MICRO LABS LIMITED

Diabetes Update

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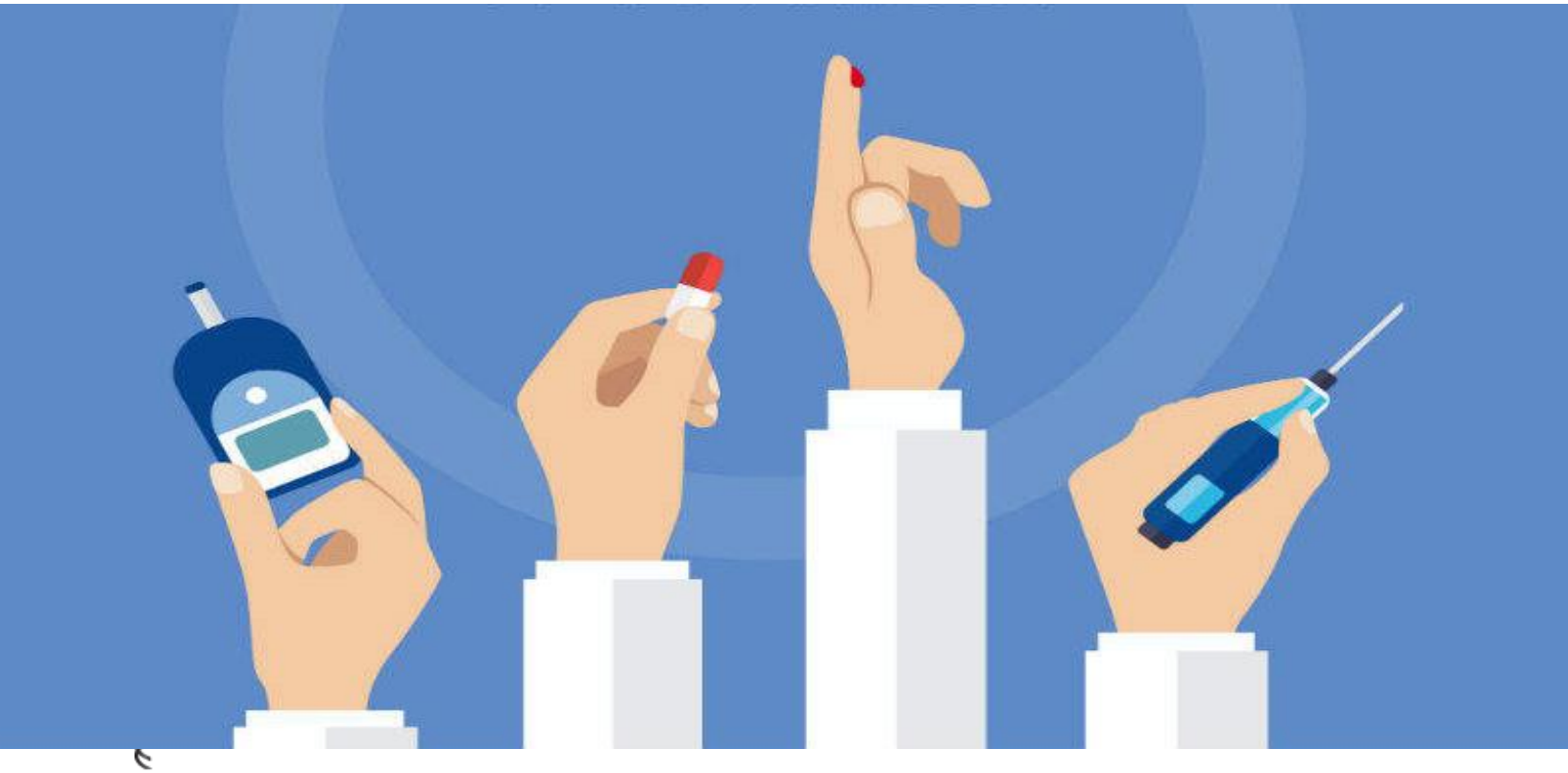


Dear Doctor,

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.

- Predicting 5- and 10-Year Mortality Risk in Older Adults With Diabetes
- Bempedoic Acid in Patients with Diabetes, Prediabetes, and Normoglycemia
- Diabetes Mellitus and Cardio-Cerebrovascular Risk in Primary Aldosteronism

Should you require any specific article or medical information, please feel free to contact us at medicalservices@microlabs.in

Looking forward to your valuable feedback

Best Regards,

Medical Team, Micro Labs Limited

Predicting 5- and 10-Year Mortality Risk in Older Adults With Diabetes

Prognostic indices obtained from administrative data can predict 5- and 10-year mortality in older adults with diabetes.

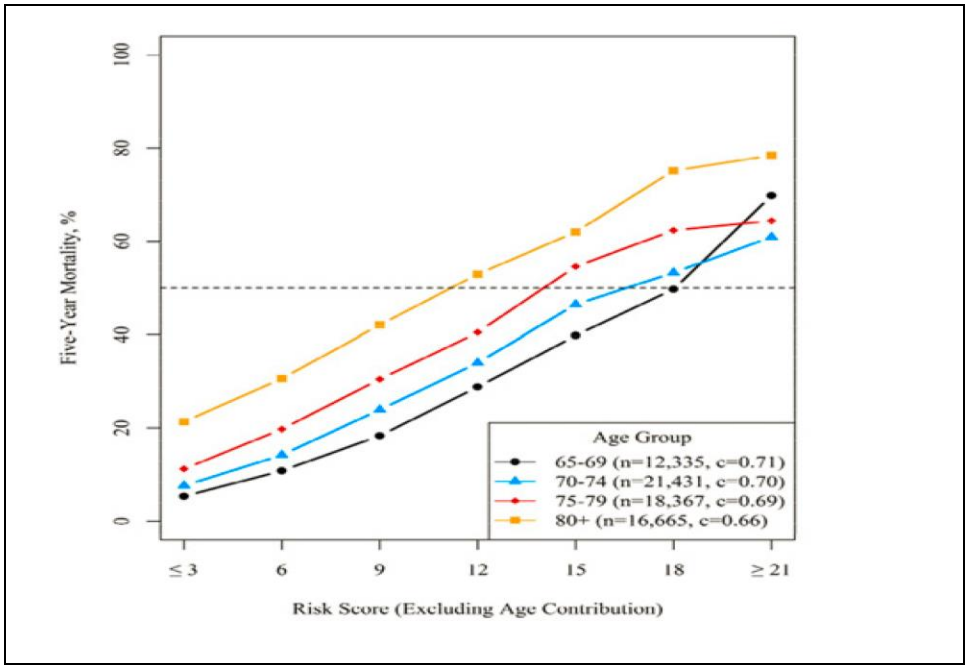
Diabetes increases the risk of macrovascular and microvascular complications and mortality. Lowering hemoglobin A1c (A1C) reduces microvascular disease risks over time but has unclear effects on cardiovascular disease and mortality, particularly in older adults.

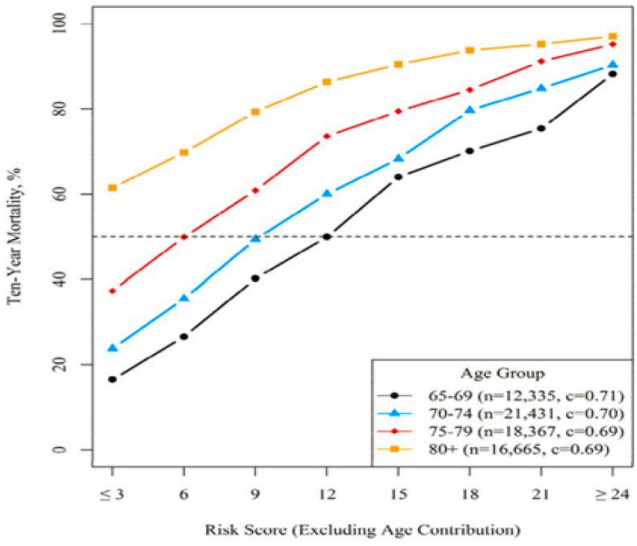
Several diabetes clinical practice guidelines suggest that treatment goals may be modified in older adults on the basis of comorbidities, complications, and life expectancy. The long-term benefits of treatment intensification may not outweigh short-term risks for patients with limited life expectancy. Because of the uncertainty of determining life expectancy for individual patients, we sought to develop and validate prognostic indices for mortality in older adults with diabetes.

Griffith et al. used a prevalence sample of veterans with diabetes who were aged ≥65 years on 1 January 2006 (N = 275,190). Administrative data were queried for potential predictors that included patient demographics, comorbidities, procedure codes, laboratory values and anthropomorphic measurements, medication history, and previous health service utilization. Logistic least absolute shrinkage and selection operator regressions were used to identify variables independently associated with mortality. The resulting odds ratios were then weighted to create prognostic indices of mortality over 5 and 10 years.

Thirty-seven predictors of mortality were identified: 4 demographic variables, prescriptions for insulin, sulfonylureas, or blood pressure medications, 6 biomarkers, previous outpatient and inpatient utilization, and 22 comorbidities/procedures. The prognostic indices showed good discrimination, with C-statistics of 0.74 and 0.76 for 5- and 10-year mortality, respectively. The indices also demonstrated excellent agreement between observed outcome and predictions, with calibration slopes of 1.01 for both 5- and 10-year mortality.

The prognostic indices had satisfactory to good accuracy when predicting mortality after excluding age from the models. Figure 1 shows mortality within age groups (65–69, 70–74, 75–79, 801years) by risk score; the indices discriminated well in all age-subgroups, with strata specific C-statistics ranging from a low of 0.66 for 5-year mortality in the 80+ group to a high of 0.71 for 5-year mortality in the 65–69 group.





Observed mortality by risk score in varying age-groups.

This graph shows mortality within age-groups (65–69, 70–74, 75–79, 801 years) by risk score calculated using prognostic indexes but excluding the points contributed by age. A horizontal line is drawn at 50% to note that such risk scores predict when mortality is more likely than not

Prognostic indices obtained from administrative data can predict 5- and 10-year mortality in older adults with diabetes. Such a tool may enable clinicians and patients to develop individualized treatment goals that balance risks and benefits of treatment intensification.

Source: Griffith KN et al. Diabetes Care 2020 Jun; dc191870. https://doi.org/10.2337/dc19-1870

Bempedoic Acid in Patients with Diabetes, Prediabetes, and Normoglycemia

Current guidelines support aggressive LDL-C lowering in patients with diabetes. We assessed the efficacy and safety of BA, a first-in-class ATP-citrate lyase inhibitor, by baseline glycemic status (diabetes, prediabetes, or normoglycemia)

in patients with hypercholesterolemia.

Four phase 3 trials randomized 3623 patients on stable lipid-lowering therapy to receive BA 180 mg or placebo (PBO) once daily for 12 to 52 weeks. Studies were grouped into 2 pools by enrollment criteria (52-weeks in patients with atherosclerotic cardiovascular disease and/or heterozygous familial hypercholesterolemia vs. 12- or 24- weeks in patients with statin intolerance). Primary efficacy endpoint was percent change from baseline to week 12 in LDL-C.

BA significantly lowered LDL-C and had a safety profile comparable to PBO, regardless of baseline glycemic status.

Percent Changes from Baseline to Week 12 in LDL-C by Study Pool

Baseline glycemic status	n[a]	BA	n[a]	Placebo	LS Mean Difference (95% CI)[b]
ASCVD/HeFH on Statins pool					
Diabetes	614	–18.6 (0.8)	317	0.6 (1.3)	–19.2 (–22.2, –16.2)
Prediabetes	994	–16.4 (0.7)	504	2.1 (1.0)	–18.5 (–20.9, –16.1)
Normoglycemic	314	–14.0 (1.1)	157	3.2 (1.9)	–17.2 (–21.4, –13.0)
Statin Intolerant pool					
Diabetes	108	–20.9 (2.3)	52	–1.9 (1.8)	–18.9 (–24.7, –13.1)
Prediabetes	215	–25.0 (1.5)	91	4.7 (2.1)	–29.7 (–34.6, –24.7)
Normoglycemic	76	–25.2 (2.2)	46	–1.6 (2.1)	–23.6 (–29.7, –17.4)

BA, bempedoic acid; CI, confidence interval. LDL, low density lipoprotein cholesterol. Data are means (standard errors) unless otherwise specified.
[a]n = number of patients with data available at both baseline and week 12.
[b]*P*<.001 for all

In both pools, BA significantly lowered LDL-C compared with PBO, regardless of baseline glycemic status (all P<.001; Table). Significant reductions with BA vs. PBO were seen in total cholesterol, non-HDL-C, apolipoprotein B, and hsCRP (all P<.01). The safety profile of BA was similar to PBO and did not vary by glycemic status. BA did not worsen measures of glycemic control or increase occurrence of new-onset diabetes mellitus compared with PBO.

Source: Leiter LA et al. Diabetes 2020 Jun; 69(Supplement 1):https://doi.org/10.2337/db20-185-OR

Diabetes Mellitus and Cardio-Cerebrovascular Risk in Primary Aldosteronism

Presence of DM as an independent risk factor for CCV events and renal complications, even in PA patients

Primary aldosteronism (PA) is major cause of secondary hypertension that affects 3.2-12.7% of hypertensive patients. PA patients are at higher risks of cardio-cerebrovascular (CCV) events compared to those with essential hypertension (EH), and the increased risk is mainly due to excess aldosterone, which induces not only a rise in blood pressure but also directly damages the myocardium and arterial walls.

Moreover, persistent exposure to excessive aldosterone is known to cause renal fibrosis and vasculopathies. This explains the high urinary albumin excretion rate in PA patients compared with EH patients. On the other hand, in patients with diabetes mellitus (DM), the risks of CCV events and proteinuria are high because of hyperglycemia.

The prevalence of diabetes mellitus (DM) in patients with primary aldosteronism (PA) is higher than in those with essential hypertension and the general population. Although DM is a common major risk factor for cardio-cerebrovascular (CCV) diseases and renal complications, details of its effects in PA have not been demonstrated. The aim of this study was to determine the effects of coexistent DM on the risk of CCV events and progression of renal

complications in PA patients. A multi-institutional, cross-sectional study was conducted.

PA patients experienced between January 2006 and October 2016 and with available data of CCV events and DM were enrolled from the Japan PA registry of the Japan Primary Aldosteronism Study/Japan Rare Intractable Adrenal Diseases Study (n = 2524). CCV events and renal complications were compared between a DM group and a non-DM group by logistic and liner-regression analysis.

DM significantly increased the odds ratio (OR) of CCV events (OR 1.59, 95% CI: 1.05-2.41) and that of proteinuria (OR 2.25, 95% CI: 1.59-3.16). DM correlated significantly with declines in estimated glomerular filtration rate (β = .05, P = .02).

Table: Risk factors for CCV events.

Variable	Univariate analysis		Multivariate analysis	
	OR (95% CI)	p	OR (95% CI)	p
Diabetes mellitus	2.53 (1.80-3.55)	<0.01	1.59 (1.05-2.41)	0.03
Sex, male	2.09 (1.53-2.86)	<0.01	1.98 (1.29-3.04)	<0.01
Age (+ 10 years)	1.70 (1.47-1.98)	<0.01	1.40 (1.15-1.71)	<0.01
Body mass index (+ 5 kg/m^2)	1.09 (0.91-1.31)	0.33	0.96 (0.76-1.22)	0.74

Systolic blood pressure (+ 10mmHg)	1.02 (0.94-1.11)	0.56	1.03 (0.94-1.14)	0.54
Duration of hypertension (+ 5years)	1.33 (1.24-1.43)	<0.01	1.21 (1.11-1.32)	<0.01
Dyslipidemia	2.34 (1.72-3.18)	<0.01	1.61 (1.11-2.34)	0.01
Current or past smoking	1.73 (1.25-2.39)	<0.01	1.58 (1.06-2.34)	0.02
Current or past drinking	0.71 (0.52-0.99)	0.04	0.50 (0.34-0.74)	<0.01

This the first report to demonstrate the presence of DM as an independent risk factor for CCV events and renal complications, even in PA patients. Management of DM should be considered in addition to the specific treatment of PA.

Source: Saiki A et al. J Clin Endocrin Metabol. 2020 July;105(7):dgaa177. https://doi.org/10.1210/clinem/dgaa177