



**Karolinska
Institutet**

Department of Oncology-Pathology

Karolinska Institutet, Stockholm, Sweden

Familial Breast Cancer

Risk populations and their surveillance

AKADEMISK AVHANDLING

som för avläggande av medicine doktorexamen vid Karolinska Institutet offentligens försvaras i Aulan, Södersjukhuset, Sjukhusbacken 10, Stockholm **Torsdagen den 16 juni, 2011, kl 13.00**

av

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ABSTRACT

Women carrying mutations in either BRCA 1 or BRCA2 have a lifetime risk of breast cancer of 80%. As little is known about the risk of other malignancies, apart from ovarian/tubal cancer in mutation carriers, the importance of other malignancies in a family with several cases of breast cancer is hard to evaluate. Women at high risk of breast cancer due to family history are offered genetic counselling and surveillance. Whether women looking for oncogenetic counselling are, in terms of socioeconomic status and health-related quality of life, comparable with women in general is not known. Mammography is a widely used screening method to detect breast cancer and has proven to reduce breast cancer mortality in women older than 50 years. The sensitivity of the method is much lower in women with dense breast and in general young women tend to have denser breast than older women. Most women under surveillance in virtue of family history of breast cancer are younger than 50, thus in a group where mammography alone has not been proved to be effective as a single screening method there is a need for other surveillance methods in women at risk of hereditary breast cancer.

We identified 803 BRCA 1/2-negative families with two or more cases of breast cancer and at least one additional malignancy. The observed proportion of different non-breast cancer in the study families was compared with the percentage distribution of non-breast cancer tumours in Sweden. Tumours in endometrium were seen in a significantly larger proportion in the study group than in the general population and could not be explained by previously known syndromes or other explanations for being overrepresented. Thus we suggest that endometrial carcinoma and breast cancer constitute a new breast cancer syndrome.

In a cross-sectional study aiming to characterize health-related quality of life and socioeconomic status among all healthy women who had ever visited the Oncogenetic Clinic, Department of Oncology, Södersjukhuset in 1998 – 2004, 306 women consented to participate (82.5%). Significantly more women in the study group were cohabiting (74.2 vs. 43.8%), had the highest education level, (56.7 vs. 39.6%) and had the highest household income (36.9 vs. 12.9 %) as compared to the reference population in the same catchment area. Study subjects reported significantly lower levels of health-related quality of life for subscales related to mental health and for general health compared to normative data, but similar levels on subscales related to physical health.

Six-hundred-and-thirty-two women (94%) from one counselling clinic consented to participate in a study aiming to find the most sensitive method to detect breast cancer in women with a familiar risk of the disease. Every woman underwent yearly, and blinded to the other methods, mammography, ultrasound and clinical breast exam. This first report describes the study design and the procedure, and the study cohort regarding hereditary pattern and sociodemographics. Further, the associations between breast density, BMI and other breast-cancer risk factors are elucidated. High breast density was associated with low BMI and young age. However, high density was not associated with *increasing* risk of breast cancer. Ultrasound and clinical breast examination caused substantially more work-up than MG. The number of detected cancers did not differ from the expected numbers. However, it is too early to draw any conclusion about the sensitivity of the three different modalities..