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Association between age at natural menopause and risk of type 2 diabetes

Menopause in women marks the loss of ovarian follicle development and the timing of the final menstrual period. The timing of menopause differs significantly among women and is seen as a marker of aging and cardiovascular health. Studies have shown a link between early onset of menopause and an increased risk of cardiovascular disease (CVD) and overall mortality, whereas menopause at age 50 to 54 years is linked to a decrease in CVD risk and mortality. The influence of age at menopause on levels of cardiovascular risk factors remains unclear. Type 2 diabetes is a major risk factor for CVD, yet no prior study examined the role of postmenopausal hormone levels in the association between age at menopause and risk of type 2 diabetes. The authors conducted a study to investigate the association between age at natural menopause and risk of developing type 2 diabetes. The study also aimed to examine the role of endogenous sex hormone levels in the association between age at natural menopause and type 2 diabetes. The authors analyzed 3,639 postmenopausal women who had participated in the Rotterdam study, a Dutch population-based prospective cohort study. They used a home interview questionnaire to obtain baseline information about current health status, medical history, medication use, smoking behavior, socioeconomic status, and other factors. Subjects were then followed up from the start of the baseline visit onward to assess the incidence of type 2 diabetes. The authors also measured the endogenous sex hormone levels in the women. They concluded that of the 3,639 postmenopausal women without diabetes at baseline, 348 developed type 2 diabetes during a median follow-up of 9.2 years. Premature menopause and early onset of natural menopause were associated with a higher risk of type 2 diabetes. This association was independent of potential intermediate risk factors for type 2 diabetes, including body mass index; glucose, insulin, and endogenous sex hormone levels; and genetic factors. The authors concluded that early onset of natural menopause is an independent marker for type 2 diabetes in postmenopausal women. Additional studies are needed to understand the mechanism and if the timing of natural menopause can add value to diabetes prediction and prevention.

Muka T, Asllanaj E, Avazverdi N, et al. Age at natural menopause and risk of type 2 diabetes: a prospective cohort study. *Diabetologia.* 2017. doi:10.1007/s00125-017-4346-8.

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Prediction of bladder cancer recurrence using somatic TERT promoter mutations

The diagnosis and treatment of urothelial bladder cancer relies on urine cytology and cystoscopy as the gold standard to detect recurrence and monitor such cancer. The advantage is that cytology is inexpensive and easy to perform, with high specificity and sensitivity to monitor high-grade tumors. However, cytology is less suitable for low-grade lesions, with an overall sensitivity for detecting tumor cells ranging from 22 to 62 percent. Biological markers that are more sensitive than cytology but lack specificity have been described. TERT (telomerase reverse transcriptase) is responsible for telomere maintenance, and when TERT activity is shut down, it leads to cell death. TERT promoter mutations have been described at high frequencies across all stages in malignant bladder tumors, but their prognostic value is not known. The authors conducted a study in which they compared the use of noninvasive detection of TERT promoter mutations in urine with cytology and cystoscopy as a predictive marker of

bladder cancer recurrence. They evaluated the urine from 348 patients treated by transurethral bladder resection for urothelial bladder cancer and compared these patients to 167 control patients. The overall sensitivity of the study was 80.5 percent and the specificity was 89.9 percent. The results were not significantly impacted by inflammation or infection. The authors found that TERT promoter mutation detection that remained positive after initial surgery was associated with residual carcinoma in situ. TERT in urine was also a reliable predictor of recurrence in nonmuscle invasive bladder cancer. In a univariate analysis, TERT-positive urine samples in patients after initial surgery increased the risk of recurrence by 5.34-fold. Even in a subset of patients with negative cystoscopy, TERT-positive mutation status was associated with recurrence. The study results demonstrated that TERT promoter mutations can be detected in urine and that the use of such mutations is a noninvasive and sensitive way to detect urothelial bladder cancer lesions, especially in low-grade UBC, for which cytology is more limited.

Descotes F, Kara N, Decaussin-Petrucci M, et al. Non-invasive prediction of recurrence in bladder cancer by detecting somatic TERT promoter mutations in urine. *Br J Cancer.* 2017;1–5. doi:10.1038/bjc.2017.210.

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