

the two groups in fasting insulin concentrations, insulin resistance, or height and weight measurements. Multivariate regression analysis showed that blood pressure and fasting glucose levels remained significantly increased in IVF-conceived children after controlling for confounding factors.

The authors suggest that the periconceptual period might contain a critical time window during which cardiometabolic function could be perturbed; they highlight the importance of continued monitoring of the postnatal development of children born after IVF.

Original article Ceelen M *et al.* (2008) Cardiometabolic differences in children born after *in vitro* fertilization: follow-up study. *J Clin Endocrinol Metab* [doi:10.1210/jc.2007-2432]

Diabetes is associated with poor outcomes after bypass surgery

Critical limb ischemia can be treated with vascular bypass surgery, but if ischemia does not resolve, lower-limb amputation might become necessary. In developed countries, the majority of such amputations are performed in patients with diabetes. Whether the outcomes of bypass surgery are less favorable in patients with diabetes than in patients without diabetes is, however, unclear. Malmstedt and colleagues performed a nationwide, population-based cohort study to compare postoperative amputation-free survival in patients with and without diabetes.

The analysis included data for 1,840 patients included in the Swedish Vascular Registry who, during 2001–2003, underwent their first unilateral, below-knee, infrainguinal, distal bypass procedure for critical limb ischemia. Of these patients, 742 had diabetes and 1,098 did not. Patients were followed up until the end of 2005.

By the end of the follow-up period, 446 and 558 patients with and without diabetes, respectively, had undergone ipsilateral amputation or died. Patients with diabetes had a shorter amputation-free survival than patients without diabetes (2.3 years, 95% CI 1.9–2.8 years versus 3.4 years, 95% CI 3.1–3.7 years). The hazard ratio for ipsilateral amputation or death in patients with diabetes—adjusted for age, sex, smoking and other confounding variables—was 1.46 (95% CI 1.26–1.69).

The authors conclude that diabetes is associated with an increased risk of amputation

or death after bypass surgery for leg ischemia. Further study is needed to find methods of reducing this excess risk and prolonging amputation-free survival.

Original article Malmstedt J *et al.* (2008) Outcome after leg bypass surgery for critical limb ischemia is poor in patients with diabetes: a population-based cohort study. *Diabetes Care* [doi:10.2337/dc07-2424]

Novel locus on chromosome 1 involved in LDL cholesterol metabolism

Studies have shown that elevated LDL cholesterol levels increase the risk of cardiovascular disease. Therapeutic strategies that target and control the biological mechanisms and regulation of LDL cholesterol metabolism might, therefore, be beneficial. Sandhu and colleagues performed a genome-wide association study to identify single-nucleotide polymorphisms (SNPs) that are linked to high LDL cholesterol levels.

The analysis included data for 293,461 autosomal SNPs in up to 11,685 patients from five studies; replication studies were also performed in two additional, independent populations to confirm the findings.

Overall, 21 SNPs were significantly associated with circulating LDL cholesterol levels. Most of these SNPs were located near to genetic loci with known involvement in LDL cholesterol metabolism (e.g. *APOB* and *APOE* genes); notably, however, three of the SNPs (rs599839, rs4970834 and rs646776) were located in close proximity to each other in the chromosome region 1p13.3. Linkage disequilibrium plots indicated that rs599839, the SNP with the strongest LDL cholesterol association, is located close to the *CELSR2* and *PSRC1* genes on chromosome 1. Compared with the major alleles, the minor alleles of all three SNPs (frequency 19–21%) were associated with significantly lower levels of LDL cholesterol.

The authors suggest that chromosome region 1p13.3 contains a locus that is related to LDL cholesterol metabolism, and that their findings might be useful for advancing our understanding of the regulation of LDL cholesterol concentrations.

Original article Sandhu MS *et al.* (2008) LDL-cholesterol concentrations: a genome-wide association study. *Lancet* 371: 483–491