

NEWS

Long-term study suggests CT scan could predict early mortality in diabetic patients

Coronary artery calcium score has been identified as an important diagnostic indicator of cardiovascular disease in patients with diabetes.

A new analysis of a 13-year study looking at the predictors of death in diabetic patients, published in *Diabetes Care*, has revealed that a CT scan could potentially be used to identify higher risk individuals. The study analyzed coronary artery calcium scores in 1500 people, demonstrating that this measure could be used to predict early death in patients with diabetes.

“With the incidence and prevalence of diabetes continuing to increase, it is clearly important to continue to analyze and understand all the associated components and risk factors of this complex disease.”

The purpose of this study was to address the varied age of death of diabetic patients, in order to accurately understand the risk factors and associated comorbidities of the disease. Speaking to *Diabetes Management*, Subhashish Agarwal, first author of the paper and a researcher at Center for Diabetes Research at Wake Forest Baptist Medical Center (Winston-Salem, NC, USA),

commented on the importance of the work: “Diabetes is a high risk condition with high CVD events. This study highlights that using a common, non-invasive test can identify a subset of the diabetes population at higher risk for CVD events. Secondly, this study was not about just CVD events such as non-fatal heart attack or stroke, but also all-cause mortality, and it highlights the risk for death in people with diabetes.”

Data for the analysis was gathered from the Diabetes Heart study, from which the researchers measured a wide range of aspects of the disease and how these affected the patients. The analysis demonstrated that patients with a high coronary artery calcium score were more likely to die at a younger age than those with a lower score. Whilst coronary artery calcium scores are associated with coronary heart disease, this study has demonstrated the importance of this measure in patients with diabetes.

The work is a very important step forward in the field of diabetes management, as the study has revealed the need for a greater understanding of cardiovascular risk in diabetes, a sentiment shared by Agarwal: “There is a perception among medical professionals that diabetes is a high risk condition by itself and additional



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tests to evaluate CVD risk will not add further information. We have shown that, within this high risk condition, coronary calcium can predict mortality independent of known traditional risk factors, as well as independent of diabetes duration.”

Whilst analysis of coronary artery calcium scores is relatively inexpensive, requiring a brief CT scan, Agarwal would like to see the work expanded into further studies of diabetes. He claims “We are doing further studies to see if these deaths are primarily driven by cardiovascular disease deaths, as well as if calcification in other vascular beds are as significant. We hope this will spur more research

in this area and in other high risk conditions, more genetic research as to why certain subgroups are afflicted more, better risk stratification strategies, and perhaps insurance coverage for this test. All of this will translate into better patient care and novel therapies.”

With the incidence and prevalence of diabetes continuing to increase, it is important to continue to analyze and understand all the associated components and risk factors of this complex disease.

Source: Agarwal S, Morgan T, Herrington DM *et al.* Coronary calcium score and prediction of all-cause mortality in diabetes: the diabetes heart study. *Diabetes Care* 34(5), 1219–1224 (2011).

Weight gain between pregnancies may be associated with gestational diabetes

A new paper published in *Obstetrics and Gynecology* has revealed an association between interpregnancy BMI changes and gestational diabetes. The team behind the project performed a retrospective cohort study analyzing BMI changes between the pregnancies of 22,351 women.

The results suggest that increasing weight between pregnancies can increase the risk of gestational diabetes, whilst a decrease in weight can reduce this risk.

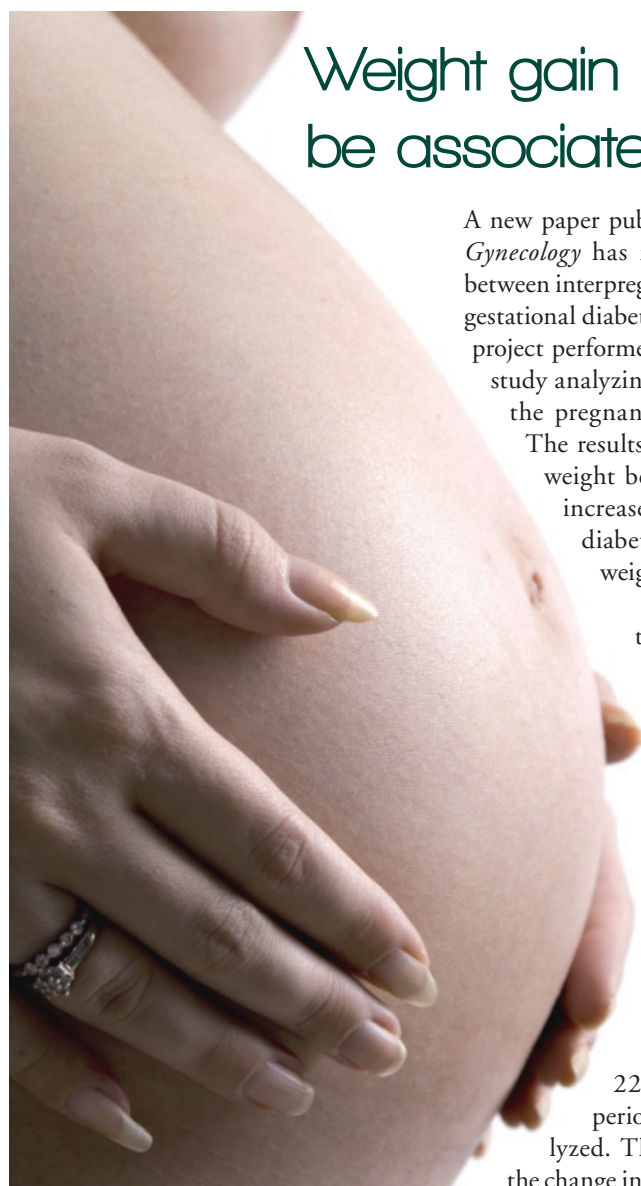
Gestational diabetes is the occurrence of diabetes in a pregnant mother who has had no previous diagnosis of diabetes. Although numerous risk factors for the occurrence of the disease have been found, this study is the first to identify an association between interpregnancy BMI changes and its incidence.

In the study, data from 22,351 patients from a period of 10 years were analyzed. The researchers measured the change in BMI of each patient over

the course of the study and the incidence of gestational diabetes. The results indicate that a rise of 2–3 units on the BMI scale in a patient was associated with a twice as likely risk of gestational diabetes compared with an individual with a constant BMI. An increase of 3 or more units in the BMI scale was associated with patients being three-times as likely to develop gestational diabetes. By contrast, a loss of 2 BMI units in overweight women resulted in a decrease in likelihood, with patients reducing their chance of gestational diabetes by 50%.

The first author of the paper, Samantha Ehrlich, Project Manager at the Kaiser Permanente Division of Research (Oakland, CA, USA) commented on the future prospects and impact of the study: “Taken together, the results support the avoidance of gestational weight retention and postpartum weight gain to decrease the risk of GDM in a second pregnancy, as well as the promotion of postpartum weight loss in overweight or obese women, particularly those with a history of GDM.”

Source: Ehrlich SF, Hedderson MM, Feng J, Davenport ER, Gunderson EP, Ferrara A. Change in body mass index between pregnancies and the risk of gestational diabetes in a second pregnancy. *Obstet. Gynecol.* 117(6), 1323–1330 (2011).





Large study suggests a link between sleep disorders and diabetes

A paper published in *Diabetes Care* has examined in detail the link between sleep and diabetes. The investigation utilized activity monitors to assess the quality of sleep in diabetic patients over 6 nights. Although there have been numerous studies looking into diabetes, few have investigated the potential relationship between sleep disorders and the disease.

Although some studies have demonstrated a decrease in the quality of sleep in patients with diabetes, this study has looked in greater detail at the biological basis and interactions found in sleep disturbances and diabetes.

In a statement to *Diabetes Management*, Kristen Knutson, Assistant Professor of Medicine at the Department of Medicine, University of Chicago (Chicago, IL, USA) and first author of the study said “Our study examined whether sleep duration and/or quality was associated with fasting glucose levels, fasting insulin levels or estimated insulin resistance (HOMA). We found that among persons with diabetes, those with poor quality sleep or insomnia had higher glucose levels, insulin levels and insulin resistance compared

with people with diabetes who did not have poor sleep quality or insomnia. Thus, the effects of impaired sleep in people with diabetes need to be examined in greater detail.”

“If ameliorating sleep does indeed help improve glucose levels, then in the future, clinical sleep studies and treatment may become an important part of diabetes management.”

Using activity monitors to measure movement during sleep (and thus quality of sleep, as movement suggests disturbed sleep) the researchers observed 40 subjects. Insulin and blood glucose levels were analyzed during clinical examinations as a quantitative measure for the investigation. The results demonstrated that diabetic patients with poorer sleep had a 48% higher blood glucose level than corresponding diabetic patients with better sleep, and these poor sleepers had 82%

higher insulin resistance than normal sleeping diabetic patients.

Knutson believes that this investigation is an important step forward in understanding diabetes and sleep disorders, but confirms that further research is required to fully understand this interaction: “The role of sleep in Type 2 diabetes needs to be examined in greater detail. For example, intervention studies that test whether improving sleep, including extending bedtimes or treating sleep disorders like insomnia or obstructive sleep apnea, can help improve glucose metabolism in people with diabetes need to be conducted. If ameliorating sleep does indeed help improve glucose levels, then in the future, clinical sleep studies and treatment may become an important part of diabetes management.”

Source: Knutson KL, Van Cauter E, Zee P, Liu K, Lauderdale DS. Cross-sectional associations between measures of sleep and markers of glucose metabolism among subjects with and without diabetes: the Coronary Artery Risk Development in Young Adults (CARDIA) sleep study. *Diabetes Care* 34(5), 1171–1176 (2011).

New genetic study indicates that there might be a 'master regulator gene' for diabetes

A new study published in *Nature Genetics* has revealed the potential existence of a regulator gene, linked to diabetes and cholesterol. In the investigation, overseen by the senior author Mark McCarthy, researcher at the University of Oxford (Oxford, UK), the multinational collaborative research project performed a genome association study to further reveal the genetic component of diabetes.

Diabetes can be classified as a metabolic disease, and has significant associations with body weight

and fat profiles in patients. The researchers found that the gene *KLF14* (previously demonstrated to be associated with the incidence of diabetes) was responsible for the control of numerous other genes that have previously been linked with diabetes.

The study was a large collaborative effort between numerous research centers and is referred to as the MuTHER study. The investigation involved the examination of 20,000 genes in the subcutaneous fat of 800 female twins. The results revealed the association of *KLF14* with numerous diabetes genes, with diverse profiles of expression around the body in different fatty areas. These genes, now believed to be controlled by *KLF14*, have been demonstrated to be involved in numerous facets of metabolic regulation, including glucose and insulin levels.

Furthermore, it was found that this *KLF14* gene was passed via the maternal side, as the corresponding gene from the paternal side is silenced.

Therefore, the control of numerous aspects of metabolism is completely dependent upon the maternal *KLF14* gene.

When talking about the future prospects of the work, McCarthy claimed "KLF14 seems to act as a master switch controlling processes that connect changes in the behaviour of subcutaneous fat to disturbances in muscle and liver that contribute to diabetes and other conditions. We are working hard right now to understand these processes and how we can use this information to improve treatment of these conditions".

Through the continued research and collaboration between institutions, the overall goal is to continue to elucidate the numerous genetic components of diabetes. This research is an important step in piecing together how these genes interact with one another, potentially leading to a better understanding of diabetes and its associated metabolic problems.

Source: Small KS, Grundberg E, Nica AC *et al.* Identification of an imprinted master regulator at the *KLF14* locus related to multiple metabolic phenotypes. *Nat. Genet.* 43(6), 561-564 (2011).