Coronary artery calcium score prediction of all cause mortality and cardiovascular events in people with type 2 diabetes: systematic review and meta-analysis

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STUDY QUESTION

What is the association of coronary artery calcium (CAC) score with all cause mortality and cardiovascular events (fatal and non-fatal) in people with type 2 diabetes?

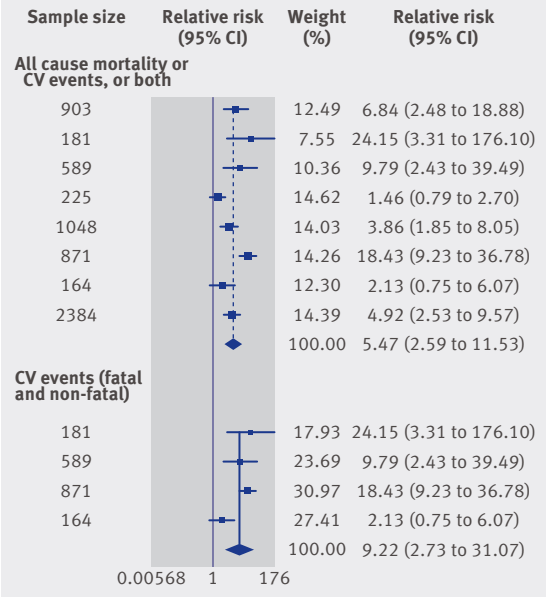
SUMMARY ANSWER

In people with type 2 diabetes a CAC score of ≥10 predicted all cause mortality or cardiovascular events, or both, with high sensitivity but low specificity. The negative likelihood ratio of a CAC score for these outcomes was low, at 0.18; people with a score of <10 were 6.8 times less likely to have an event.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

In this study of people with type 2 diabetes, a CAC score of ≥10 compared with <10 predicted all cause mortality or cardiovascular events, or both, with high sensitivity but low specificity, as it does in the general population. For people with type 2 diabetes with a CAC score of <10, however, the post-test probability of all cause mortality or cardiovascular events, or both was reduced by 6.8-fold from the pretest probability.

Meta-analyses of association between coronary artery calcium score ≥10 and outcome in people with type 2 diabetes CV=cardiovascular (both fatal and non-fatal events)



Selection criteria for studies

Studies were identified from Embase, PubMed, and abstracts from the 2011 and 2012 annual meetings of the American Diabetes Association, European Association for the Study of Diabetes, American College of Cardiology, and American Heart Association (2011). We included prospective studies that evaluated baseline CAC score in people with type 2 diabetes and subsequent all cause mortality or cardiovascular events (fatal and non-fatal), or both. Two independent reviewers extracted the data. A random effects model was used to assess the predictive value of the CAC score.

Primary outcome

Incidence of all cause mortality or cardiovascular events, or both.

Main results and role of chance

Eight studies were included (n=6521; 802 events; mean follow-up 5.18 years). The relative risk for all cause mortality or cardiovascular events, or both comparing a total CAC score of ≥10 with a score <10 was 5.47 (95% confidence interval 2.59 to 11.53; I^2=82.4%, P<0.001). The overall sensitivity of a total CAC score of ≥10 for this composite outcome was 94%, with specificity 34%. The positive and negative likelihood ratios were 1.41 (95% confidence interval 1.20 to 1.66) and 0.18 (0.10 to 0.30), respectively. For people with a CAC score of <10, the post-test probability of the composite outcome was about 1.8%, representing a 6.8-fold reduction from the pretest probability.

Bias, confounding, and other reasons for caution

The question remains whether using the CAC score test can affect the incidence of events. Randomised controlled trials evaluating the impact of using the CAC score for screening on mortality are needed.

Study funding/potential competing interests

This study was supported by intramural funds from the Leadership Sinai Centre for Diabetes. BZ has served as a consultant for Merck, Boehringer Ingelheim, Novo Nordisk, and Eli Lilly, received grants from Merck, Boehringer Ingelheim, and Novo Nordisk, and received payment for lectures for Merck and Novo Nordisk; JLG has served on boards for Bristol-Myers Squibb, GlaxoSmithKline, Novo Nordisk, Sanofi-Aventis, and Eli Lilly, and has received payment for the development of educational presentations for Bristol-Myers Squibb, Novo Nordisk, and Eli Lilly; LHC has served on a board for Janssen Cilag; RR has served as a consultant for Merck and Novo Nordisk, received grants from Merck and Novo Nordisk, and received payment for lectures for Eli Lilly; no other relationships or activities that could appear to have influenced the submitted work.

Effect of behavioural-educational intervention on sleep for primiparous women and their infants in early postpartum: multisite randomised controlled trial

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STUDY QUESTION

Does a behavioural-educational sleep intervention in the early postpartum have any effect on sleep in the mother and baby at six and 12 weeks after birth?

SUMMARY ANSWER

A nurse delivered behavioural-educational sleep intervention had no effect on maternal and infant sleep or other important health outcomes in the early postpartum. While the women allocated to the sleep intervention group valued receiving information about sleep and reported using many of the suggested strategies, there were no differences in the main outcomes between groups.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

Maternal sleep disturbance is common in the postpartum period, with primiparous women particularly affected. In trials of behavioural interventions to increase infant sleep parents have reported an increase in infant sleep and fewer infant awakenings. The current study, however, showed that a behavioural-educational intervention delivered in the early postpartum in hospital and in the first weeks at home was ineffective in improving maternal and infant sleep in the first months postpartum.

Design

Randomisation was centrally controlled, concealed, in random blocks of four and six, and stratified by centre with a secure web based randomisation service. Women randomised to the sleep intervention group received a 45-60 minute meeting with a nurse to discuss sleep information and strategies to promote maternal and infant sleep, a 20 page booklet with the content discussed, and phone contacts at one, two, and four weeks postpartum to reinforce information, provide support, and problem solve. The usual care group received phone calls at weeks one, two, and four to maintain contact without provision of advice.

Models for outcomes (sleep intervention minus usual care) related to sleep, postpartum depression, and breast feeding

	Difference/rate ratio (95% CI)	Standard error, P value
Nocturnal sleep, maternal	5.97* (−7.55 to 19.49)	6.90, 0.39
Longest stretch of nocturnal sleep, infant	−0.18*(−16.13 to 15.76)	8.13, 0.98
EPDS score	0.21* (−0.62 to 1.04)	0.42, 0.62
Night awakenings, maternal	−0.012† (−0.12 to 0.10)	0.056, 0.83
Night awakenings, infant	0.036† (−0.043 to 0.12)	0.040, 0.37

EPDS=Edinburgh postnatal depression scale.
*Mean difference.
†Log rate ratio.

Participants and setting

246 primiparous women and their healthy term infants were randomised in the postpartum units of two university affiliated hospitals in Toronto, Canada.

Primary outcomes

Maternal nocturnal (9 pm to 9 am) sleep (in minutes) at six and 12 weeks postpartum, as measured by actigraphy, an objective measure of sleep.

Main results and the role of chance

Longitudinal mixed effects model analyses indicated no significant differences between groups on any of the outcomes. The estimated mean difference in maternal nocturnal sleep between the sleep intervention and usual care groups was 5.97 minutes (95% confidence interval −7.55 to 19.49 minutes, P=0.39).

Harms

No harms associated with the intervention were reported.

Bias, confounding, and other reasons for caution

We used actigraphy to objectively measure both maternal and infant sleep, thereby avoiding bias introduced by parents' reports and knowledge of group assignment. Research assistants who analysed objective sleep data were blinded to group assignment.

Generalisability to other populations

Although our sample was racially diverse, participants were predominantly socially advantaged, thereby limiting generalisability. Baseline rates of postpartum depression were lower and rates of social support and exclusive breast feeding higher than in the general population (at 12 weeks, 71/103 (69%) in the intervention group and 66/100 (66%) in the usual care group were exclusively breast feeding). We did not preferentially enrol new mothers deemed at high risk of sleep difficulties as we viewed the intervention as a means to prevent sleep problems in a population in which sleep disturbance was to be expected.

Study funding/potential competing interests

This work was funded by a Canadian Institutes of Health Research grant (No MCT 84658). This trial was conducted and data analysed with complete independence of the researchers from the Canadian Institutes of Health Research. RS is a recipient of a Canadian Institutes of Health Research new investigator award and an Ontario Ministry of Research and Innovation early researcher award.

Trial registration ISRCT No 13501166

Effect of routine controlled cord traction as part of the active management of the third stage of labour on postpartum haemorrhage: multicentre randomised controlled trial (TRACOR)

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STUDY QUESTION

What is the impact of controlled cord traction on the incidence of postpartum haemorrhage in a high resource setting?

SUMMARY ANSWER

Controlled cord traction for the management of placental expulsion had no significant effect on the incidence of postpartum haemorrhage and other markers of postpartum blood loss.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

The management of third stage of labour without controlled cord traction does not increase the risk of severe postpartum haemorrhage in low and middle income countries. The use of controlled cord traction in a high resource setting had no significant effect on the incidence of postpartum haemorrhage and other markers of postpartum blood loss.

Design

This was a randomised controlled trial with block randomisation and computer generated allocation. 2175 women were randomly assigned to third stage of labour managed by controlled cord traction and 2180 to standard placenta expulsion (awaiting spontaneous placental separation before facilitating expulsion). In the two arms prophylactic oxytocin was administered and the cord clamped and cut within two minutes after birth.

Participants and setting

This trial took place in five French university hospital maternity units. Participants were women aged 18 or more with a singleton fetus at a gestational age of 35 or more weeks and a planned vaginal delivery.

Primary outcome

The primary outcome was the incidence of postpartum haemorrhage ≥500 mL as measured in a collector bag.

Main results and the role of chance

The incidence of postpartum haemorrhage did not differ between the controlled cord traction arm (9.8%, 196/2005) and standard placenta expulsion arm (10.3%, 206/2008): relative risk 0.95 (95% confidence interval 0.79 to 1.15). There was no significant difference in the mean peripartum change in haemoglobin and haematocrit values. The need for manual removal of the placenta was significantly less frequent in the controlled cord traction arm (4.2%, 85/2033) compared with the standard placenta expulsion arm (6.1%, 123/2024): relative risk 0.69, 0.53 to 0.90); as was third stage of labour of more than 15 minutes (4.5%, 91/2030 and 14.3%, 289/2020, respectively): relative risk 0.31, 0.25 to 0.39. Women in the controlled cord traction arm reported a significantly lower intensity of pain and discomfort during the third stage than those in the standard placenta expulsion arm.

Harms

No uterine inversion occurred in either arm.

Bias, confounding, and other reasons for caution

The study was not blinded, therefore we cannot exclude a patient preference bias for secondary outcomes related to the women' experience of the third stage of labour.

Generalisability to other populations

Exclusion criteria were few and women enrolled were comparable to the general population of parturient women in most high resource countries. In consequence, the results are generalisable to women having vaginal delivery in high resource settings.

Study funding/potential competing interests

The TRACOR trial was funded by the French Ministry of Health under its clinical research hospital programme (contract No P081206).

Trial registration number

ClinicalTrials.gov NCT01044082.

Trial outcomes. Values are number with outcome/number in group (percentage) unless stated otherwise

Outcomes	Controlled cord traction	Standard placenta expulsion	Relative risk (95% CI)	Mean difference (95% CI)
Blood loss ≥500 mL	196/2005 (9.8)	206/2008 (10.3)	0.95 (0.79 to 1.15)	—
Blood loss ≥1000 mL	34/2005 (1.7)	37/2008 (1.8)	0.92 (0.58 to 1.46)	—
Mean (SD) peripartum change in haemoglobin (g/L)	8.6 (0.3) (n=1961)	8.7 (0.3) (n=1953)	—	−0.2 (−1.0 to 0.7)
Mean (SD) peripartum change in haematocrit (%)	2.1 (0.1) (n=1904)	2.2 (0.1) (n=1890)	—	−0.05 (−0.29 to 0.19)
Third stage ≥15 min	91/2030 (4.5)	289/2020 (14.3)	0.31 (0.25 to 0.39)	—
Manual removal of placenta	85/2033 (4.2)	123/2024 (6.1)	0.69 (0.53 to 0.90)	—
Maternal pain during third stage	109/1892 (5.8)	138/1868 (7.4)	0.78 (0.61 to 0.99)	—

One year outcomes in patients with acute lung injury randomised to initial trophic or full enteral feeding: prospective follow-up of EDEN randomised trial

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STUDY QUESTION

Does initial low energy permissive underfeeding ("trophic feeding") compared with full calorie enteral feeding ("full feeding") in the intensive care unit affect physical function and other physical, psychological, and cognitive outcomes in patients with acute lung injury?

SUMMARY ANSWER

There was no difference between the two feeding regimens in physical function, survival, or multiple secondary physical, psychological, and cognitive outcomes at six and 12 month follow-up.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

A previous trial had shown that initial trophic feeding compared with full feeding had no effect on short term mortality and days without ventilator use. This follow-up study from the trial showed that there was substantial physical, psychological, and cognitive impairment, reduced quality of life, and impaired return to work in both feeding groups, and that the initial type of feeding did not affect outcomes up to 12 months later.

Design

This study is a prospective longitudinal follow-up evaluation of the EDEN trial, in which patients were randomised to trophic or full enteral feeding for up to six days; thereafter, all patients still requiring mechanical ventilation received full feeding. As part of the EDEN protocol, both groups received evidence based treatment with low tidal volume ventilation and fluid conservative haemodynamic management. Follow-up assessments occurred at six and 12 months after acute lung injury.

Participants and setting

Participants were 525 patients from 41 hospitals in the United States who had survived acute lung injury and were free from cognitive impairments before admission to hospital. The average age was 52 (SD 16) years and 49% were women. More than 80% were previously living independently without assistance. Follow-up visits occurred from April 2008 to April 2012.

Selected outcomes in patients with acute lung injury at 12 month follow-up

Outcome measure	Result
Mean (SD) SF-36 physical function domain score* (norm 82, SD 9)	55 (32)
Mean (SD) SF-36 mental health domain score* (norm 76, SD 3)	65 (25)
Mean (SD) EQ-5D visual analogue scale score*	69 (22)
Cognitive impairment	21%
Clinically important symptoms of:	
Fatigue	67%
Anxiety	42%
Depression	37%
Post-traumatic stress disorder	23%

* Score ranges from 0 to 100, with higher score indicating better quality of life.

Primary outcome

The primary outcome was the physical function domain score of SF-36, adjusted for age and sex.

Main results and the role of chance

Of all eligible patients, this study had 95% cohort retention rate at 12 month follow-up and minimal missing data for each survey instrument evaluated. Despite some improvement between six and 12 months, at 12 month follow-up, survivors still commonly had substantial impairments, including an overall rating of "some difficulty" on functional activity assessment, 56% requiring either institutionalisation or outpatient physiotherapy, and 48% of previously employed patients not working, primarily citing health related reasons for their unemployment. The initial method of feeding (trophic versus full) did not affect mean 12 month physical function (55 (SD 33) *v* 55 (SD 31), P=0.539) or survival through 12 months (65% *v* 63%, P=0.632). There was also no difference between the feeding groups for most secondary outcomes. The treatment effect at six compared with 12 month follow-up did not significantly differ across the primary outcome and almost all secondary outcomes.

Harms

There were no differences in mortality or in a comprehensive range of physical, psychological, and cognitive outcome measures at six and 12 month follow-up between the two feeding groups.

Bias, confounding, and other reasons for caution

The EDEN trial had an open label design. In this follow-up study, however, outcome assessors and investigators were blinded to randomised treatment allocation.

Generalisability to other populations

The EDEN trial excluded malnourished patients. The most common risk factor for acute lung injury was pneumonia or non-pulmonary sepsis. The patients evaluated were relatively young and overweight (mean BMI 30, SD 8). Generalisability to older, malnourished, or critically ill patients without infection might be limited.

Study funding/potential competing interests

The National Heart, Lung and Blood Institute funded this study (N01HR56170, R01HL091760 and 3R01HL091760-02S1) and the EDEN trial (contracts HHSN268200536165C to HHSN268200536176C and HHSN268200536179C).

Trial registration number

NCT No 00719446.