Should Fallopian Tubes Be Removed During Hysterectomy Procedures? – A Statement by AGO Ovar

Sollen die Tuben im Rahmen der Hysterektomie entfernt werden? – Ein Statement der AGO Ovar

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Introduction

The detection of premalignant cells in the epithelia of the fallopian tubes has revolutionized the theories on the genesis of ovarian cancer. Occurrence of serous tubal intraepithelial carcinomas (STIC) has been established in carriers of the germline mutation of the BRCA1/2 gene, with STICs now considered as a possible origin of serous high-grade carcinomas which frequently occur in this patient population. Bilateral salpingo-oophorectomy leads to a significant decrease in the risk of developing this carcinoma. It is recommended that this prophylactic surgery be performed between the age of 40 and 45 years.

Removal of the fallopian tubes has been propagated analogously in women with no proven genetic or identifiable familial risk of ovarian cancer. Fallopian tube removal has been proposed during surgery for benign disease, for example in women in whom hysterectomy is indicated. Such "prophylactic" or "opportunistic" salpingectomy procedures could prevent carcinoma development in later years. Critics warn that such an intervention could result in inadequate blood supply to the ovaries, resulting in morbidity associated with early hormone deficiency. It is still unclear how effective opportunistic salpingectomy could be as a primary prevention strategy and how such a strategy should best be implemented.

Are All Serous Ovarian Cancers Tubal Carcinomas?

The detection of a group of in-situ lesions in the tubal fimbria [1] abruptly shifted the scientific focus to the fallopian tubes; most putative ovarian cancers could have a tubal origin with spread to the ovarian cortex occurring through drainage to the ovarian surface or through displacement of transformed tubal epithelium during ovulation and thus only appear to originate in the ovary.

Histopathologically, this tubal cancerogenesis must be understood as a stepwise process, starting with p53 signature and moving from proliferative p53 signature to serous intraepithelial carcinoma (STIC) [2–13]. Intensive workup of the distal fallopian tubes demonstrated the following incidence for STIC:

- in 2–7% of cases undergoing risk-reduction salpingo-oophorectomy (BRCA1/2-positive women or women with a familial risk) [14],
- in up to 80% of surgical specimens of BRCA1/2 patients with serous high-grade carcinoma, and
- in 46% of cases with sporadic ovarian cancer [12, 15].

Development from a tubal precursor cannot be proven in 40–80% of cases if the patient with ovarian cancer has no underlying BRCA 1 or 2 mutation. A causal relationship is likely when STIC occurs coincidentally with serous high-grade carcinoma, but parallel independent occurrence as a result of field cancerogenesis is also conceivable. It is therefore unlikely that all serous ovarian cancers originate from tubal epithelia; rather, it is likely that there are several different pathways for the development of serous high-grade cancers. Prophylactic tubal removal will not prevent the development of all cancers in later years.

Advantages and Disadvantages of Prophylactic Adnexal Surgery

The removal of both adnexae during hysterectomy procedures to prevent the development of ovarian cancer has reduced the incidence in prospective cohort studies but did not reduce mortality [16, 17]. Premenopausal women develop a higher risk of osteoporosis and cardiovascular dis-

ease, which appears statistically to compensate for the prophylactic effect on carcinogenesis [18].

Ovarian function is assumed to play an important role on sexual function and quality-of-life even after menopause, so that there are no general recommendations whether and from what age the adnexae should be removed during hysterectomy.

Tubal removal during hysterectomy can affect blood supply to the ovaries and lead to detrimental degenerative effects and earlier menopause [19]. A number of studies using various methods and end-points such as Doppler measurement of ovarian blood flow or serial hormonal measurements (FSH, LH, estradiol, anti-Müllerian hormone) showed no effect on ovarian reserve [20–23]. But because of the relatively small patient populations investigated in these studies, it is not possible to come to a conclusive evalution. There are no controlled studies on the potential early start of menopause after salpingectomy. Perioperative morbidity after hysterectomy with bilateral salpingectomy was not increased compared to hysterectomy without salpingectomy [24].

Conversely, hysterectomy with retention of fallopian tubes or sterilization is associated with more adverse effects compared to the potential disadvantages of hysterectomy procedures with salpingectomy. Subsequent hydrosalpinx can require surgical investigation. Retention of fallopian tubes doubles the risk for later surgery of adnexae, indicating a benefit of tubal removal [24,25].

How Effective Could Removal of the Fallopian Tubes Be?

Around 125,000 hysterectomies are performed annually in Germany [26]. If salpingectomy performed during hysterectomy procedures is the only measure taken to reduce the incidence of ovarian cancer, a simple calculation puts the hopes of a significant impact into perspective: out of 8000 new cases with disease (including those of genetic origin) round 70% are serous high-grade carcinomas. If opportunistic salpingectomy were to be carried out immediately in **all** hysterectomy procedures and would thereby prevent the development of **all** serous cancers, the incidence of ovarian cancer would be reduced by around 2.3% in 20 years – if **all** hysterectomies were carried out together with bilateral salpingectomies and thus **all** serous cancers could be prevented. If – as is assumed – other mechanisms can also lead to the development of serous high-grade cancers even after bilateral salpingectomy, the effect will be lower. It is not clear to what extent tubal removal has a protective effect against the development of endometrioid or clear-cell ovarian cancers. Epidemiological data have shown an overall lower risk of developing ovarian cancer after tubal sterilization. It is possible that carcinogenic substances are transported through the tubes; opportunistic salpingectomy could thus reduce the incidence of non-serous subtypes.

How Could Opportunistic Salpingectomy be Implemented as a Primary Prevention Strategy?

If prophylactic surgical tubal removal is considered as a preventive strategy, the greatest reduction in the incidence of ovarian cancer in a low-risk population could be achieved if tubal removal is carried out rigorously and frequently. The presumably simplest and currently most common form of opportunistic salpingectomy is carried out during abdominal or laparoscopic hysterectomies where surgical access provides a good opportunity to carry out ovarian and tubal procedures. But should a general recommendation for salpingectomy then also apply to vaginal hysterectomy procedures in which salpingectomy is technically not always easy? Should the recommendation be expanded to include other gynecological procedures such as surgery for ovarian cysts? Should every woman be offered bilateral salpingectomy after she has completed her family if she is scheduled for intra-abdominal surgery, e.g., cholecystectomy? Will this result in a modification of the standard technique for tubal sterilization with the procedure changed to bilateral salpingectomy for preventive reasons? Could failure to educate a patient about tubal removal have legal ramifications if a patient later develops serous high-grade cancer and she was not informed about the potential association prior to undergoing hysterectomy? Answers to these questions and any conclusive assessment of the effects of opportunistic salpingectomy procedures will probably only be possible in several years' time.

Conclusion

In practice, the evidence of precancerous lesions in the fallopian tubes has resulted in diagnoses for opportunistic salpingectomy during hysterectomy being given with a liberal hand. There are no indications that opportunistic salpingectomy is associated with increased morbidity; the rates for surgical interventions required at a later date appear to be much lower in women who underwent opportunistic salpingectomy than for women with retained fallopian tubes. Based on the current scientific data it is not possible to give a general recommendation in support of opportunistic salpingectomy for cancer prevention. Prospective registries and long-term data collection will be necessary prior to making such a recommendation. During patient consultations and discussions prior to undergoing surgery, the patient must be informed about the possibility of tubal removal and the potential risks and benefits associated with bilateral salpingectomy.

A detailed description of the current scientific position on opportunistic salpingectomy has been published in Archives of Gynecology and Obstetrics [27].

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