

**Impact of birthweight on macrovascular complications in type 2 diabetes: a cohort study**

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**Background and aims:** Low birthweight (BW) is a risk factor for type 2 diabetes (T2D) and has been associated with severer clinical presentation at disease onset, including markedly lower age at onset, less obesity, less family history of diabetes, and a higher prevalence of comorbidities. It is, unknown if lower BW increases risk of incident macrovascular complications and mortality after T2D diagnosis.

**Materials and methods:** Midwife records were traced for 6920 recently diagnosed patients (median age 62 years) in the Danish Center for Strategic Research in T2D cohort. Participants were enrolled starting in 2010 and followed for first occurrence of a composite endpoint of major cardiovascular disease (CVD) (myocardial infarction, coronary revascularization, unstable angina, stroke, heart failure, peripheral revascularization, or cardiovascular death) and for all-cause mortality, using linkage to electronic health records available up to 2018. Adjusted hazard ratios (aHRs) were calculated comparing the lowest 25% of BW (<3000g) and highest 25% of BW (>3700g), with BW of 3000-3700g as reference. Adjusted cumulative incidence curves with 3- and 5-year risks were estimated using G-computation with cause-specific Cox regression, accounting for the competing risk of non-cardiovascular death. Analyses were adjusted for sex, year of birth, family history of T2D, born-at-term, and lifestyle (smoking, alcohol, and physical activity).

**Results:** A total of 585 CVD events were recorded with median follow-up of 4.6 years. Compared to participants with a BW of 3000-3700g, a BW <3000g yielded a 5-year cumulative CVD incidence of 9.8% (95% CI, 7.9-11.6) (n=126 events) vs 9.1% (95% CI, 8.0-10.1) (n=292 events) corresponding to an aHR of 1.08 (95% CI, 0.85-1.38). The slight risk increase was driven primarily by peripheral revascularization; aHR = 1.55 (95% CI, 0.74-3.22) and cardiovascular death; aHR = 1.56 (95% CI, 0.85-2.85). Participants with BW >3700g had a 5-year cumulative incidence of 9.4% (95% CI, 8.0-10.8) (n=167 events), corresponding to an aHR of 1.04 (95% CI, 0.86-1.26) compared to those with BW 3000-3700g, with a tendency towards higher risk of heart failure; aHR = 1.28 (95% CI, 0.86-1.91). For all-cause mortality, participants with a BW <3000g and BW 3000-3700 g had similar 5-year cumulative incidences of 5.9% (95% CI, 4.5-7.3) vs 5.7% (95% CI, 4.9-6.5) corresponding to an aHR of 1.04 (95% CI, 0.77-1.41). Those with BW >3700g had a 5-year cumulative incidence of 5.4% (95% CI, 4.4-6.5) and an aHR of 0.95 (95% CI, 0.75-1.21).

**Conclusion:** A BW <3000g compared with a BW of 3000-3700g was associated with a slightly and statistically imprecisely higher 5-year risk of CVD. We observed 50-60% higher hazards of peripheral revascularization and cardiovascular death associated with BW <3000 g, but the estimates lacked statistical precision. All-cause mortality was similar across BW categories. Follow-up data through 2022 will be presented at EASD 2023.

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