Cardiovascular disease

Standing more and sitting less may benefit cardiometabolic health

Spending less time sitting and more time standing, stepping, or both, improves markers of cardiometabolic health, a study from Australia has shown.

The researchers studied participants from the 2011/12 Australian Diabetes, Obesity, and Lifestyle Study who wore the posture-based activPAL3 monitor. This activity monitor has been shown to be highly accurate and directly measures posture from the thigh position. There were 698 adults in this subsample aged 36-80 years (mean 57.9) of which 57% were women.

Using data collected from postural sensors the authors modelled cross-sectional associations with cardiometabolic risk biomarkers of reallocating time (2h/day) from sitting to standing or to stepping.

Association of activPAL3 derived mean daily time sitting, standing and stepping with the following parameters was examined: BMI, waist circumference, BP, HbA_{1c}, fasting glucose and lipids (HDL cholesterol, LDL cholesterol, total:HDL cholesterol ratio, and triglycerides), and 2-hour plasma glucose.

After adjusting for confounding factors, each 2h/day sitting to standing reallocation was significantly associated with:

- 2% lower fasting plasma glucose
- 11% lower triglycerides
- 6% lower total:HDL cholesterol ratio
- 0.06 mmol/L higher HDL cholesterol

Each 2 h/day sitting to stepping reallocation was significantly associated with:

- 11% lower BMI
- 7.5 cm smaller waist circumference
- 11% lower 2-h plasma glucose
- 14% lower triglycerides
- 0.10 mmol/L higher HDL cholesterol

Standing to stepping reallocations were significantly associated with:

- 10% lower BMI
- 7 cm smaller waist circumference
- 11% lower 2-h plasma glucose

The healthy lifestyle message is generally well understood and our patients know that they should avoid smoking, exercise frequently and eat healthily. However, our lives are increasingly sedentary and perhaps the risk of excessive sitting time is less well documented.

The authors conclude that sitting reduction strategies targeting increased standing, stepping, or both, may benefit cardiometabolic health. Standing is a feasible alternative to sitting and they feel this warrants further examination in prospective and intervention studies.

This is a simple message and should encourage us all to get out of our chairs more even if just to stand while making that phone call.

DR PETER SAVILL

● **Healy GN, Winkler EAH, Owen N et al. Replacing sitting time with standing or stepping: associations with cardio-metabolic risk biomarkers. *Eur Heart J.* DOI: http://dx.doi.org/10.1093/eurheartj/ehv308**

Diabetes

Low birthweight combined with unhealthy lifestyle boosts diabetes risk

A recently published study in the *BMJ* has supported a synergistic effect between low birthweight and poor lifestyle on the risk of developing type 2 diabetes in adults.

The study used pooled data from three continuing long-term prospective cohort studies that had gathered data on health and lifestyle. The Health Professionals Follow-Up Study, the Nurses' Health Study and Nurses' Health Study II were started in 1986, 1980 and 1991 respectively. Participants completed a food frequency questionnaire at the beginning of each study that was used as a baseline for this study. The food frequency questionnaires were repeated at approximately four-year intervals.

The study was concerned with adult modifiable lifestyle habits on type 2 diabetes, so the scoring for risk did not include raised blood pressure, or adverse lipid profiles. The five factors selected were: diet, body mass index, physical activity, smoking, and alcohol consumption. Patients were scored 0 or 1 according to absence or presence of the risk factor.

New incident cases of diabetes were obtained by self-reporting, validated on a supplementary questionnaire. This methodology has been shown to be accurate. Birthweight was also based on self-reporting at the commencement of the studies.

Self-reporting of birthweight is not quite as accurate as the self-reporting of diabetes, but the average error margin was known and adjustments could be made.

In total the pooled studies gave 149,794 participants who were free of cardiovascular disease, cancer or diabetes at entry to the study, and with no missing data on lifestyle.

For each of the three cohorts the participants were divided into categories according to birthweight. Prevalence of the lifestyle variables was similar across each weight category in all three cohorts.

In the 20-30 years of follow-up, 11,709 new cases of diabetes were documented.

The authors found a consistent association between low birthweight and risk of type 2 diabetes in all three cohorts. After adjustment for current BMI, the relative risk for those with the lowest birthweight (< 2.5 kg) compared with those in the middle birthweight category (3.18-3.82 kg) was 1.55 (95% CI:1.46-1.64).

After adjusting for confounding variables, the results showed a consistent relationship between each unhealthy risk factor and the risk of developing diabetes, which was again

consistent across all three cohorts.

For patients with unhealthy lifestyle scores and low birthweight, the risk of developing new type 2 diabetes was increased by more than the simple sum of the two individual risk factors.

Across the cohorts studied, the new cases of type 2 diabetes could be attributed as follows:

- Low birthweight alone 22% (95% CI: 18.3-26.4%)
- Poor lifestyle alone 59% (95% CI: 57.1-61.5%)
- Additive interaction between low birthweight and unhealthy lifestyle 18% (95% CI: 13.9-21.3%)

Low birthweight is a surrogate for intrauterine stress, which is known to produce hyperglycaemia and increase the risk of diabetes. Poor lifestyle, especially obesity, an unhealthy diet and lack of exercise, is already strongly linked to the current high incidence of type 2 diabetes. This study shows that a combination of the two increases the risk by more than the addition of the risks associated with each individual factor.

The authors conclude: 'The finding suggests that most cases of type 2 diabetes could be prevented by the adoption of a healthier lifestyle, but simultaneous improvement of both prenatal and postnatal factors could further prevent additional cases.'

This is another brick in the wall of evidence that change at population level is needed to stem the current flood of new diabetes cases that underlie the statistics.

DR MATTHEW LOCKYER

- **Li Y, Ley SH, Tobias DK et al. Birth weight and later life adherence to unhealthy lifestyles in predicting type 2 diabetes: prospective cohort study. *BMJ* 2015;351:h3673**

Addiction

Arrhythmia risk higher with methadone than buprenorphine

Buprenorphine appears to be a safer option to methadone in terms of reduced risk of ventricular arrhythmia and sudden death from cardiac arrest, a study from the United States has shown.

The authors used pharmacovigilance data routinely submitted to the US Food and Drug Administration between 1969 and 2011 to analyse methadone- and buprenorphine-related adverse events.

The primary outcome was the composite of ventricular arrhythmia and cardiac arrest, and the secondary outcome the composite of QTc prolongation and torsade de pointes. The proportional reporting ratio (PRR) was used to identify disproportionate reporting.

A total of 4,418,215 cases were evaluated, of which 7,283 involved buprenorphine and 14,915 methadone. There were 132 (1.8%) cases of ventricular arrhythmia/cardiac arrest and 19 (0.3%) cases of QTc prolongation/torsade de pointes associated with buprenorphine prescribing compared with 1,729 (11.6%) cases of ventricular arrhythmia/cardiac arrest and 390 (2.6%) cases of QTc prolongation/torsade de pointes involving methadone prescribing.

PRR for buprenorphine was not significant for ventricular arrhythmia/cardiac arrest, 1.10 (95% CI: 0.93-1.31) or QTc prolongation/torsade de pointes, 1.03 (95% CI: 0.66-1.62) but was for methadone 7.20 (95% CI: 6.88-7.52) and 10.7 (95% CI: 9.66-11.8) respectively.

When choosing between the two drugs, the prescribing physician will balance the benefits associated with each (methadone has a cost advantage and is associated with better engagement in treatment for example) against potential problems, including the risk of adverse effects.

In the UK, as in the Unites States, there are only two opioid medications licensed for the management of opioid dependence – methadone and buprenorphine. Both are known to have the potential to delay cardiac repolarisation causing prolongation of the QTc interval, and predisposing to the potentially fatal arrhythmia torsade de pointes.

However, in vitro data suggest that the impact of buprenorphine in this area is relatively small, and there is some epidemiological evidence to suggest that buprenorphine prescribing is associated with a lower risk of sudden death than methadone.

As a result buprenorphine has been recommended as a safer alternative to methadone in patients at risk of QTc prolongation. Despite this, one recent study has suggested that some patients treated with high-dose transdermal buprenorphine may develop significant QTc prolongation.

Acknowledging the limitations necessarily associated with data from voluntary reporting, and the differing timelines for marketing approval for the two drugs and relative prescribing volumes, the authors of this study conclude that, pending direct safety-related research, buprenorphine appears to be a safer option to methadone in terms of reduced risk of ventricular arrhythmia and sudden death from cardiac arrest.

DR JEZ THOMPSON

- **Kao DP, Haigney MCP, Mehler PS et al. Arrhythmia associated with buprenorphine and methadone reported to the food and drug administration. *Addiction* 2015;110:1468-75**

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