

## Title: Hyperglycaemia and antidiabetic medication as prognostic factors in ovarian cancer

### Authors:

*Tiina Jääntti (MD), Synnöve Staff (MD, PhD, associate prof.), Aino Siltari (PhD), Teemu Murtola (MD, PhD, prof.).*

### Keywords:

cancer, epidemiology, clinical medicine, diabetes, hyperglycaemia

### Abstract

Ovarian cancer (OC) is the second most common gynaecological cancer, with a poor prognosis. Diabetes and antidiabetic medications may influence the prognosis of OC. High-quality, population level studies on the relationship between medication use and OC prognosis are needed.

The aim of this study is to clarify the association between antidiabetic medication use, hyperglycaemia and OC prognosis.

The study population consisted of all new OC cases diagnosed in Finland in 1995–2020 (N=14 000). Cohort follow-up continued until 31.12.2020. The association of hyperglycaemia and antidiabetic medication use with OC mortality was evaluated with Cox regression model. We separately analysed different groups of antidiabetic medication use and glycaemic status before and after OC diagnosis.

In multivariate analyses, metformin use before OC diagnosis was associated with elevated risk of OC death (HR 1.21, 95% CI 1.08–1.35). No risk elevation was observed for post-diagnostic metformin use. Insulin use was associated with increased risk of OC death both for pre-diagnosis use (HR 1.24, 95% CI 1.06–1.44) and post-diagnosis use (HR 1.39, 95 % CI 1.23–1.54). Both pre-diagnostic (HR 0.63, 95 % CI 0.47–0.84) and post-diagnostic (HR 0.63, 95 % CI 0.43–0.93) use of thiazolidinediones was associated with lowered risk of OC death. Elevated fasting glucose both before and after OC diagnosis as well as elevated post-diagnostic HbA1c level were associated with higher OC and overall mortality.

Hyperglycaemia appears to be a poor prognostic factor in OC, whereas some antidiabetic drug groups, especially thiazolidinediones, may have a beneficial effect on OC prognosis. Further research into mechanisms behind these risk associations is required.