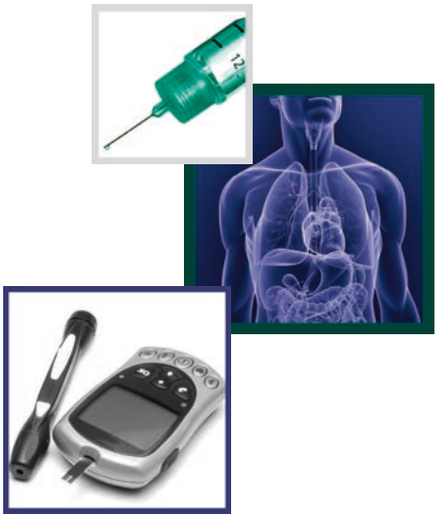
JOURNAL WATCH

Our panel of experts highlight the most important research articles across the spectrum of topics relevant to the field of diabetes management



Expert panel: **Pranav Dalal,** University of Missouri, Columbia, MO, USA; **Prasad Bichu**, University of Missouri, Columbia, MO, USA; **Preethi Yerram,** University of Missouri, Columbia, MO, USA; **Adam Whaley-Connell,** University of Missouri, Columbia, MO, USA; **Dominique Hansen,** Hasselt University, Faculty of Medicine, Belgium; **Charlie Dong,** Indiana University School of Medicine, IN, USA

Chakkera HA, Weil EJ, Swanson CM, Dueck AC. Pretransplant risk score for new-onset diabetes after kidney transplantation. *Diabetes Care* 34(10), 2141–2145 (2011).

Using a single-center retrospective cohort of 318 pretransplant patients, the authors constructed a risk score for new-onset diabetes after transplantation (NODAT). A simple risk score of 0–7 was calculated from seven pretransplant variables, including age, triglycerides, BMI, fasting glucose, use of gout medicine, family history of Type 2 diabetes and planned corticosteroid therapy, to predict the incidence of NODAT at 1 year post-transplant. The risk of NODAT ranged from 7% for a score of 0 to 56% for a score of ≥4. This simple risk score can be useful to predict post-transplant NODAT. The major limitations include that it is a single-center study, its retrospective nature and the unavailability of precise time to the event.

– By Pranav Dalal, Preethi Yerram, Prasad Bichu & Adam Whaley-Connell

The DCCT/EDIC research group. Intensive diabetes therapy and glomerular filtration rate in Type 1 diabetes. *N. Engl. J. Med.* 365(25), 2366–2376 (2011).

The Diabetes Control and Complications Trial (DCCT), a multicenter, randomized, controlled trial of 1441 patients with Type 1 diabetes, demonstrated that intensive glucose control was associated with lower glycated hemoglobin levels and a reduced risk of microalbuminuria and macroalbuminuria compared with conventional therapy. The Epidemiology of Diabetes Interventions and Complications (EDIC) study – an observational extension of the DCCT – followed 1375 participants for 16 years. Over a median follow-up of 22 years, the research found that the patients who received intensive diabetes therapy early in the course of disease had a 50% lower risk of developing an impaired glomerular filtration rate (GFR) than patients who received conventional diabetes therapy.

– By Pranav Dalal, Preethi Yerram, Prasad Bichu & Adam Whaley-Connell

Silveiro SP, Araújo GN, Ferreira MN, Souza FD, Yamaguchi HM, Camargo EG. Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation pronouncedly underestimates glomerular filtration rate in Type 2 diabetes. *Diabetes Care* 34, 2353–2355 (2011).

GFR in individuals with or without diabetes has been shown to be an independent predictor of cardiovascular and renal outcomes. Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI), like modification of diet in renal disease (MDRD), is an equation to estimate GFR and there have been recent studies to demonstrate

Future Medicine part of fsg

its performance in diabetic patients. In a cross-sectional study including 105 Type 2 diabetic patients (44% with microalbuminuria and 13% with macroalbuminuria), GFR was measured by Cr-EDTA method and estimated by the MDRD and CKD-EPI equations. Cr-EDTA-measured GFR was 103 ± 23 and estimated CKD-EPI GFR was 83 ± 15, and MDRD-GFR was 78 ± 17 ml/min/1.73m^2 ($p < 0.001$). Accuracy was 67% (58–74) for CKD-EPI and 64% (56–75) for MDRD. Therefore, this study showed that the CKD-EPI equation and MDRD equations may underestimate GFR in Type 2 diabetes patients.

– By Pranav Dalal, Preethi Yerram, Prasad Bichu & Adam Whaley-Connell

Zoppini G, Targher G, Chonchol M *et al.* Serum uric acid levels and incident chronic kidney disease in patients with Type 2 diabetes and preserved kidney function. *Diabetes Care* 35(1), 99–104 (2012).

Recent studies have suggested an association between hyperuricemia and adverse renal outcomes in nondiabetic populations. This study (conducted as a part of the Verona Diabetes Study, an observational longitudinal study) evaluated whether baseline serum uric acid levels predict the subsequent development of chronic kidney disease (CKD) in patients with Type 2 diabetes with preserved kidney function. A total of 1449 Type 2 diabetic patients with normal kidney function and without overt proteinuria were followed for 5 years for the occurrence of incident CKD (defined as overt proteinuria or estimated GFR <60 ml/min/1.73 m^2). During a 5-year follow-up period, the cumulative incidence of CKD was significantly greater in patients with hyperuricemia than in those without hyperuricemia (29.5 vs 11.4%; $p < 0.001$). It was shown that the presence of hyperuricemia roughly doubled the risk of developing CKD ($p < 0.001$). Also, one standard deviation increment in the serum uric acid level was significantly associated with a 21% increased risk of CKD. This may indicate that in Type 2 diabetic individuals with preserved kidney function, hyperuricemia may be an independent risk factor for the development of incident CKD.

– By Pranav Dalal, Preethi Yerram, Prasad Bichu & Adam Whaley-Connell

Joseph AM, Joanisse DR, Baillot RG, Hood DA. Mitochondrial dysregulation in the pathogenesis of diabetes: potential for mitochondrial biogenesis-mediated interventions. *Diabetes Res.* 2012, 642038 (2012).

Muscle mitochondrial metabolism is a tightly controlled process that involves the coordination of signaling pathways and factors from both the nuclear and mitochondrial genomes. Perhaps the most important pathway regulating metabolism in muscle is mitochondrial biogenesis. In response to physiological stimuli such as exercise, retrograde signaling pathways are activated that allow crosstalk between the nucleus and mitochondria, upregulating hundreds of genes and leading to higher mitochondrial content and increased oxidation of substrates. With Type 2 diabetes, these processes can become dysregulated and the ability of the cell to respond to nutrient and energy fluctuations is diminished. This, coupled with reduced mitochondrial content and altered mitochondrial morphology, has been directly linked to the pathogenesis of this disease. In this paper, the authors discuss our current understanding of mitochondrial dysregulation in skeletal muscle as it relates to Type 2 diabetes, placing particular emphasis on the pathways of mitochondrial biogenesis and mitochondrial dynamics, and the therapeutic value of exercise and other interventions.

– By Dominique Hansen

Stafne SN, Salvesen K, Romundstad PR, Eggebø TM, Carlsen SM, Mørkved S. Regular exercise during pregnancy to prevent gestational diabetes: a randomized controlled trial. *Obstet. Gynecol.* 119(1), 29–36 (2012).

The objective was to assess whether exercise during pregnancy can prevent gestational diabetes and improve insulin resistance. A total of 855 women in gestational week 18–22 were randomly assigned to receiving a 12-week standard exercise program (intervention group) or standard antenatal care (control group). The exercise program followed standard recommendations and included moderate-intensity to high-intensity activity 3 or more days per week. Primary outcomes were gestational diabetes and insulin resistance estimated by the homeostasis model assessment method. At 32–36 weeks of gestation there were no differences between groups in prevalence of gestational diabetes: 25 of 375 (7%) in the intervention group compared with 18 of 327 (6%) in the control group ($p = 0.52$). There were no differences in insulin resistance between groups when adjusting for baseline values. Only 55% of women in the intervention group managed to follow the recommended exercise protocol. No serious adverse events related to physical exercise were seen, and the outcomes of pregnancy were similar in the two groups. There was no evidence that offering women a 12-week standard exercise program during the second half of pregnancy prevents gestational diabetes or improves insulin resistance in healthy pregnant women with normal BMIs.

– By Dominique Hansen

Bostrom P, Wu J, Jedrychowski MP *et al.* A PGC-1-a-dependent myokine that drives brown-fat-like development of white fat and thermogenesis. *Nature* 481(7382), 463–468 (2012).

In recent years, brown adipose tissue has been suggested to play a significant role in the protection against obesity and diabetes in rodents and also humans. In this study, a novel myokine named irisin has been demonstrated to function as an important exercise-induced hormone for the induction of brown adipocyte differentiation and thermogenesis in subcutaneous white adipose tissue. Biochemical studies revealed that irisin is a C-terminally-cleaved *FNDC5* gene

product and secreted into the blood circulation at a concentration of ~40 nM in mice. Interestingly, blood levels of irisin were increased by 65 and 100% in 3-week exercised mice and 10-week exercised human subjects, respectively. The pathophysiological significance of irisin was tested in high-fat treated mice by adenovirus-mediated Fndc5 overexpression; and the results showed that increased irisin improved oxygen consumption and glucose tolerance and lowered body weight and fasting plasma insulin levels. Although the way in which irisin regulates white adipose tissue physiology is not quite clear, PPARα was shown to be at least one of the downstream mediators. Based on their findings, the authors suggested that irisin could have a broad implication in therapeutics for obesity, Type 2 diabetes and other diseases that can be improved by exercise.

– By Charlie Dong

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The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

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