

## JOURNAL WATCH

Our 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; Braxton D Mitchell, University of Maryland, MD, USA; Dominique Hansen, Hasselt University, Faculty of Medicine, Belgium

**Wahl P, Xie H, Scialla J *et al.*: Chronic Renal Insufficiency Cohort Study Group. Earlier onset and greater severity of disordered mineral metabolism in diabetic patients with chronic kidney disease. *Diabetes Care* 35(5), 994–1001 (2012).**

Using Chronic Renal Insufficiency Cohort (CRIC) study data, the authors examined the association between diabetic status and disordered mineral metabolism in chronic kidney disease (CKD) patients. Participants with diabetes ( $n = 1820$ ) had lower estimated glomerular filtration rate, a lower serum albumin and higher urinary protein excretion, compared with those without diabetes ( $n = 1936$ ). Diabetic patients also had higher levels of serum phosphate, parathyroid hormone and FGF23, and lower vitamin D levels compared with nondiabetic patients. In addition, hyperphosphatemia, secondary hyperparathyroidism and FGF23 excess occurred earlier in the course of CKD in those with diabetes. The authors concluded that derangements of mineral metabolism begin earlier, and are more severe in diabetic CKD patients than those without. However, these results may not be generalizable, as the CRIC database predominantly represents African-American and Hispanic participants.

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

**Wiseman AC, Gralla J. Simultaneous pancreas kidney transplant versus other kidney transplant options in patients with Type 2 diabetes. *Clin. J. Am. Soc. Nephrol.* 7(4), 656–664 (2012).**

Renal failure patients with Type 2 diabetes may have the option of undergoing simultaneous pancreas–kidney transplantation (SPK), deceased-donor kidney transplantation alone (DDKA) or living-donor kidney transplantation alone (LDKA). Using the Scientific Registry of Transplant Recipients database, the authors compared the outcomes of Type 2 diabetes patients, aged 18–59 years with a BMI of 18–30 kg/m<sup>2</sup>, who underwent SPK ( $n = 424$ ), DDKA ( $n = 4005$ ), or LDKA ( $n = 1987$ ) from 2000 through to 2008. The 5-year patient and graft survival were better with LDKA than SPK. The patient, but not graft, survival was higher for SPK versus DDKA. On multivariate analysis, survival advantage for SPK versus DDKA was related not to pancreas transplantation, but younger donor and recipient ages in the SPK cohort.

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

**Schauer PR, Kashyap SR, Wolski K *et al.* Bariatric surgery versus intensive medical therapy in obese**



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**patients with diabetes. *N. Engl. J. Med.* 366(17), 1567–1576 (2012).**

While observational studies have shown improvements in glycemic control following bariatric surgery, this has yet to be demonstrated in a controlled setting. To address this gap, the authors randomized 150 obese patients with uncontrolled diabetes to receive medical therapy alone versus medical therapy in conjunction with Roux-en-Y gastric bypass or sleeve gastrectomy. After 1 year of follow-up, 12% of patients in the medical therapy alone group achieved the target HbA1c of 6.0%, compared with 42% in the gastric bypass and 37% in the sleeve gastrectomy groups. The two surgery groups further experienced greater weight loss and a greater reduction in the use of glucose, lipid and blood pressure-lowering medications.

– By Braxton D Mitchell

**Biensø RS, Ringholm S, Kiilerich K *et al.* GLUT4 and glycogen synthase are key players in bed rest-induced insulin resistance. *Diabetes* 61(5), 1090–1099 (2012).**

To elucidate the molecular mechanisms behind physical inactivity-induced insulin resistance in skeletal muscle, 12 young, healthy male subjects completed 7 days of bed rest with vastus lateralis muscle biopsies obtained before and after. In six of the subjects, muscle biopsies were taken from both legs before and after a 3-h hyperinsulinemic euglycemic clamp performed 3 h after a 45-min, one-legged exercise. Blood samples were obtained from one femoral artery and both femoral veins before and during the clamp. Glucose infusion rate and leg glucose extraction during the clamp were lower after bed rest than before. This bed rest-induced insulin resistance occurred together with reduced muscle GLUT4, hexokinase II, protein kinase B/Akt1 and Akt2 protein levels, and there was a tendency for reduced 3-hydroxyacyl-CoA dehydrogenase activity. The ability of insulin to phosphorylate Akt and activate glycogen synthase (GS) was reduced with normal GS site 3 but abnormal GS site 2 + 2a phosphorylation after bed rest. Exercise enhanced insulin-stimulated leg glucose extraction both before and after bed rest, which was accompanied by higher GS activity in the prior-exercised leg than the rested leg. The

present findings demonstrate that physical inactivity-induced insulin resistance in the muscle is associated with lower content/activity of key proteins in glucose transport/phosphorylation and storage.

– By Dominique Hansen

**van Dijk JW, Tummers K, Stehouwer CD, Hartgens F, van Loon LJ. Exercise therapy in Type 2 diabetes: is daily exercise required to optimize glycemic control? *Diabetes Care* 35(5), 948–954 (2012).**

Given the transient nature of exercise-induced improvements in insulin sensitivity, it has been speculated that daily exercise is preferred to maximize the benefits of exercise for glycemic control. The current study investigates the impact of daily exercise versus exercise performed every other day on glycemic control in Type 2 diabetic patients. Thirty Type 2 diabetic patients (age:  $60 \pm 1$  years, BMI:  $30.4 \pm 0.7$  kg/m<sup>2</sup> and HbA<sub>1c</sub>  $7.2 \pm 0.2\%$ ) participated in a randomized crossover experiment. Subjects were studied on three occasions for 3 days under strict dietary standardization but otherwise free-living conditions. Blood glucose homeostasis was assessed by continuous glucose monitoring over 48 h during which subjects performed no exercise (control) or 60 min of cycling exercise (50% maximal workload capacity) distributed either as a single session performed every other day or as 30 min of exercise performed daily. The prevalence of hyperglycemia (blood glucose  $>10$  mmol/l) was reduced from  $7:40 \pm 1:00$  h:min per day ( $32 \pm 4\%$  of the time) to  $5:46 \pm 0:58$  and  $5:51 \pm 0:47$  h:min per day, representing  $24 \pm 4$  and  $24 \pm 3\%$  of the time, when exercise was performed either daily or every other day, respectively ( $p < 0.001$  for both treatments). No differences were observed between the impact of daily exercise and exercise performed every other day. A short 30-min session of moderate intensity endurance-type exercise substantially reduces the prevalence of hyperglycemia throughout the subsequent day in Type 2 diabetic patients. When total work is being matched, daily exercise does not further improve daily glycemia compared with exercise performed every other day.

– By Dominique Hansen

**Balducci S, Zanuso S, Cardelli P *et al.*; for the Italian Diabetes Exercise Study (IDES) Investigators. Changes in physical fitness predict improvements in modifiable cardiovascular risk factors independently of body weight loss in subjects with Type 2 diabetes participating in the Italian Diabetes and Exercise Study (IDES). *Diabetes Care* 35(6), 1347–1354 (2012).**

Physical fitness is inversely related to mortality in the general population and in subjects with Type 2 diabetes. Here, the authors present data concerning the relationship between changes in physical fitness and modifiable cardiovascular risk factors in subjects with Type 2 diabetes from the IDES. Sedentary patients with Type 2 diabetes ( $n = 606$ ) were enrolled in 22 outpatient diabetes clinics and randomized to twice-a-week supervised aerobic and resistance training plus exercise counseling versus counseling alone for 12 months. Baseline to end-of-study changes in cardiorespiratory fitness, strength and flexibility, as assessed by  $\text{VO}_{2\text{max}}$  estimation, a 5–8 maximal repetition test and a hip–trunk flexibility test, respectively, were calculated in the whole cohort, and multiple regression analyses were applied to assess the relationship with cardiovascular risk factors. Changes in  $\text{VO}_{2\text{max}}$ , upper and lower body strength,

and flexibility were significantly associated with the variation in the volume of physical activity,  $\text{HbA}_{1c}$ , BMI, waist circumference, high-sensitivity C-reactive protein, coronary heart disease risk score and, inversely, HDL cholesterol. Changes in fitness predicted improvements in  $\text{HbA}_{1c}$ , waist circumference, HDL cholesterol, high-sensitivity C-reactive protein and coronary heart disease risk score, independent of study arm, BMI and, in the case of strength, waist circumference. Physical activity/exercise-induced increases in fitness, particularly muscular, predict improvements in cardiovascular risk factors in subjects with Type 2 diabetes independently of weight loss, thus indicating the need for targeting fitness in these individuals, particularly in subjects who struggle to lose weight.

– By Dominique Hansen

#### **Financial & competing interests disclosure**

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