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Cervical and vaginal cancer
-aspects on risk factors, prevention and treatment

Akademisk avhandling

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Avhandlingen baseras på följande delarbeten

I. Alfonzo E, Andersson Ellström A, Nemes S, Strander B, 2016, **Effect of Fee on Cervical Cancer Screening Attendance-ScreenFee, a Swedish Population-Based Randomised Trial**, PLoSOne 2016 Mar 17;11(3): e0150888

II. Alfonzo E, Holmberg E, Sparén P, Milsom I, Strander B, 2020, **Risk of vaginal cancer among hysterectomised women with cervical intraepithelial neoplasia: a population-based national cohort study,** BJOG 2020 MAR;127(4):448-454

III. Alfonzo E, Holmberg E, Daneshpip F, Milsom I, Strander B, **Swedescore and the effectiveness of colposcopy in the Swedish screening program**, Manuscript

IV. Alfonzo E, Wallin E, Ekdahl L, Staf C, Flöter Rådestad A, Reynisson P, Stålberg K, Falconer H, Persson J, Dahm-Kähler P, **No survival difference between robotic and open radical hysterectomy for women with early stage cervical cancer: results from a nationwide population-based cohort study,**
Eur J Cancer 2019 Jul;116:169-177

SAHLGRENSKA AKADEMIN
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Cervical and vaginal cancer
-aspects on risk factors, prevention and treatment

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Abstract

Background: Participation in screening is associated with a major risk reduction in cervical cancer, but there is a lack of knowledge on whether the cost to the individual has an effect on the participation rate. Women with abnormal findings at screenings are referred for colposcopy. The use of the Swedescore scoring system is recommended by the Swedish national guidelines for cervical cancer prevention. There is, however, a lack of effectiveness studies evaluating this assessment. Previous studies have shown that women with cervical high-grade lesions have an increased risk for vaginal cancer, but there is a knowledge gap regarding the risk for hysterectomised women with and without risk factors. Women with early-stage cervical cancer are treated with radical hysterectomy, which can be performed via open or minimally invasive surgery (MIS). Inferior oncologic results of MIS have been reported in international studies, which emphasises the need for further assessment of the technique's oncological safety.
Aims: To study factors influencing the prevention of cervical and vaginal cancer by means of the screening programme for cervical cancer and to evaluate surgical treatment modalities for early-stage cervical cancer.
Material and methods: Paper I was a randomised controlled trial (RCT) performed on female (n = 3124) residents of low-resource areas of Gothenburg in 2013. The intervention group did not have a fee, and the control group had the standard fee. Attendance was defined as registered cytological smear within three months of invitation. In paper II, population-based register data from the National Patient Register and the Swedish Cancer Register were used in a cohort study design 1987–2011. The cohort was divided into four groups: hysterectomised with benign cervical history, hysterectomised with a history of cervical intraepithelial lesion grade 3 (CIN3), hysterectomised with prevalent CIN at surgery and non-hysterectomised. The main outcome was vaginal cancer. Paper III was a cross-sectional study linking data from the Swedish National Cervical Screening Registry (NKCx) with histological samples and a Swedescore assessment and/or colposcopic assessment by identifiable colposcopists. In Paper IV, five-year overall survival (OS) and disease-free survival (DFS) were assessed in a population-based cohort study that included all Swedish women with IA1-IB1 cervical cancer treated with radical hysterectomy from 2011 to 2017. The Swedish Quality Register for Gynecological Cancer (SQRGC) was used for identification.
Results: Paper I: No difference in attendance was noted between the intervention and control groups (RR=0.93 95% CI 0.83-1.02). Nor were there any differences according to previous participation or non-participation or between the districts. Paper II: 898 vaginal cancers were included. Women with prevalent CIN at hysterectomy had a high incidence rate (IR 51.3/100 000 95% CI 34.4-76.5), followed by women with CIN3 history (IR 17.1/100 000 95% CI 12.5-23.4). Paper III: 11 317 colposcopic assessments by Swedescore were included. Sensitivity at Swedescore ≥2 was 97.5%, and the negative predictive value (NPV) was 90.2%. Specificity at ≥8 was 93.3%, and the positive predictive value (PPV) was 60.1%. Area under the ROC curve (AUC) = 0.71. In total, 24 362 colposcopies with identifiable colposcopists were analysed for accuracy. The variability in accuracy differed significantly (p-value <0.001), no effect of experience was noted (k= 0.0024). Paper IV: In total, 864 women, 236 open and 628 robotic radical hysterectomies were identified and included. There was no difference in five-year OS between groups (Hazard Ratio (HR) 1.00; 95% CI 0.50-2.01) or DFS (HR 1.08 95% CI 0.66-1.78).
Conclusions: Abolishment of a fee in low-resource settings did not increase attendance. Surveillance should be offered to hysterectomised women with prevalent CIN since their risk of vaginal cancer is elevated. Abstaining from biopsy is not recommended at any Swedescore step; a referral smear should be taken into consideration before 'see and treat' to lower the risk for overtreatment. The experience of colposcopists did not affect accuracy. Long-term oncological outcomes did not differ between open and robotic radical hysterectomies.
Keywords: cervical cancer, uterine cervical neoplasms, cervical screening, medical fee, vaginal cancer, hysterectomy, Swedescore, effectiveness screening, robotic radical hysterectomy, oncological outcomes.

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