≪ 19 years old and using the CKD-Epi question for participants ≥ 19 years old.
[b] Bivariate *p*-value of the association between binary adverse renal outcome and demographic and clinic characteristics calculated using chi-square tests for categorical characteristics and Wilcoxon Rank-Sum tests for continuous characteristics.
[c] Multivariable *p*-values calculated using a multivariable logistic regression with stepwise selection procedure adjusted for use of anti-hypertensive medication. Only factors remaining after the stepwise selection procedure will display a p-value.

disease. Socioeconomic factors impede treatment of a chronic disease that is expensive, time-consuming and requires attention to details. The DCCT/EDIC studies clearly demonstrate both the benefits of early glycemic control and the difficulties maintaining that level of control in 'usual care' settings.[7] ACEi/ARB therapy has proven beneficial for preventing the progression of diabetic nephropathy,[12] but may not prevent DKD,[8] and is not suitable for or tolerated by all (e.g., teratogenic effects can deter treatment in women of reproductive age, hypotension or hyperkalemia may prohibit use).

Follow-up of the T1D Exchange Registry cohort reveals a 17% incidence of DKD over 5 years, diagnosed by either new onset albuminuria (7%), reduced eGFR to ≪60 ml/min/1.73 m^2 (8%) or both parameters (2%) within 5 years of enrolling in the Registry. The high rate of reduced eGFR without albuminuria attests to the need to monitor both albuminuria and serum creatinine with calculation of eGFR to diagnose this important diabetes complication. Our findings also indicate that both age and duration of diabetes are important risk factors and suggest that surveillance for DKD should continue across the age spectrum in adults. The modestly higher HbA1c among those with incident DKD compared to those without (8.0% ± 1.3% vs 7.6% ± 1.0%) is a reminder that glucose control across the lifespan continues to be an important factor in the development of diabetes complications and that poor metabolic control early in the disease may have long-term consequences, as shown in the DCCT/EDIC study.[11,18] Clinical trials report better glucose control among CGM users, providing hope that these devices may lead to reductions of both acute and chronic complications of diabetes.[19,20] Achievement and persistence of good to excellent glycemic control remains challenging, as evidenced by recent data from the T1D Exchange Clinic Network showing that glycemic control has not improved from 2010 to 2012 to 2016–2018 despite significant increases in the use of insulin pumps and CGM systems.[21]

Hypertension has been associated with adverse renal outcomes, and blood pressure control is often recommended as a strategy to prevent DKD and other microvascular and macrovascular complications of diabetes.[22,23] The blood pressure target of ≪140/90 mmHg has been recommended by the American Diabetes Association (ADA) in recently published Standards of Care guidelines for persons with both type 1 and type 2 diabetes without distinction.[5,24] In this observational study, mean systolic blood pressures of participants with DKD were only slightly higher than those without DKD, and were below targets recommended by ADA and KDOQI. Nonetheless, persons without incident DKD at follow-up examinations had lower systolic blood pressures than those with albuminuria, reduced eGFR, or both ($P \ll 0.001$). Interestingly, the diastolic blood pressure was higher in the group without incident DKD compared to groups with incident albuminuria or reduced eGFR ($P \ll 0.001$), suggesting that elevated pulse pressure might be a hidden risk factor for DKD. Prior studies of small vessel elasticity and pulse pressure in the prediction of microvascular complications in persons with T1D have been inconsistent.[25,26] In the DCCT/EDIC studies, time-updated blood pressures ≪ 120/80 mmHg were associated with substantially lower risk of adverse renal outcomes independent of initial glucose-control treatment assignment.[22] This finding was true whether persons were treated or not treated for hypertension, suggesting that the blood pressure level of ≪120/80 mmHg is protective of adverse renal outcomes in T1D regardless of hypertension treatment.[22] Whether blood pressure targets for persons with T1D should be lower than the recommended targets for all persons with diabetes is unclear due to the lack of prospective randomized clinical trials.

Socioeconomic factors have been implicated in the development of diabetes complications in multiple observational studies of persons with T1D.[27–29] In this follow-up study of well characterized patients with T1D from the T1D Exchange Clinic Network, both lower education levels and lower household income were associated with greater risk of adverse renal outcomes ($P \ll 0.001$ for both characteristics in bivariate analyses). Prior studies have shown similar results. Lower attained education level was associated with ESRD and cardiovascular disease in the Pittsburgh Epidemiology of Diabetes Complications study, while lower household income predicted autonomic neuropathy and peripheral arterial disease.[28] A long-term follow-up study of patients with T1D in Sweden showed a much greater risk of ESRD in those with lower

personal and family education levels.[29] The complexity and burdens of self-care for persons with T1D may put those with limited education and resources at risk for diabetes complications, including adverse renal outcomes.

The interesting finding that continuous glucose monitoring (CGM) use was associated with lower risk of adverse renal outcomes in bivariate analysis, but was not significant in multivariate analysis deserves more study. Short-term studies have consistently shown that CGM use improves glucose control in persons with T1D, whether used in conjunction with insulin pumps or with insulin injections.[19,20] Likewise, use of insulin pumps has been shown to improve glucose control in clinical trials, an effect confirmed in observational studies.[30] Long-term use of insulin pump therapy has been shown to both improve glycemic control and reduce incident albuminuria.[31] The relatively high penetration of insulin pump use compared to CGM use may have mitigated the non-independent effects noted in this cohort.

In conclusion, multiple risk factors, including age, duration of diabetes, HbA1c, blood pressure and socioeconomic factors such as attained education level and household income were associated with incident adverse renal outcomes in this T1D Exchange Clinic Network follow-up study. While age and duration of diabetes are not modifiable, ongoing surveillance for DKD is certainly indicated throughout the lifespan of persons with T1D. Lower HbA1c, early in the course of diabetes or as soon as it can be achieved, has been shown in numerous studies to reduce the risk of adverse kidney outcomes,[32] and is confirmed by this study. Whether ongoing efforts to control glucose levels by expanded use of CGM and sensor-augmented insulin pumps will reduce the frequency of these complications requires further study.[32] An unexpected finding from this observational study is that lower mean diastolic blood pressure and modestly higher systolic blood pressure within the target range of ≪140/90 mmHg is associated with higher risk of incident adverse kidney outcomes. Review of blood pressure targets and frequency of monitoring based on diabetes duration for persons with T1D may be warranted by guideline committees. Socioeconomic factors associated with poorer outcomes in people with T1D may not be modifiable. Future research should seek to identify interventions and support systems that can improve the trajectory of complications that disproportionately impact morbidity and mortality in these high risk persons with T1D. Based on findings in this report, screening for DKD should include both urine albumin and eGFR measurements, since declining kidney function in the absence of albuminuria is a common presentation for DKD. While the minimum age for screening for DKD is not identified in this study, it is clear that screening should continue across the adult years in patients with T1D.

Acknowledgments

The authors would like to thank all the participants in the T1D Exchange clinic registry and their families.

Funding: This work was supported by the Leona M. and Harry B. Helmsley Charitable Trust.

References

1. Krolewski AS, Niewczas MA, Skupien J, et al. Early progressive renal decline precedes the onset of microalbuminuria and its progression to macroalbuminuria. Diabetes Care 2014;37:226-34.
2. Molitch ME, Steffes M, Sun W, et al. Development and progression of renal insufficiency with and without albuminuria in adults with type 1 diabetes in the diabetes control and complications trial and the epidemiology of diabetes interventions and complications study. Diabetes Care 2010;33:1536-43.
3. Caramori ML, Fioretto P, Mauer M. Low glomerular filtration rate in normoalbuminuric type 1 diabetic patients: an indicator of more advanced glomerular lesions. Diabetes 2003;52:1036-40.
4. Drummond K, Mauer M. International Diabetic Nephropathy Study G. The early natural history of nephropathy in type 1 diabetes: II. Early renal structural changes in type 1 diabetes. Diabetes 2002;51:1580-7.
5. American DA. 11. Microvascular complications and foot care: standards of medical Care in Diabetes-2019. Diabetes Care 2019;42:S124-38.
6. Kdoqi. KDOQI clinical practice guidelines and clinical practice recommendations for diabetes and chronic kidney disease. Am J Kidney Dis 2007;49:S12-154.
7. Diabetes C. Complications Trial/Epidemiology of Diabetes I, Complications Research G, et al. Modern-day clinical course of type 1 diabetes mellitus after 30 years' duration: the diabetes control and complications trial/epidemiology of diabetes interventions and complications and Pittsburgh epidemiology of diabetes complications experience (1983-2005). Arch Intern Med 2009;169:1307-16.
8. Mauer M, Zinman B, Gardiner R, et al. Renal and retinal effects of enalapril and losartan in type 1 diabetes. N Engl J Med 2009;361:40-51.
9. National KF. K/DOQI clinical practice guidelines for chronic kidney disease: evaluation, classification, and stratification. Am J Kidney Dis 2002;39:S1-266.
10. Diabetes C, Complications Trial Research G, Nathan DM, et al. The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. N Engl J Med 1993;329:977-86.
11. Group DER. de Boer IH, Sun W, et al. Intensive diabetes therapy and glomerular filtration rate in type 1 diabetes. N Engl J Med 2011;365:2366-76.
12. Group TES. Sustained effect of intensive treatment of type 1 diabetes mellitus on development and progression of diabetic nephropathy: the Epidemiology of Diabetes Interventions and Complications (EDIC) study. JAMA 2003;290:2159-67.
13. Laffel LM, McGill JB, Gans DJ. The beneficial effect of angiotensin-converting enzyme inhibition with captopril on diabetic nephropathy in normotensive IDDM patients with microalbuminuria. North American Microalbuminuria Study Group Am J Med 1995;99:497-504.
14. Lewis EJ, Hunsicker LG, Bain RP, Rohde RD. The effect of angiotensin-converting-enzyme inhibition on diabetic nephropathy. The Collaborative Study Group. N Engl J Med 1993;329:1456-62.
15. Beck RW, Tamborlane WV, Bergenstal RM, Miller KM, Dubose SN, Hall CA. The T1D exchange clinic registry. J Clin Endocrinol Metab 2012;97:4383-9.
16. Levey AS, Stevens LA, Schmid CH, et al. A new equation to estimate glomerular filtration rate. Ann Intern Med 2009;150:604-12.
17. Schwartz GJ, Munoz A, Schneider MF, et al. New equations to estimate GFR in children with CKD. J Am Soc Nephrol 2009;20:629-37.
18. Effect of intensive diabetes treatment on albuminuria in type 1 diabetes: long-term follow-up of the Diabetes Control and Complications Trial and Epidemiology of Diabetes Interventions and Complications study. *Lancet Diabetes Endocrinol.* 2014;2(10):793–800.
19. Beck RW, Riddlesworth T, Ruedy K, et al. Effect of continuous glucose monitoring on glycemic control in adults with type 1 diabetes using insulin injections: the DIAMOND randomized clinical trial. JAMA 2017;317:371-8.
20. Tumminia A, Crimi S, Sciacca L, et al. Efficacy of real-time continuous glucose monitoring on glycaemic control and glucose variability in type 1 diabetic patients treated with either insulin pumps or multiple insulin injection therapy: a randomized controlled crossover trial. Diabetes Metab Res Rev 2015;31:61-8.
21. Foster NC, Beck RW, Miller KM, et al. State of Type 1 Diabetes Management and Outcomes from the T1D Exchange in 2016-2018. Diabetes Technol Ther 2019;21(2):66-72.
22. Ku E, McCulloch CE, Mauer M, Gitelman SE, Grimes BA, Hsu CY. Association between blood pressure and adverse renal events in type 1 diabetes. Diabetes Care 2016;39:2218-24.
23. Orchard TJ, Forrest KY, Kuller LH, Becker DJ. Pittsburgh Epidemiology of Diabetes Complications S. Lipid and blood pressure treatment goals for type 1 diabetes: 10-year incidence data from the Pittsburgh epidemiology of diabetes complications study. Diabetes Care 2001;24:1053-9.
24. Tuttle KR, Bakris GL, Bilous RW, et al. Diabetic kidney disease: a report from an ADA consensus conference. Am J Kidney Dis 2014;64:510-33.
25. Benitez-Aguirre PZ, Januszewski AS, Cho YH, Craig ME, Jenkins AJ, Donaghue KC. Early changes of arterial elasticity in type 1 diabetes with microvascular complications - a cross-sectional study from childhood to adulthood. J Diabetes Complicat 2017;31:1674-80.
26. Gordin D, Waden J, Forsblom C, et al. Pulse pressure predicts incident cardiovascular disease but not diabetic nephropathy in patients with type 1 diabetes (The FinnDiane Study). Diabetes Care 2011;34:886-91.
27. Lievre M, Marre M, Robert JJ, et al. Cross-sectional study of care, socio-economic status and complications in young French patients with type 1 diabetes mellitus. Diabetes Metab 2005;31:41-6.
28. Secrest AM, Costacou T, Gutelius B, Miller RG, Songer TJ, Orchard TJ. Associations between socioeconomic status and major complications in type 1 diabetes: the Pittsburgh epidemiology of diabetes complication (EDC) study. Ann Epidemiol 2011;21:374-81.
29. Toppe C, Mollsten A, Schon S, Dahlquist G. Socio-economic factors influencing the development of end-stage renal disease in people with type 1 diabetes - a longitudinal population study. Diabet Med 2017;34:676-82.
30. Karges B, Schwandt A, Heidtmann B, et al. Association of insulin pump therapy vs insulin injection therapy with severe hypoglycemia, ketoacidosis, and glycemic control among children, adolescents, and young adults with type 1 diabetes. JAMA 2017;318:1358-66.
31. Rosenlund S, Hansen TW, Andersen S, Rossing P. Effect of 4 years subcutaneous insulin infusion treatment on albuminuria, kidney function and HbA1c compared with multiple daily injections: a longitudinal follow-up study. Diabet Med 2015;32:1445-52.
32. Heinemann L, Fleming GA, Petrie JR, Holl RW, Bergenstal RM, Peters AL. Insulin pump risks and benefits: a clinical appraisal of pump safety standards, adverse event reporting, and research needs: a joint statement of the European Association for the Study of Diabetes and the American Diabetes Association Diabetes Technology Working Group. Diabetes Care 2015;38:716-22.