HOPPSA-associated studies:

AMH-HOPPSA, a nested trial of anti-Müllerian hormone (AMH) levels

Background

There is a theoretical rationale that salpingectomy may disturb the vascular and nervous supply to the ovary, possibly causing impairment in ovarian function. Two previous studies, one RCT and one cohort study, has studied AMH levels three months after hysterectomy, comparing the change in AMH if a salpingectomy was performed at the same time or not (Findley et al and Morelli et al). No difference was observed between groups. None of these studies evaluated any clinical outcome related to ovarian function, but only surrogate outcomes. In the HOPPSA study, the primary outcome for ovarian function is based on clinical symptoms related to menopause. In order to strengthen the hypothesis of non-inferiority for ovarian function if salpingectomy is performed, an analysis of serum-AMH is planned in a nested trial within HOPPSA. The serum level of AMH is an indirect measure of ovarian function.

Methods

This nested trial will be conducted at the Sahlgrenska University Hospital and the associated laboratory. Consecutive patients in the HOPPSA study will be asked for blood samples. Specific written and oral information will be provided for this group. Blood samples are taken at baseline and after one year. Samples are handled according to laboratory instructions, frozen and stored in a biobank for later analysis, when the entire cohort will be analyzed at the same time. Results will not be available until after one year of follow-up. Measurements of AMH will be added manually to the one-year follow-up dataset in GynOp. The primary outcome is *absolute change in AMH*. Secondary outcomes are *relative change in AMH* and *level of AMH* one year after surgery.

Sample size calculation

A decrease in AMH from baseline to one year after surgery is expected in both groups, based on a negative effect of hysterectomy on ovarian function and also on increasing age. Baseline before surgery is estimated to be 0.5 mg/L and one year post-operatively 0.25 mg/L in the group with hysterectomy only. If non-inferiority is defined as 0.125 mg/L AMH, the higher limit of the two-sided 95% CI for the difference in change between the two groups shall not exceed 0.125 (SD for change 0.1) with a probability of 80% (β=20%), and an estimation of up to 0.05 larger change in the salpingectomy group, 29 patients per randomization group is needed to show non-inferiority. Estimating a 20% loss to follow-up (a second blood sample not taken), 75 patients will be recruited in this nested trial.

Statistics

A two-sided 95% CI for the mean difference in *absolute change in AMH* will be constructed using Fisher's exact permutation test. The lower limit of the 95% CI shall not exceed the non-inferiority margin of 0.125.