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ADA 82ND SCIENTIFIC SESSIONS New Orleans, 2022

Presents

AMERICAN DIABETES ASSOCIATION

82nd SCIENTIFIC SESSIONS

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SESSION-1 :
Joint ADA/ASN Symposium: Turning the Tides (Diabetic Kidney Disease)

REVEAL-CKD: Undiagnosed Chronic Kidney Disease in Patients with Type 2 Diabetes in Germany and France

Monday, 6th June 2022

This paper was presented by Drs. Markus P. Schneider, Jean B. Virgitti, Emily Peach, from Erlangen, Germany, Orry La Ville, France, Cambridge, United Kingdom, as a part of the symposium "Joint ADA/ASN Symposium: Turning the Tides (Diabetic Kidney Disease)" on Monday June 6th 2022 at the 82nd Scientific Sessions of the American Diabetes Association held in New Orleans.

Early recognition of chronic kidney disease (CKD) is crucial to slow its progression, yet underdiagnosis remains high. This study assesses prevalence of and factors associated with undiagnosed stage 3 CKD in patients with pre-existing type 2 diabetes (T2D).

REVEAL-CKD is a multi-national secondary data study. Data were extracted from THIN (Cegedim Health Data, France) and Disease Analyzer (IQVIA, Germany). Patients were aged ≥18 years with 2 consecutive estimated glomerular filtration rate (eGFR) results 30-59 mL/min/1.73 m^2 recorded 90-730 days apart in 2015-2021. T2D was identified by a diagnosis code before 2nd eGFR. Patients with no CKD code before 1st eGFR and ≤6 months after 2nd eGFR were considered undiagnosed.

The cohorts included 3,532 patients with T2D and stage 3 CKD in France and 6,935 in Germany. In both cohorts, undiagnosed CKD was high (94% and 74%, respectively), and was greater in those aged ≥65 years and in females. In patients with additional pre-existing comorbidities undiagnosed CKD remained high, ranging between 65% - 96% (Table 1).

A high prevalence of undiagnosed CKD in patients with T2D was observed for France and

Table 1. Prevalence of undiagnosed stage 3 CKD by baseline characteristics in patients with type 2 diabetes

Variable	UNDIAGNOSED CKD PREVALENCE[1] (%) THIN Cegedim, France	Disease Analyzer, Germany
OVERALL	3311/3532 (93.7%)	5145/6935 (74.2%)
AGE AT INDEX (YEARS)		
<45	3/4 (75.0%)	6/9 (66.7%)
45-64	317/343 (92.4%)	502/689 (72.9%)
65-74	1029/1109 (92.8%)	1376/1827 (75.3%)
≥75	1962/2076 (94.5%)	3261/4410 (73.9%)
SEX		
FEMALE	1451/1532 (94.7%)	2775/3675 (75.5%)
MALE	1860/2000 (93.0%)	2370/3260 (72.7%)
COMORBIDITIES		
HYPERTENSION	2490/2680 (92.9%)	3629/4991 (72.7%)
HEART FAILURE	210/235 (89.4%)	1037/1550 (66.9%)
AF	330/359 (91.9%)	936/1323 (70.7%)
MI	149/156 (95.5%)	248/379 (65.4%)
STROKE	115/125 (92.0%)	216/303 (71.3%)

Notes: [1] (undiagnosed CKD/overall population)*100; CKD, chronic kidney disease; AF, atrial fibrillation; MI, myocardial infarction

Germany. Older patients and females were particularly vulnerable to undiagnosed CKD.

Machine Learning Approach to Evaluate the Prospective Kidney Failure Risk of the Complement Proteome in T1D

Monday, 6th June 2022

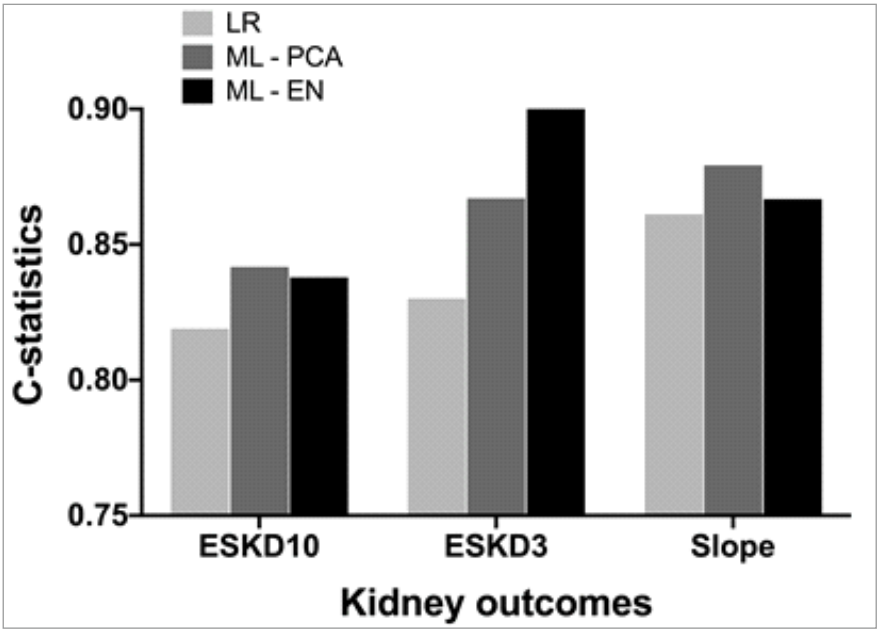
This paper was presented by Drs. Zaipul Md Dom, Salina Moon, Sara Pickett, Simon Dillon, Monika Niewczas from, Boston, MA, as a part of the symposium "Joint ADA/ASN Symposium: Turning the Tides (Diabetic Kidney Disease)" on Monday June 6th 2022 at the 82nd Scientific Sessions of the American Diabetes Association held in New Orleans.

"We tested the Complement proteome's prognostic accuracy for kidney outcomes in T1D using a machine learning (ML) approach."

This prospective cohort study comprised 193 Joslin Kidney Study subjects with T1D and an overt diabetic kidney disease at baseline followed for 10 years. We performed urinary measurements of the Complement proteins (n=82) using aptamer proteomics. The outcomes of interest included developing end-stage kidney disease (ESKD) in 10 or 3 years and a kidney slope. We tested biostatistical logistic regression (LR) and 7 ML models (principal component (PCA); decision tree: random forest (RF) and generalized boosting (GB); penalized regression: elastic net (EN), lasso (LS) and ridge (RD); and neural network (NN)).

The LR model with the top protein had decent model accuracy (c=0.80-0.86) across the kidney outcomes, which was further improved in the ML model with 10 proteins (PCA). The performance of the 7 ML was comparable or higher with the best ML model being EN (AUC=0.80-0.90). Accuracy was better for the shorter follow-up period or slope-based outcomes (Figure 1). Models fed with 82 proteins did not much improve performance.

Multiple Complement proteins are strongly associated with short-to-long term kidney outcomes in T1D and offer attractive prognostic accuracy in ML models to complement biostatistical tools.



Lessons Learned from A Patient-Centered, Team-Based Intervention for Patients with Type 2 Diabetes at High Cardiovascular Risk: Year 1 Results from the CINEMA Program

Monday, 6th June 2022

This paper was presented by Drs. Ian Neeland, Sadeer G. Al-Kindi, Nour Tashtish, Elke Eaton, Sara Rahmani, Diamond Berg from, Cleveland OH, as a part of the symposium "Joint ADA/ASN Symposium: Turning the Tides (Diabetic Kidney Disease)" on Monday June 6th 2022 at the 82nd Scientific Sessions of the American Diabetes Association held in New Orleans.

Persons with type 2 diabetes mellitus (T2DM) often experience fragmented and complex care and across multiple specialties. We implemented a patient-centered, multidisciplinary team-based intervention called CINEMA to improve care delivery and outcomes.

Patients with T2DM at high-risk for cardiovascular disease events, including those with established atherosclerotic cardiovascular disease, elevated coronary artery calcium score >100, chronic heart failure with reduced ejection fraction, and/or chronic kidney disease stages 2-4 were included in the program in Cleveland, OH. The program included 5 cardiologists with a special focus on T2DM, a pharmacist, a certified diabetes care and education specialist/dietician, a nurse navigator, and collaboration with endocrinologists and nephrologists. Data was collected from baseline within 3 months prior to patients' first visit to up to 1 month after the follow-up visit. From May 2020 through May 2021, there were 316 referrals to the program. Of those referred, 47% met inclusion criteria. Among eligible patients, 96 (64%) completed a baseline and follow-up visit, with mean (std dev) follow-up time of 105 (34) days. Among patients completing the initial 3-month visit, 50% were ≥age 60 years with 48% female and 34% Black patients. Patients had significant reductions from baseline in Hb A1c (-8.7%), total (-10.4%), LDL (-15.7%), and non-HDL (-14.9%) cholesterol, body weight (-3.7%), and body mass index (-3.8%) ($p<0.001$ for all). In addition, among eligible patients, 87.5% were started on evidenced-based therapy with SGLT2i (n=24), GLP-1 RA (n=40), or both (n=20) to reduce the risk of CVD.

A team-based, patient-centered approach to high-risk disease management appears to be a promising paradigm for care delivery associated with greater use of evidence-based therapies and improved control of multiple CV risk factors.

SESSION-2 : Breakthrough! Effective Treatments for Diabetic Kidney Disease

More Pronounced Effect of Empagliflozin-Losartan Combination Therapy on Measured GFR and Blood Pressure Vs. Either of the Drugs: A Crossover RCT in People with Type 2 Diabetes

Monday, 6th June 2022

This paper was presented by Drs. Daniël Van Raalte, Hiddo L. Heerspink, Rosalie Scholtes, Amsterdam, Netherlands, Groningen, Netherlands, as a part of the symposium

"Breakthrough! Effective Treatments for Diabetic Kidney Disease" on Monday June 6th 2022 at the 82nd Scientific Sessions of the American Diabetes Association held in New Orleans.

Sodium-glucose cotransporter-2 inhibitors (SGLT2i) and renin-angiotensin system inhibitors (RASi) improve kidney outcomes in people with type 2 diabetes (T2D). Both drugs favorably affect kidney hemodynamic function which is characterized an acute GFR drop (reflecting reduced glomerular pressure) which, in part, underlies their protective effects. However, the interaction of these drugs on systemic and kidney hemodynamics is unstudied.

During this 4-arm, cross-over, placebo-controlled, double-blind intervention trial, twenty-four T2D patients on metformin and/or sulfonylurea therapy, (age 66±6 years, HbA1c 7.4±0.9%, measured GFR 108±20 mL/min, hypertension treated by beta blockers) were randomized to one-week treatment with empagliflozin (EMPA) 10mg QD, losartan (LOS) 50mg QD, empagliflozin+losartan (EMPA+LOS) and placebo. Fasting GFR was measured by steady-state plasma iohexol clearances. Blood pressure and heart rate (HR) were recorded. Statistical comparisons were done by Friedman test and Wilcoxon rank test correcting for multiple comparisons.

Versus placebo, EMPA and LOS monotherapy reduced GFR by 7.0 mL/min (p=0.003) and 7.3 mL/min (p=0.01) respectively, while EMPA+LOS reduced by GFR by 10.7 mL/min (p<0.001). Versus placebo, all treatment lowered blood pressure: EMPA -8.7 mmHg (p=0.04), LOS -12.4 mmHg (p=<0.001) and EMPA+LOS -15.1 mmHg (p<0.001). HR was unchanged. No safety concerns were observed.

In people with T2D and preserved kidney function, empagliflozin-losartan therapy induces more pronounced effects on measured GFR and blood pressure versus either of the drugs. These data support their combined use to improve kidney outcomes.

Efficacy of Dapagliflozin by Baseline Diabetes Medications: A Prespecified Analysis from the DAPA-CKD Study

Monday, 6th June 2022

This paper was presented by Drs. Peter Rossing, Niels Jongs, Glenn M. Chertow, Fan Fan Hou, Priya Vart, from Herlev from Denmark, Gentofte, Denmark, Groningen, Netherlands, as a part of the symposium "Breakthrough! Effective Treatments for Diabetic Kidney Disease" on Monday June 6th 2022 at the 82nd Scientific Sessions of the American Diabetes Association held in New Orleans.

The sodium-glucose cotransporter 2 inhibitor dapagliflozin improved kidney and cardiovascular (CV) outcomes in persons with chronic kidney disease (CKD) with and without type 2 diabetes (T2D) in the DAPA-CKD study. In this prespecified analysis we investigate the effects of dapagliflozin on kidney, CV, and mortality outcomes according to baseline diabetes drug class or number of diabetes drugs.

We enrolled participants with CKD with eGFR 25-75 ml/min/1.73m^2 and UACR 200-5000 mg/g, and included those with T2D at baseline in this analysis. The primary endpoint was a composite of sustained decline in eGFR of ≥50%, end-stage kidney disease, or death from kidney or CV causes. Secondary outcomes included a kidney-specific composite (the same as the primary without CV death), composite of hospitalizations for heart failure and CV mortality, and all-cause mortality. We determined the effect of dapagliflozin, compared with placebo, in subgroups by use or not of diabetes drug classes at baseline: metformin, sulfonylureas, DPP4 inhibitors, GLP-1 receptor

agonists and insulin, and by the number of diabetes medications at baseline.

Of 4304 participants enrolled 2906 (68%) had T2D, of which 1598 (55%) were on insulin, 1244 (43%) on metformin, 774 (27%) on sulfonylureas, 742 (26%) on DPP4 inhibitors, and 122 (4%) on GLP-1 receptor agonists. At baseline 327 (11%) were without diabetes treatment, 1442 (50%) were treated with one diabetes drug, 943 (32%) with two drugs and 194 (7%) with three or more. The effect of dapagliflozin on the primary composite outcome was consistent across comparisons of baseline drug class (all pint>0.19), and according to number of drugs (pint=0.08). Similarly, we found consistent benefit of dapagliflozin compared to placebo on the secondary endpoints regardless of background drug class or number of drugs.

Dapagliflozin reduced kidney and CV events in T2D with CKD independent of baseline diabetes drug class or number.

Optimization of Albuminuria Lowering Treatment by Crossover Rotation to Four Different Drug Classes

Monday, 6th June 2022

This paper was presented by Drs. Viktor Rotbain Curovic, Marjolein Y.A. Kroonen, Niels Jongs, Taha Se from Leiden, Netherlands, Groningen, as a part of the symposium "Breakthrough! Effective Treatments for Diabetic Kidney Disease" on Monday June 6th 2022 at the 82nd Scientific Sessions of the American Diabetes Association held in New Orleans.

Renin-angiotensin system (RAS) inhibitors decrease urinary albumin:creatinine ratio (UACR) and are guideline recommended drugs for kidney protection but are ineffective in lowering UACR in up to 40% of cases. We hypothesized that rotation to another drug class overcomes resistance to RAS inhibition and tested this hypothesis in a randomized cross-over trial.

We assigned 26 adults with type 1 diabetes and 37 with type 2 diabetes and UACR ≥30 and ≤500 mg/g to 4-week treatment periods with telmisartan 80 mg, empagliflozin 10 mg, linagliptin 5 mg, and baricitinib 2 mg in random order, separated by 4-week wash-out periods. Participants were then re-exposed for 4-weeks to the individual drug that induced the largest UACR reduction. Primary outcome was the difference in UACR response between the first and second exposure to the best performing drug, versus the difference in UACR response between the best performing drug and the other three drugs.

There was substantial between person variation in the best performing drug: telmisartan was best performing in 33 (52%) participants, followed by empagliflozin and linagliptin in 11 (17%) participants each, and baricitinib in 8 (13%) participants. The individual best performing drug changed UACR during the first exposure by -39.6% (95%CI -44.8, -33.8, p<0.001) and by -22.4% (95%CI -29.7, -12.5, p<0.001) at re-exposure (between exposure difference: 22.1% [95%CI 12.5, 30.8; p<0.001]). The difference in UACR response between the individual best performing drug and the other three drugs was -40.5% (95%CI -45.9, -34.6, p<0.001 vs. between exposure difference). The correlation in UACR response of the best performing drug at exposure and re-exposure was r=0.389, p=0.017.

We demonstrated a large and reproducible variation in UACR lowering responses to different drug classes reinforcing the need for personalized therapy approaches to overcome therapy resistance to guideline recommended treatment.

SESSION-3:
Joint ADA/EASD: Management of Hyperglycemia in Type 2 Diabetes

A Personalized Retrospective Continuous Glucose Monitoring (CGM) Report Improves Engagement and Glycemic Control in a Remote Monitoring Diabetes Program (RDMP)

Monday, 6th June 2022

This paper was presented by Drs. Robert J. Ellis, Tejaswi Kompala, Kevin Weng, Robert J. Brooks, Atousa Salehi, Roberta James, Hau Liu from Aurora, CO, Mountain View, CA, New York, NY as a part of the symposium "Joint ADA/EASD: Management of Hyperglycemia in Type 2 Diabetes" on Monday June 6th 2022 at the 82nd Scientific Sessions of the American Diabetes Association held in New Orleans.

Retrospective review of CGM data is associated with improved glycemic control in people with diabetes, but self-initiated data review is uncommon. The objective of this study was to examine the impact of a novel "CGM-powered Insights Report" on program engagement and glycemic control within Livongo for Diabetes, a RDMP.

Members enrolled in the RDMP and who authorized data sharing of their existing Dexcom CGM automatically received biweekly Insight Report emails. These Reports provided personalized analysis of CGM trends and suggested next steps within the digital coaching program. The impact of engaging with Insight Reports was assessed via (1) odds ratios and Fisher's exact tests on the relative recency of key RMDP program feature utilization; and (2) linear regression to quantify its impact on changes in glycemic control.

1105 members (436 T1D, 464 T2D using insulin, 205 T2D not using insulin) who received their first report by February 1, 2022 were included for analysis. On average, members received 7 Reports and opened 51% of them. Members who opened at least one Report (vs. opened no Reports) were more likely to subsequently utilize the mobile app (OR 1.6), web portal (OR 1.9), food logger (OR 1.8) and 1-on-1 coach chat feature (OR 3.2) (all $p < .05$). After controlling for demographic and clinical characteristics, baseline glucose metrics, and number of Reports received, members who opened more Reports were more likely to show improvements in mean sensor glucose, Time In Range, and Time Above Range (all $p < .05$).

For CGM users within an RDMP, engagement with a personalized Insights Report is associated with increased engagement across other program features, and improvements in glycemic control. Beyond the benefits of CGM itself, surfacing actionable insights within an RDMP adds value by driving members towards increased program engagement, specifically digital coaching.

Impact of Flash Glucose Monitoring in People with Type 2 Diabetes Inadequately Controlled with Noninsulin Antihyperglycemic Therapy: IMMEDIATE Study

Monday, 6th June 2022

This paper was presented by Drs Ruth E. Brown, Ronnie Aronson from Toronto, ON, Canada, as a part of the symposium "Joint ADA/EASD: Management of Hyperglycemia in Type 2 Diabetes" on Monday June 6th 2022 at the 82nd Scientific Sessions of the American Diabetes Association held in New Orleans.

Continuous glucose monitoring (CGM) has been shown to improve glycemic outcomes in people with diabetes using insulin therapies. In this multi-site, randomized trial, we studied adults with T2D inadequately controlled with non-insulin antihyperglycemic therapy to evaluate the impact of flash glucose monitoring (FGM) on glycemic and patient-reported outcomes.

Participants received FGM + diabetes self-management education (DSME) or matched DSME alone for 16 weeks. Primary outcome was assessed by a blinded CGM device worn at baseline and at outcome. Among 116 participants enrolled (age 58.4 ± 10.1 years; T2D duration 10.1 ± 6.1 years; HbA1c 8.6 ± 1.1%), the initial 82 completers (41 FGM + DSME, 41 DSME) showed time in range significantly greater in the FGM + DSME arm (76.1 ± 16.9%) compared to DSME arm (64.3 ± 23.2%) ($p<0.01$).

Time above range was similarly lower in the FGM + DSME arm (21.5 ± 17.8% vs. 31.3 ± 25.6%, $p=0.03$). Hypoglycemia was rare in both arms. Glucose monitoring satisfaction scores improved in the FGM + DSME arm only (0.6 ± 0.5 vs. 0.0 ± 0.5, $p<0.01$). Change in HbA1c was also greater in the FGM + DSME arm (-0.9 ± 0.9% vs. -0.5 ± 0.9%, $p=0.03$). In this interim analysis, FGM users with T2D using non-insulin therapies had significantly greater time in range, satisfaction with glucose monitoring, and a greater reduction in HbA1c.

Table. FGM metrics at 16 weeks in the FGM + DSME and DSME arms

	FGM + DSME	DSME	Adjusted difference (95% CI)	Adjusted p-value
n	41	41		
Glucose (mmol/L)	8.1 ± 1.5	8.9 ± 2.5	-0.8 (-1.7 to 0.0)	0.06
SD (mmol/L)	2.2 ± 0.5	2.4 ± 0.6	-0.2 (-0.5 to 0.0)	0.07
CV (%)	27.0 ± 6.7	27.8 ± 7.0	-0.7 (-3.9 to 2.4)	0.64
Time in range (%) (3.9-10 mmol/L)	76.1 ± 16.9	64.3 ± 23.2	11.5 (3.1 to 20.0)	<0.01
Tight time in range (%) (3.9-7.8 mmol/L)	49.2 ± 22.0	39.2 ± 23.4	8.9 (-0.3 to 18.1)	0.06
Time above range (%) (>10.0 mmol/L)	21.6 ± 17.6	32.0 ± 25.3	-9.6 (-18.4 to -0.8)	0.03
Time below range (%) (<3.9 mmol/L)	2.3 ± 5.0	3.7 ± 8.7	-1.4 (-4.6 to 1.8)	0.38
Time below range level 2 (<3.0 mmol/L)	0.5 ± 2.0	0.9 ± 3.2	-0.4 (-1.6 to 0.8)	0.49
Frequency of hypoglycemia	1.0 (5.0)	0.0 (5.0)		
Frequency of nocturnal hypoglycemia	0.0 (3.0)	0.0 (4.0)		
Frequency of level 2 hypoglycemia	0.0 (1.0)	0.0 (1.0)		

Data is expressed as mean ± SD or as mean (95% CI). Frequency of hypoglycemia is expressed as median (IQR). Linear mixed models were used to compare differences between arms, with arm and baseline HbA1c as fixed effects, and site as a random effect.

SESSION-4:
Diabetes with Cardiomyopathy: Does Anybody Have a Map?

Prevalence of Diabetic Cardiomyopathy in An Electronic Health Record–Based Cohort

Monday, 6th June 2022

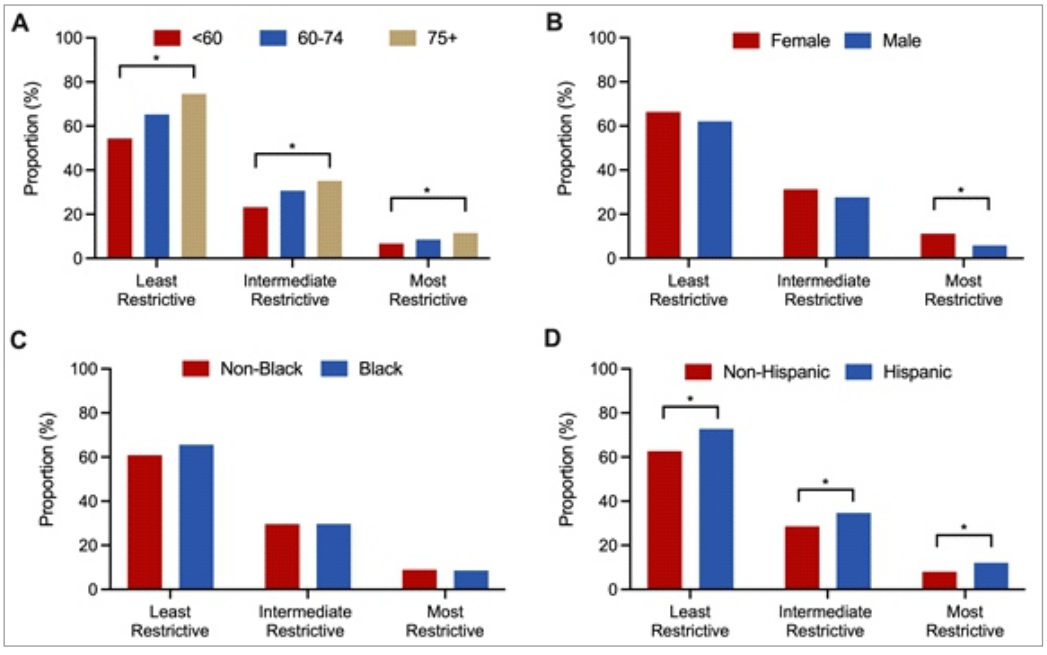
This paper was presented by Drs. Matthew W. Segar, Kershaw Patel, Muthiah Vaduganathan, Alvin Chandra, Duwayne L. Willett, Ambarish Pandey from Houston, TX, Boston, MA, Dallas, TX, as a part of the symposium "Diabetes with Cardiomyopathy: Does Anybody Have a Map?" on Monday June 6th 2022 at the 82nd Scientific Sessions of the American Diabetes Association held in New Orleans.

Diabetic cardiomyopathy (DbCM) is characterized by abnormal cardiac structure/function, associated with incident HF, and has a 67% prevalence in the community. However, the prevalence of DbCM in a real-world, electronic health record (EHR) system is not known.

Adult patients with DM in a single center EHR free of CVD with available data on HF risk factors were included. The presence of DbCM was defined using different definitions (Figure). DbCM prevalence was compared across subgroups with differences assessed using the chi-squared test. Adjusted logistic regression models were constructed to evaluate significant predictors of DbCM.

Among 1,921 individuals with DM, prevalence of DbCM in the overall cohort was 8.7% and 64.4% in the most and least restrictive definitions, respectively. Across all definitions, increasing age and Hispanic ethnicity was associated with higher proportion of DbCM (Figure A,D). No consistent differences in DbCM prevalence were observed across sex and race-based subgroups across definitions (Figure B-C). In multivariable-adjusted logistic regression, higher creatinine and longer QRS duration were associated with higher risk of DbCM across all definitions.

In a single-center, EHR cohort, the prevalence of DbCM was up to 64.4%. Increasing age and Hispanic ethnicity had a higher prevalence of DbCM.



WATCH-DM Identifies Diabetic Cardiomyopathy: A Multicohort Analysis

Monday, 6th June 2022

This paper was presented by Drs. Matthew W. Segar, Kershaw Patel, Muthiah Vaduganathan, Alvin Chandra, Duwayne L. Willett, Ambarish Pandey from Houston, TX, Boston, MA, Dallas, TX, as a part of the symposium "Diabetes with Cardiomyopathy: Does Anybody Have a Map?" on Monday June 6th 2022 at the 82nd Scientific Sessions of the American Diabetes Association held in New Orleans.

Diabetic cardiomyopathy (DbCM), a transitional phenotype that may precede overt heart failure (HF) onset, is characterized by abnormalities in cardiac structure or function in DM in the absence of cardiovascular disease (CVD) or major risk factors. Whether WATCH-DM, a validated risk score to identify incident heart failure (HF) among individuals with DM, can identify DbCM is unknown. Adults without known prevalent CAD or overt HF were pooled from 2 community-based cohort studies (ARIC and CHS). Presence of DbCM in patients with DM was defined using different definitions (Figure). Adjusted logistic regression and restricted spline models were used to evaluate the association of WATCH-DM and the individual components of DbCM.

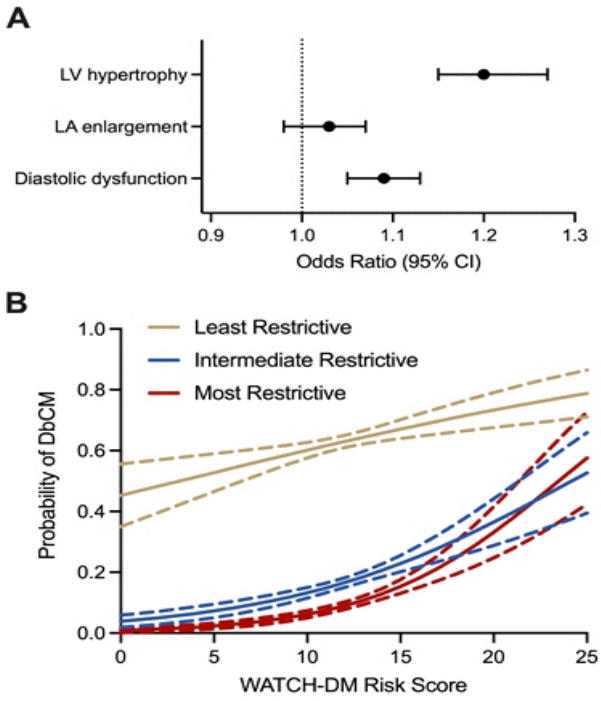


Figure. Adjusted association of WATCH-DM risk score and the **A)** individual components of DbCM and the **B)** different definitions of DbCM. Models were adjusted for sex, race, hypertension medication, smoking, alcohol use, and total cholesterol. The dashed lines represent the 95% CI. DbCM was defined using different definitions: a) least restrictive: ≥1 echocardiographic abnormality (left atrial enlargement, left ventricle hypertrophy, diastolic dysfunction); b) intermediate restrictive: ≥2 echocardiographic abnormalities; c) most restrictive: elevated NT-proBNP levels (>125 in normal/overweight or >100 pg/mL in obese) plus ≥2 echocardiographic abnormalities.
Abbreviations:
CI, confidence interval; DbCM, diabetic cardiomyopathy; LA, left atrial; LV, left ventricle

Among 2,241 individuals with DM, the prevalence of DbCM was 9.8% and 62.8% applying the most and least restrictive definitions, respectively. For every 1-unit increase, the WATCH-DM score was associated with higher risk of LV hypertrophy and diastolic dysfunction (odds ratio [95% CI] = 1.20 [1.15-1.27] and 1.09 [1.05-1.13], respectively), but not LA enlargement (Figure A). Across definitions, higher WATCH-DM scores were associated with a higher risk of DbCM (Figure B). The WATCH-DM risk score is associated with higher prevalence of DbCM and may be a useful tool in screening for DbCM.

Aldose Reductase Inhibition by AT-001 Limits Diastolic Dysfunction and Adverse Remodelling in Diabetic Cardiomyopathy

Monday, 6th June 2022

This paper was presented by Drs. Qutuba G. Karwi, Keshav Gopal, Seyed Amirhossein Tabatabaei Dakhili, from Edmonton, AB, Canada, Devon, AB, as a part of the symposium "Diabetes with Cardiomyopathy: Does

Anybody Have a Map?" on Monday June 6th 2022 at the 82nd Scientific Sessions of the American Diabetes Association held in New Orleans.

Diabetic cardiomyopathy (DbCM) increases mortality and morbidity in type 2 diabetes (T2D) subjects. Increased cardiac aldose reductase (AR) activity has been correlated with impaired cardiac function and less effective energy metabolism in DbCM subjects. The aim of the present study was to evaluate the effect AT-001, a potent and selective AR inhibitor, on cardiac function, structure, and energy metabolism in diabetic cardiomyopathic mice that overexpress the human AR (hAR-Tg).

The effects of AT-001 were compared to those of dapagliflozin, a sodium-glucose cotransporter inhibitor that decreases the risk of cardiovascular death. DbCM was induced in human AR overexpressing transgenic (hAR-Tg) mice by subjecting them to a high-fat diet (60% kcal from lard) for 10-wk with a single intraperitoneal streptozotocin injection (75 mg/kg) at 4-wk. Male mice were randomized to receive either vehicle, AT-001 (40 mg/kg/day),or dapagliflozin (1 mg/kg/day) for the final 3-wk. AT-001 treatment improved diastolic function in vivo (a decrease in the E/e' ratio and an increase in the E'/A') and reduced left ventricular mass (LV) mass in DbCM mice compared to vehicle-treated DbCM mice.

Cardioprotection by AT-001 was associated with reduced cardiac AR activity, decreased circulating blood sorbitol levels, and a reduction in cardiac fatty acid oxidation rates in the DbCM mice. Treatment with dapagliflozin did not significantly affect either diastolic function or LV mass in DbCM mice. In addition, dapagliflozin did not have a significant effect on cardiac fatty acid oxidation rates.

In summary, the present study demonstrates that AT-001 attenuates diastolic dysfunction and cardiac hypertrophy in DbCM. AT-001-induced cardioprotection is accompanied by reduced cardiac fatty oxidation rates in DbCM.

SESSION-5: Updates on Inpatient Diabetes Management

Inpatient Glycemic Control and Glucose Variability by Continuous Glucose Monitoring in Older Adults with Type 2 Diabetes

Monday, 6th June 2022

This paper was presented by Drs. Haer Idrees, Rodolfo J. Galindo, Maria A. Urrutia, Iris A. Castro-Revoredo from Atlanta, GA, as a part of the symposium "Updates on Inpatient Diabetes Management" on Monday June 6th 2022 at the 82nd Scientific Sessions of the American Diabetes Association held in New Orleans.

Few studies have reported on differences in glycemic control and glucose variability by continuous glucose monitoring (CGM) in hospitalized insulin-treated older adults with type 2 diabetes (T2D). Accordingly, we combined data from 3 inpatient randomized clinical trials using CGM in insulin-treated patients with T2D. Glycemic parameters were compared in 103 older adults (≥60 years) and 160 younger adults (<60 years). Older adults, as compared to younger adults, had significantly lower HbA1c and blood glucose (BG) upon admission, and had lower overall mean daily CGM glucose values and higher percent time in range between 70-180 mg/dl during hospital stay.

Glycemic variability (GV) did not differ between the two groups when assessed through direct univariate comparisons using coefficient of variation (CV), mean amplitude of glucose excursion (MAGE), and standard

Variable	Age<60 years (N=160)	Age >60 years (N=103)	P-value
Age	49.5± 7.5	65.7± 4.8	<.001
BMI, Kg/m^2	33.6± 8.8	34.9± 12	0.84
HbA1c, %	10.2± 2.3	8.7± 1.8	<.001
GFR ≥ 60 / < 60 ml/min, %	69/31	57 / 43	0.06
Total insulin, units/day	43.5 ± 28.5	41.4 ± 27.8	0.51
Overall Mean CGM, mg/dl	182.1 ± 44	172.7 ± 40.9	0.06
% CGM BG			
Time in range 70-180 mg/dl, %	51± 26.1	58.9± 25.5	0.012
Time above range >180 mg/dl, %	46.3± 27.2	38.6± 26.5	0.026
Time below range			
<70 mg/dl, %	2.7± 5.4	2.5± 4.7	0.69
<54 mg/dl, %	1.0± 2.7	0.9± 2.3	0.83
CGM GV			
MAGE, %	67.9± 39	67.2± 34.6	0.93
CV, %	0.28± 0.09	0.29± 0.08	0.68
SD, %	50.5± 16.2	49.3± 17.5	0.32

BMI: body mass index; **GFR**: glomerular filtration rate; **GV**: glycemic variability; **MAGE:** mean amplitude of glucose excursion; **SD**: standard deviation; **CV:** coefficient of variation

deviation (SD); however, a multivariate analysis adjusted for GFR, BMI, admission BG and HbA1c, indicated that older adults have higher GV during the hospital stay compared to younger adults.

Our study indicates that older adults with T2D have better glycemic control on admission (BG and HbA1c) and had higher % time in range (70-180 mg/dl), no difference in hypoglycemia, but greater GV during hospitalization compared to younger adults.

Diabetes Mobile Apps: A Resource for Inpatient Education and Support?

Monday, 6th June 2022

This paper was presented by Drs. Jodi S. Krall, Jason Ng, Linda M. Siminerio, from Pittsburgh, PA, as a part of the symposium "Updates on Inpatient Diabetes Management" on Monday June 6th 2022 at the 82nd Scientific Sessions of the American Diabetes Association held in New Orleans.

Diabetes mellitus (DM)-related hospitalizations are recognized as important opportunities for self-management intervention. Yet, there remains a need for practical delivery strategies.

The objective was to assess provider perspectives on DM mobile apps as a tool for self-management education and support in the inpatient setting.

Healthcare professionals (n=33) who oversee or provide DM care and education to hospitalized patients completed a validated survey about DM mobile apps.

Only 21% of respondents had previously used an app for DM education. Of those who had never used a DM app, 100% indicated that they would consider recommending one to their patients. For 82% of respondents, patient access to and interest in app use were rated as the most important factors in their decision to recommend apps. Patient acuity and time were also noted as key considerations. In fact, 54% of respondents were only willing to spend 5 minutes to download and teach app use. Hospitalized patients considered best candi-

dates for apps are those newly diagnosed with DM, new to insulin, admitted with a DM-related complication, or requiring additional education/support (change in treatment plan). Perceived benefits of apps in relation to self-management were to reinforce education (71%), support education with trustworthy information (62%), and serve as a resource after discharge (56%). Some respondents also foresaw a role for apps in teaching patients during hospitalization, especially younger patients generally viewed as more interested in apps. Most respondents agreed the following features are important for apps in education and support: Content is developed by DM experts (91%), provide answer to basic DM self-management questions (96%), user experience can be customized (91%), and include features for logging/tracking glucose results (91%).

Hospital-based providers offer valuable insights into DM app use. Exposing them to apps to support patient self-management warrants strong consideration.

Management of Inpatient Hyperglycemia Guided by Continuous Glucose Monitoring (CGM) in Insulin-Treated Patients with Diabetes—A Randomized Clinical Trial

Monday, 6th June 2022

This paper was presented by Drs. Ilias (Elias) Spanakis, Maria A. Urrutia, Maria F. Scioscia, Rodolfo J. Galindo, Priyathama Vellanki, from Atlanta, GA, Rosedale, MD, CA, Baltimore, MD, as a part of the symposium "Updates on Inpatient Diabetes Management" on Monday June 6th 2022 at the 82nd Scientific Sessions of the American Diabetes Association held in New Orleans.

Inpatient use of CGM results in higher detection of hypoglycemic and hyperglycemic events compared to point of care testing (POC) but its efficacy and safety in adjusting insulin therapy has not been evaluated. This randomized controlled trial included 181 general medicine and surgery patients with type 1 (n= 18) and type 2 (n= 155) diabetes treated with a basal bolus insulin regimen. All patients underwent POC testing AC & HS. Patients in the POC group wore a blinded Dexcom G6 CGM with insulin dose adjusted based on POC results; while in the CGM group, insulin adjustment was based on daily Dexcom G6 CGM profile review. Hypoglycemia alarms were set at 80 mg/dl in the CGM group. Primary endpoints were differences in time in range (70-180 mg/dl) and hypoglycemia (<70 mg/dl and <54 mg/dl).

There were no differences on admission clinical characteristics, HbA1c or diabetes type between POC and CGM groups. There were no differences in mean daily glucose (186.8±39 mg/dl vs. 183.2±40 mg/dl, p=0.36), total daily insulin dose (36.1±28 U/day vs. 40.7±29 U/day, p=0.33), % patients with CGM values <70 mg/dl (39% vs. 36%, p=0.68) or <54 mg/dl (24% vs. 14%, p=0.12) between the two groups. Among patients with ≥ 1 hypoglycemic event, compared to POC, CGM use resulted in significant reduction in hypoglycemia recurrence with an incidence-ratio for glucose <70 mg/dl (0.53, 95% CI:0.31-0.92) and incidence-ratio for glucose <54 mg/dl (0.37 (95% CI:0.17-0.83). The percent time <70 mg/dl among those with hypoglycemia was smaller in the CGM (1.9±3.3% vs. 5.5±8.5, p=0.024) compared to the POC group, with group difference in hypoglycemia confirmed by zero-inflated Beta Regression analysis (p<0.001).

Our results indicates that the inpatient use of Dexcom G6 CGM is safe and effective in guiding insulin adjustment resulting in similar improvement in glucose control and in significant reduction of recurrent hypoglycemic events compared to POC testing.

SESSION-6:
Individualizing Diabetes Care & Education: Children, Teens & Young Adults

INNOVATIONS: Improving Care of Patients with Type 1 Diabetes Mellitus Through Utilization of Telemedicine and Outreach

Monday, 6th June 2022

This paper was presented by Drs. Lisa E. Rasbach, Virginia Purrington, Deanna Adkins, Robert Benjamin from Durham, NC, as a part of the symposium "Individualizing Diabetes Care & Education: Children, Teens & Young Adults" on Monday June 6th 2022 at the 82nd Scientific Sessions of the American Diabetes Association held in New Orleans.

Frequent diabetes support and glucose review via telehealth may help decrease hospitalization rates and improve glycemic control for high-risk youth. This support may also help with uptake and durability of diabetes technology. Eligible youth had insulin dependent diabetes, Medicaid insurance, ages 8-18, and willing to use a continuous glucose monitor (CGM).

The quality improvement project provided weekly check-ins with a diabetes educator, visit reminders, and monthly video visits with a nurse practitioner. 10-item Likert questionnaire (1=not at all comfortable; 5=very comfortable) given at baseline assessed diabetes related comprehension. A needs assessment evaluated a family's interest in learning about certain areas of diabetes management. A1c was done at quarterly clinic visits and ED/hospitalization rates tracked. 3-month data presented. Youth (N=29, 62% female, 79% NHB), aged 8-18 yr, diabetes duration 6.3±4.3 years, had baseline mean A1c 12.3±1.7%; 28% on CSII. Mean baseline score of diabetes comprehension was 4.0±0.6. Baseline A1c correlated negatively with diabetes comprehension ($r=-0.40$, $p<0.05$). There was no difference between A1c at baseline and at 3 months ($p=0.14$) and no differences in ED/hospitalization rates compared to 2 years prior when controlled for time. There was an increase in CGM use from 3 months prior to the intervention (36% of participants) to 3 months after baseline (64%), though this was not statistically significant ($p=0.09$). There was no difference in clinic visit adherence at 3 months despite reminders.

Preliminary data reveal that those patients with the highest HbA1c often have the lowest comprehension regarding optimal diabetes care, and may benefit from education reinforcement. CGM use increased with greater understanding of this technology, and may become clinically significant over time. Further research is needed to assess the long-term impact of telehealth interventions.

Improving CGM Uptake in Minority Youth and Youth with Poorly Controlled T1D

Monday, 6th June 2022

This paper was presented by Drs. Yger L. Lin, Jacquelyn A. Manfredo, Nicole Illesca, Kai Abiola, Nearry Hwang, Maureen Seel, Elizabeth A. Brown, Risa M. Wolf from Baltimore, MD, as a part of the symposium "Individualizing Diabetes Care & Education: Children, Teens & Young Adults" on Monday June 6th 2022 at the 82nd Scientific Sessions of the American Diabetes Association held in New Orleans.

Continuous glucose monitoring (CGM) improves glycemic control for youth with type 1 diabetes (T1D). Despite these benefits, less than half of youth with T1D use CGM.

Objective: To determine if trial CGM use (10-days) increases CGM uptake and is associated with improved glycemic control among minority youth and youth with poorly controlled T1D. We also examined barriers to CGM use.

This prospective study was conducted at an academic Pediatric Diabetes Center. Youth with T1D for more than 3 months, with no previous CGM usage, or no CGM usage in the last year were enrolled. Diabetes staff placed CGM at the point of care (POC) and provided CGM education. Barriers to prior CGM use, hemoglobin A1c (HbA1c), and demographic information were recorded. Participants received 5 and 10-day follow up calls from the diabetes team to review glycemic trends. At 3 months, participants' use of CGM and HbA1c were recorded.

Youth with T1D (n=22) were enrolled (13 first time CGM users, 9 past users), mean age 14.1 years (SD 3.1), 41% non-Hispanic black, 68% female, mean diabetes duration 6.3 ± 4.4 years, and baseline mean HbA1c of 10.8%. Patient-cited barriers to prior CGM use included technical difficulties (n=5), unawareness of CGM (n=4), difficulty obtaining CGM (n=4), general apprehension (n=3), not wanting devices (n=3), and pain, fear of needles, and new diabetes diagnosis (n=1 each). Of participants, 20 completed some follow-up, and 18/20 (90%) cited wanting to use CGM long-term. Of 13 participants who completed 3 and/or 6-month follow-up visits, only 9 were actively using CGM. Further barriers to use included insurance issues (n=2) and CGM falling off (n=1). There was no change in mean HbA1c from baseline to follow-up (10.8 ±2.4% vs. 10.3 ±2.3%, p=0.46).

There are many barriers to CGM uptake in youth. Providing a trial use of CGM at the POC may increase uptake of CGM use in at-risk diabetes populations, but further investigation of additional barriers that impact long-term adherence to CGM is needed.

Trends in Incidence and Age at Diagnosis of Youth-Onset Type 2 Diabetes, 2002–2018 — The SEARCH for Diabetes in Youth Study

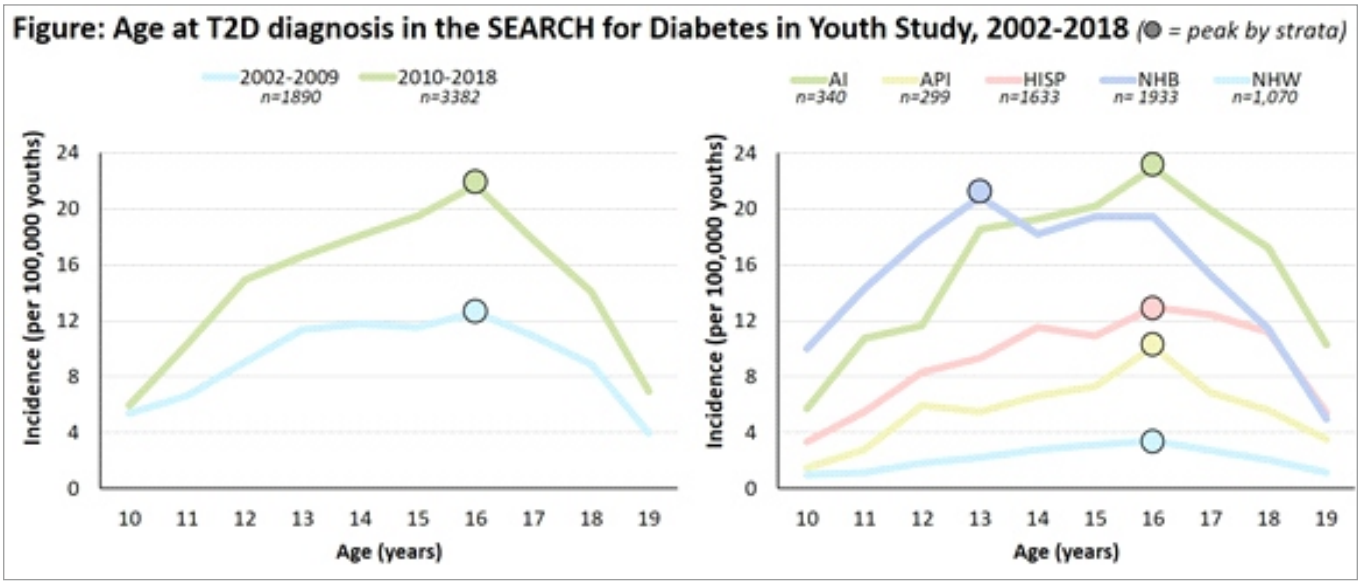
Monday, 6th June 2022

This paper was presented by Drs. Katherine A. Sauder, Lynne E. Wagenknecht, Angela D. Liese, Dana Dabelea, from Aurora, CO, Winston-Salem, NC, Columbia, SC, as a part of the symposium "Individualizing Diabetes Care & Education: Children, Teens & Young Adults" on Monday June 6th 2022 at the 82nd Scientific Sessions of the American Diabetes Association held in New Orleans.

The SEARCH study ascertained individuals with type 2 diabetes (T2D) diagnosed at <20 years of age at 5 study centers in the US from 2002 to 2018 and calculated annual incidence as number of cases divided by the population <20 years in the catchment area (~5 million annually based on US Census or health-plan member counts).

"We estimated incidence trends using a generalized autoregressive (2-year) moving average model. From annual incidence, we calculated peak age at T2D diagnosis overall population and within period, sex, race and ethnicity strata. Incidence increased from 2002-2009 to 2010-2018 (p<0.0001); however, the peak age at diagnosis did not change (16 years; Figure)."

Across all years, the peak age at diagnosis was similar between females (16 years [95% CI 15-18]) and males (16 years [16-18]). The peak age at diagnosis was younger for non-Hispanic



Black youth (NHB; 13 years), while similar for American Indian (AI), Asian and Pacific Islander (API), Hispanic (HISP), and non-Hispanic White (NHW) youth (16 years; Figure).

These data indicate continued increases in T2D incidence across ages associated with the pubertal transition, with a rapid decline following the incidence peak. They also highlight an earlier T2D onset among NHB youth. These results highlight the need for pre-pubertal or early pubertal intervention to mitigate risk of youth-onset T2D.

SESSION-7:
Definition & Interpretation of Remission in Type 2 Diabetes

Remission of Type 2 Diabetes and Improvement in Metabolic Markers with the Twin Precision Treatment Technology (TPT)–A Multicenter, Randomized, Controlled Trial

Monday, 6th June 2022

This paper was presented by Drs. Paramesh Shamanna, Lisa Shah, Jahangir Mohammed, from Bangalore, India, Mountain View, CA, as a part of the symposium "Definition & Interpretation of Remission in Type 2 Diabetes" on Monday June 6th 2022 at the 82nd Scientific Sessions of the American Diabetes Association held in New Orleans.

Table: Mean baseline and 180 day secondary outcome measures in the TPT and SC groups

Clinical & Biochemical parameters	TPT Group				SC Group			
	Baseline Mean (SD)	180 days Mean (SD)	Mean difference (SD)	P value	Baseline Mean (SD)	180 days Mean (SD)	Mean difference (SD)	P value
HbA1C (%)	9.0 (1.8)	5.7 (0.5)	-3.3 (1.8)	<0.001	8.5 (2.0)	8.1 (1.7)	-0.4 (1.4)	0.0279
Fasting Plasma Glucose (mg/dl)	170.2 (59.9)	95.9 (18.2)	-74.3 (60.4)	<0.001	159.8 (62.5)	155.0 (60.2)	-6.3 (85.4)	0.552
Time In Range (TIR) (%)	52.8 (32.3)	81.1 (20.3)	28.3 (40.4)	<0.001	61.2 (29.2)	51.6 (25.2)	-10.0 (24.8)	0.003
TAR1 (%)	24.9 (17.3)	1.2 (2.9)	-23.7 (17.6)	<0.001	19.9 (15.7)	21.4 (14.1)	1.5 (17.0)	0.472
TAR2 (%)	19.3 (25.9)	0.1 (1.2)	-19.2 (25.9)	<0.001	15.4 (24.4)	23.7 (24.5)	8.3 (20.0)	0.001
GMI (%)	7.7 (1.6)	5.6 (0.4)	-2.2 (1.5)	<0.001	7.3 (1.7)	7.7 (1.4)	0.4 (1.4)	0.0432
CV (%)	23.3 (6)	17.1 (5.4)	-6.2 (7.2)	<0.001	24.6 (5.4)	22.7 (4.6)	-1.9 (5.6)	0.0096
SBP (mmHg)	127.3 (11.4)	116.9 (10.4)	-10.4 (9.8)	<0.001	132.3 (17.1)	130.1 (14.9)	-2.2 (17.1)	0.3126
DBP (mmHg)	84.7 (7.3)	78.1 (7.1)	-6.6 (7.1)	<0.001	86.9 (11.0)	84.0 (9.4)	-2.9 (10.7)	0.0361
Weight (kg)	78.5 (14.2)	67.7 (11.4)	-10.7 (5.9)	<0.001	72.3 (12.7)	72.0 (12.1)	-0.3 (3.4)	0.5503
BMI (kg/m2)	27.3 (4.4)	23.5 (3.5)	-3.8 (2.2)	<0.001	28.1 (4.2)	28.1 (4.1)	-0.007 (1.5)	0.9703
WC (cm)	97.7 (11)	86.7 (7.8)	-10.9 (6.8)	<0.001	94.8 (10.9)	95.3 (12.2)	0.5 (10.9)	0.7219
LDL-C (mg/dL)	127.5 (38.1)	130 (37.9)	2.5 (40.5)	0.387	116.7 (31.8)	115.7 (34.9)	-1.0 (28.7)	0.7733
HDL-C (mg/dL)	34.8 (6.9)	43.3 (8.9)	8.5 (8.2)	<0.001	35.4 (7.0)	35.3 (7.4)	-0.01 (5.1)	0.8727
TG/HDL	7.1 (7.5)	3.2 (2.1)	-3.9 (2.1)	<0.001	6.4 (3.6)	7.0 (5.5)	0.5 (4.7)	0.3684
TG (mg/dL)	223.5 (181.5)	128.7 (72.3)	-94.8 (172.8)	<0.001	214.2 (97.1)	222.0 (128.9)	7.8 (100.6)	0.5403
HOMA 2IR (%)	1.9 (0.9)	1 (0.5)	-0.9 (0.8)	<0.001	1.9 (1.0)	2.2 (1.4)	0.3 (1.2)	0.0968
HOMA 2B (%)	51.5 (30.6)	88 (31.3)	36.5 (38.5)	<0.001	60.4 (38.5)	66.9 (41.6)	6.4 (40.2)	0.2101
NAFLD Fibrosis Score	-2.3 (1)	-3.3 (1.1)	-1 (1.1)	-1.9 (1.2)	-2.1 (1.3)	-0.2 (0.8)	0.0166	-1.9 (1.2)
NAFLD Liver Fat Score	0.7 (1.8)	-1.6 (1)	-2.3 (1.7)	0.8 (2.1)	0.9 (1.9)	0.2 (2.1)	0.5871	0.8 (2.1)
Urine Microalbumin to Creatinine ratio (mg/g)	39.6 (98.8)	15.6 (60.9)	-23.9 (89.8)	<0.001	31.1 (60.2)	41.6 (115.0)	10.5 (86.0)	0.3363

The study was designed to determine the effect of TPT vs. standard care (SC) on change in A1C and T2DM remission at 90-day intervals, in addition to multiple secondary endpoints.

The TPT intervention uses the Whole-Body Digital Twin Platform, with AI and Internet of Things, to integrate multi-dimensional data to give precision nutrition and health recommendations via the TPT app and by coaches.

Baseline mean age, diabetes duration and A1C obtained in 319 pts were 45y (±9.7y), 3.9y (±2.9y) and 9.0% (±1.9%), respectively. Interim analysis of 262 pts (TPT n=199; SC n=63) who reached 180d showed 94.9% (189/199) of TPT pts had A1C < 6.5%, on no medications or metformin only; 83.9% (167/199) achieved diabetes remission based on ADA criteria. All 9 insulin-using pts stopped insulin before 90d.

The Table shows significant improvement in secondary endpoints in TPT pts at baseline and 180d, including A1C (9.0% to 5.7%, P<0.001). TPT pts had -3.3% change in A1C (95% CI -3.6 to -3%, P=<0.001) compared to SC with -0.39% (95% CI -0.73 to -0.043%, P=0.028), with a significant between-group difference (P=<0.0001). The TPT intervention in pts with T2DM allowed for significant reduction in A1C, diabetes remission (~84%) and improvement in multiple metabolic parameters at 6 months. Future long-term studies are needed to support these initial findings.

Remission of Type 2 Diabetes and Improvement in Incretins, Cardiovascular Risk Factors, and Weight Loss with a High-Protein Diet

Monday, 6th June 2022

This paper was presented by Drs. Frankie B. Stentz, Ann Ammons, John V. Christman from Memphis, TN as a part of the symposium "Definition & Interpretation of Remission in Type 2 Diabetes" on Monday June 6th 2022 at the 82nd Scientific Sessions of the American Diabetes Association held in New Orleans.

The incretins GLP-1 and GIP have important roles in insulin sensitivity and have been shown to be effective in pharmacological treatment of type 2 diabetes (T2D). Therefore, we studied these incretin level changes with remission of T2D and weight loss using a high protein (HP) diet in 12 obese women and men with T2D.

Our studies have shown that subjects with T2D on a 6-month HP diet (30% protein, 30% fat, 40% CHO) had 100% remission of T2D compared to only 33% on a HC diet (15% protein, 30% fat, 55% CHO). Effects of HP and HC diets on ghrelin levels were determined since HP subjects had increased satiety compared to HC diet. GLP-1, GIP, and Ghrelin levels were determined with a Meal Tolerance Test (MTT) at baseline and after 6 mo on HP and HC diets where all food was provided.

Since cardiovascular risk factors (CVRF) decreased more in the HP than the HC diet, we determined if the B-Type Natriuretic Peptide (BNP) released from the heart was affected by either diet. As shown in Table, HP diet had a greater increase in GLP-1and GIP than the HC diet. BNP decrease demonstrates improvement in heart tissue with the HP diet having a greater effect than the HC diet.

Weight loss was similar (9.8% in HP vs. 11.3% in HC, p=0.692). this study demonstrates that the HP diet increases GLP-1 and GIP which may be responsible in part for the improved insulin sensitivity and decreased BNP with greater improvement in CVRF with remission of T2D.

Remission of Type 2 Diabetes After Weight Loss in "Normal" Weight People–The ReTUNE Study

Monday, 6th June 2022

This paper was presented by Drs. Roy Taylor, Keaton M. Irvine, Alison C. Barnes, Tara L. Kelly from Newcastle Upon Tyne, United Kingdom, Edinburgh, United Kingdom as a part of the symposium "Definition & Interpretation of Remission in Type 2 Diabetes" on Monday June 6th 2022 at the 82nd Scientific Sessions of the American Diabetes Association held in New Orleans.

Mechanisms underlying weight loss induced remission of type 2 diabetes (T2DM) have been reported only in people with BMI >27 kg/m^2. The Personal Fat Threshold hypothesis postulated that the same mechanisms in people with BMI <27 kg/m^2. Pathophysiology during stepwise dietary weight loss was studied in this group.

People with T2DM (13/20 female, mean (±1SD) 59.3±7.1 years, BMI 24.8±1.7 kg/m^2) were studied before and after up to three 5% weight loss cycles, each comprising a 2–4-week low energy diet (800kcal/day formula meal replacements plus non starchy vegetables), followed by 4-6 weeks of weight maintenance. All hypoglycemic agents were stopped before weight loss. Studies were repeated at 12 months. Outcomes were compared to normoglycemic matched controls (n=20). Intrahepatic and intrapancreatic fat was quantified by magnetic resonance, and a standard meal test assessed insulin secretion by Disposition Index (DI).

70% achieved remission (HbA1c <6.5%; 14/20), accompanied by decrease in adipose tissue distress (Median (IQR) PAI-1 8.64 (6.97-11.01) to 5.99 (3.94-7.73) p<0.02 [control 4.87(3.49-7.03]

ng/ml; GDF-15591 (439-872) to 444 (395-554) [446 (383-614] pg/ml $p<0.05$. Between baseline and 12 months, decrease was (mean±SE; control data in square brackets): BMI 24.8±0.4 to 22.5±0.4 kg/m^2 ($p<0.0001$) [21.5±0.5]; total body fat 32.1±1.5 to 27.6±1.8% ($p<0.0001$) [24.6±1.5]; Fasting plasma insulin 47±6 to 24±6pmol/l ($p<0.001$) [23±2]; liver fat 4.0±0.6 to 1.6±0.2% ($p=0.02$) [1.9±0.3]; plasma triglycerides 1.4±0.2 to 0.9±0.1mmol/l ($p<0.02$) [0.9±0.1]; Intrapancreatic fat (6.1±0.5 to 5.0±0.6% ($p=0.03$) [4.1±0.3]. DI increased from median (IQR) 289 (183-373) to 774 (486-1709) dl/kg/min per pmol/l ($p<0.05$) but remained subnormal [2751 (1524-3526].

Mechanistic changes underpinning remission after weight loss in non-obese people with T2DM are the same as in obese people. T2DM occurs if a person becomes too heavy for their own constitution, irrespective of BMI. Weight loss of ~10% can bring about T2DM remission in people classified as having a 'normal' BMI.

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