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Diabetes Update

Vol. 2 | Issue 30| 2021

Dear Doctor,

Greetings from Micro Labs Limited. We are happy to bring you "DIABETES UPDATE" which contains latest and interesting news in the field of Diabetes and Endocrinology.

- Interpretation between trajectory patterns of albuminuria, rates of end-stage kidney disease and all-cause mortality in diabetic kidney disease
- Insulin resistance in COVID-19 and diabetes
- Role of Dapagliflozin on ventricular arrhythmias, resuscitated cardiac arrest, or sudden death

Interpretation between trajectory patterns of albuminuria, rates of end-stage kidney disease and all-cause mortality in diabetic kidney disease

Worldwide, diabetic kidney disease (DKD) is leading cause of end stage kidney disease (ESKD) and premature death. Albuminuria is an indication for diabetic kidney disease and risk factor for end stage kidney disease and all-cause death. The risk assessment of ESKD and mortality rate allows the understanding of longitudinal trajectory of albuminuria. This study focuses on the association of 2-year

longitudinal trajectory patterns of albuminuria with end-stage kidney disease and all-cause mortality using joint latent class mixed models.

Kidney biopsy based study involved 895 patients with type 2 diabetes aged 30-82 years who underwent clinical kidney biopsy. 329 patients with 30mL/min/1.73m^2 of glomerular filtration rate (eGFR) and no events of ESKD were included in the study. Data such as patients age, gender, urine albumin to creatinine ratio (UACR) and medication usage was obtained and number of serum creatinine and UACR measurements during the 2year follow-up period was also reported. Pathological findings such as glomerular and interstitial lesions (grades 0-3) were evaluated according to the Renal Pathology Society Diabetic Nephropathy classification.

Three classes of mean UACR trajectories were obtained based on the mean posterior class membership probabilities; class 1 containing high increasing albuminuria (n=254, 77.2%) during the 2-year follow-up. Class 2 containing high decreasing albuminuria (n=24, 7.3%) during 2-year follow-up and class 3 contained low stable albuminuria (n=51, 15.5%) during 2-year follow-up. When comparing baseline characteristics by the trajectory patterns of UACR, fewer risk factors associated with ESKD was observed in low stable group.

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Figure 1: Trajectories of UACR over 2 years of follow up by the mean posterior class membership probabilites.

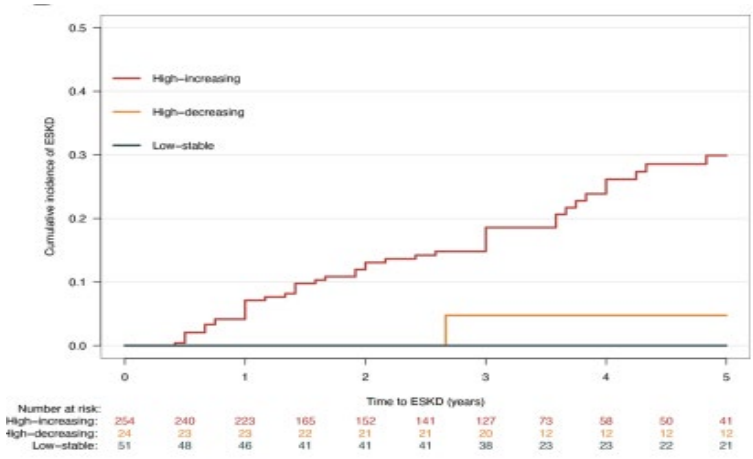
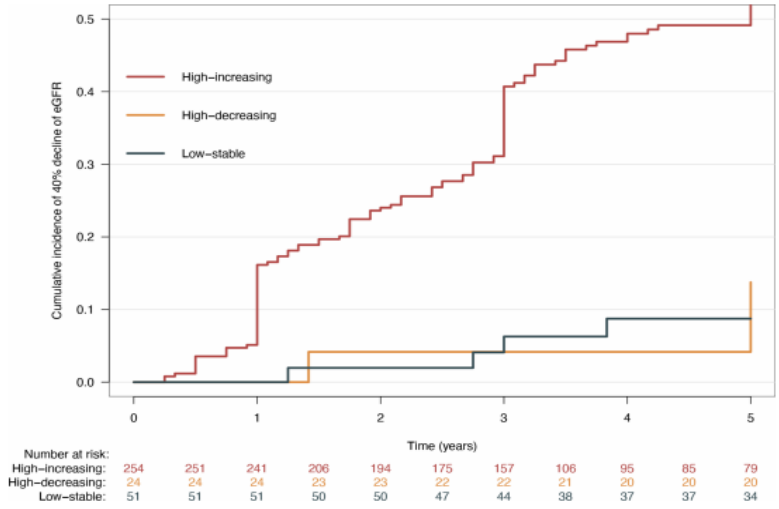


Figure 2: Cumulative incidence of ESKD by the mean posterior class membership probabilities



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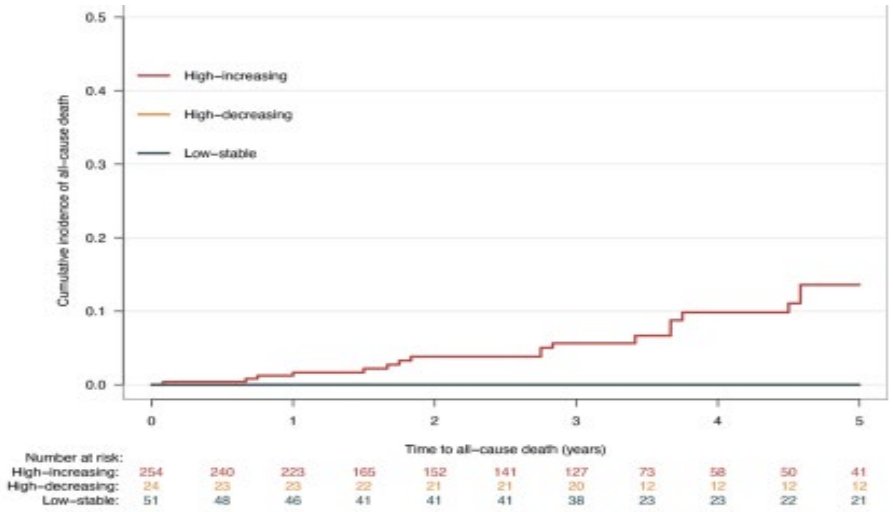

Figure 3: Cumulative incidence of all cause death before ESKD by the mean posterior class membership probabilities

The cumulative incidence of ESKD increased in the order of low stable group, high decreasing group, high increasing group and all cause-death was observed highest in high increasing group. Cumulative incidence showed no difference between the high decrease group and low stable group. Compared with the reference group, ESKD was 5.77 for high decreasing group and 10.61 for the high increasing group. The sub distribution of all-cause death was highest in high increasing group, but no difference observed between high decreasing group and low stable group. The crude incidence rates of ESKD and all-cause death were lower in the high decreasing group compared with high decreasing group. 40% decline in eGFR was observed during median follow up and 40% decline in eGFR increased in the order of low stable group, high decreasing group and high increasing group according to the cumulative incidence.

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Three different groups of 2 years longitudinal UACR trajectory that linked to ESKD and all-cause death was identified, from this findings more individualized therapy can be established to alleviate disease towards ESKD and all-cause death.

Reference: Yamanouchi M, et al. BMJ Open Diab Res Care 2021;9:e002241

Insulin resistance in COVID-19 and diabetes

The epidemiology of COVID-19 is affected by advanced age, gender, immunocompromisation and co-morbidities such as diabetes mellitus, hypertension, cardiovascular disorders and respiratory disease. Patients with history of diabetes and insulin resistance experience the severity of COVID-19 with decline of immune function.

The present study aimed at investigating the effects of COVID-19 infection on insulin resistance in patients with diabetes. SARS-CoV2 stability and infectivity was tested under controlled laboratory conditions, Viral RNA was detected by reverse transcriptase PCR and infectivity was detected by VERO E6 CPE test. Physical examination, hemoglobin A1c test and blood tests such as fasting plasma glucose test and oral glucose tolerance test was done for patients with insulin resistance.

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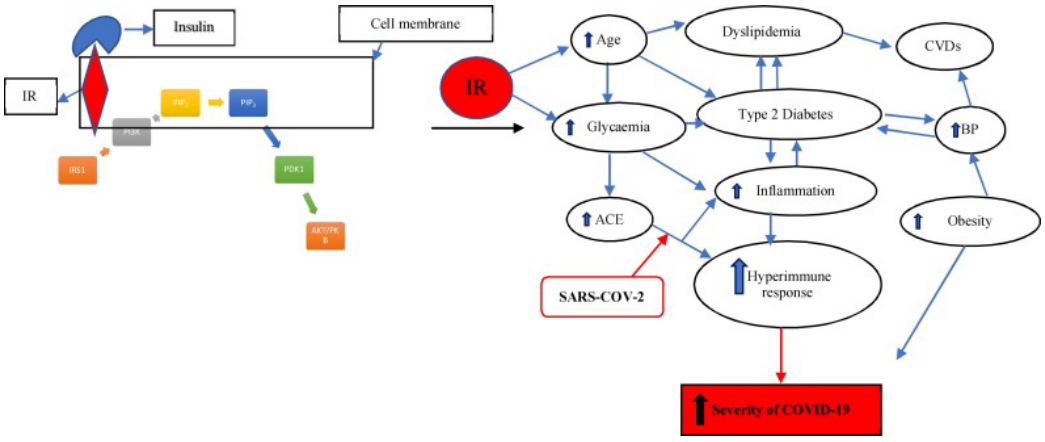
The data shows the viral binding to Angiotensin Converting Enzyme 2 (ACE2) increases angiotensin II associating it has the main cause in the synergy of insulin resistance and cardiovascular disease. It is observed that the expression of ACE2 decreased this results in overstated activity of Ang II with insulin resistance, inflammation and cardiac dysfunction. Increased insulin resistance leads to increased pancreatic expression showed high affinity for the spike protein to bind causing increased vulnerability COVID-19 infection. Patients with insulin resistance and diabetes mellitus lead to severe pathological symptoms during COVID-19 and subsequent mortality. Thus, insulin resistance in diabetes causes hyperinsulinemia, chronic inflammation and lung dysfunction.

Figure 1: Insulin signalling pathway and insulin resistance in COVID-19 and diabetes



This study demonstrated that insulin resistance is key facilitator between COVID-19 and diabetes which initiates inflammatory response causing respiratory distress. However, more studies are required to provide to the accurate results to confirm if insulin resistance be used as predictor for both COVID-19 and diabetes.

Reference: Govender N, et al. Prim Care Diabetes. 2021 Aug;15(4):629-634.

Role of Dapagliflozin on ventricular arrhythmias, resuscitated cardiac arrest, or sudden death

The aim of this study was to examine the effect of dapagliflozin on the incidence of ventricular arrhythmias and sudden death in patients with heart failure and reduced ejection fraction (HFrEF).

In a post hoc analysis of DAPA-HF, we examined serious adverse event reports related to ventricular arrhythmias or cardiac arrest, in addition to adjudicated sudden death. The effect of dapagliflozin, compared with placebo, on the composite of the first occurrence of any serious ventricular arrhythmia, resuscitated cardiac arrest, or sudden death was examined using Cox proportional hazards models. A serious ventricular arrhythmia was reported in 115 (2.4%) of the 4744 patients in DAPA-HF (ventricular fibrillation in 15 patients, ventricular tachycardia in 86, 'other' ventricular arrhythmia/tachyarrhythmia in 12, and torsade de pointes in 2 patients). A

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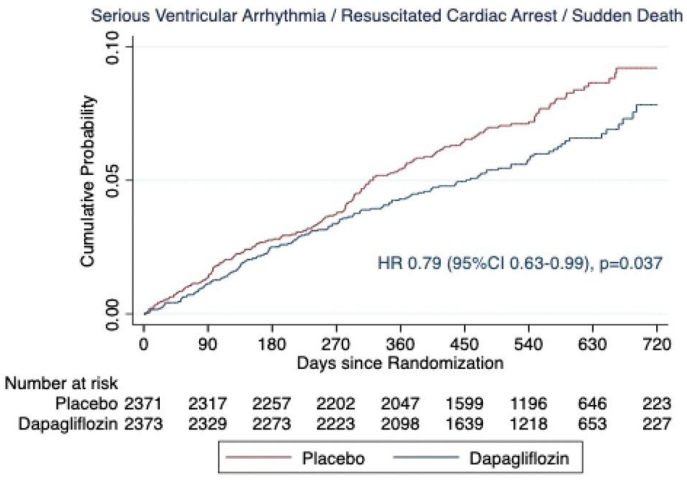
total of 206 (41%) of the 500 cardiovascular deaths occurred suddenly. Eight patients survived resuscitation from cardiac arrest. Independent predictors of the composite outcome (first occurrence of any serious ventricular arrhythmia, resuscitated cardiac arrest or sudden death), ranked by chi-square value, were log-transformed N-terminal pro-B-type natriuretic peptide, history of ventricular arrhythmia, left ventricular ejection fraction, systolic blood pressure, history of myocardial infarction, male sex, body mass index, serum sodium concentration, non-white race, treatment with dapagliflozin, and cardiac resynchronization therapy. Of participants assigned to dapagliflozin, 140/2373 patients (5.9%) experienced the composite outcome compared with 175/2371 patients (7.4%) in the placebo group [hazard ratio 0.79 (95% confidence interval 0.63–0.99), P = 0.037], and the effect was consistent across each of the components of the composite outcome.



Kaplan–Meier curves for time-to-first serious ventricular arrhythmia, resuscitated cardiac arrest, or sudden death according to treatment assignment.

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Predictor variable[a]	Odds ratio (95% CI)	*P*-value[b]	χ^2
Log-transformed NT-proBNP (per 1 unit increase)	1.54 (1.34–1.77)	<0.001	36.0
Previous ventricular arrhythmia	1.93 (1.41–2.64)	<0.001	16.8
LVEF (per 5% increase)	0.86 (0.78–0.94)	0.001	11.9
Systolic BP (per 10 mmHg increase)	0.88 (0.81–0.96)	0.004	8.1
Previous MI	1.42 (1.11–1.82)	0.005	7.8
Male sex	1.53 (1.10–2.12)	0.012	6.3
BMI (per 1 kg/m^2 increase)	1.03 (1.00–1.05)	0.020	5.4
Sodium (per 1 mmol/L increase)	0.96 (0.92–0.99)	0.039	4.3
Non-white race	0.85 (0.72–0.99)	0.038	4.3
Dapagliflozin	0.80 (0.63–1.02)	0.067	3.4
Cardiac resynchronization therapy	0.64 (0.39–1.04)	0.070	3.3
Previous HF hospitalization	0.99 (0.78–1.27)	0.985	0.0

Backward stepwise logistic regression multivariable model to predict any serious ventricular arrhythmia, resuscitated cardiac arrest, or sudden death

Dapagliflozin reduced the risk of any serious ventricular arrhythmia, cardiac arrest, or sudden death when added to conventional therapy in patients with HFrEF.

Source: Curtain JP et al. Eur Heart J. 2021 Aug 27:ehab560. doi: 10.1093/eurheartj/ehab560. Epub ahead of print.