occurred in the treated group versus none in the control group. Poisson test for all cancers was highly significant $P < 0.001$). We did not observe a difference in endometrial cancers due to the small number of events in our study. The difference between groups for ovarian and peritoneal cancers can probably be explained by the well known association between breast and ovarian cancer rather than by tamoxifen intake. Our results confirmed that tamoxifen increased the endometrial thickness. In any case, the true endometrial pathologies under tamoxifen were more often benign (55/62).

These results support the hypothesis that tamoxifen, in association with breast cancer, seems to be a 'revealing agent' of benign endometrial abnormalities found in a normal population. The small number of true endometrial pathologies found supports our policy of using an endovaginal echography as the first screening test. Because of the lack of a peak of incidence of pathology under tamoxifen, we propose an annual endovaginal echography as follow-up of the patients treated by tamoxifen.

The design of our study does not allow us to attribute the observed effects to tamoxifen intake alone, but to the global exposition to breast cancer and tamoxifen. Perhaps our current prospective study of women, for which we have an ultrasonography before and during tamoxifen intake, will provide further arguments about the specific effects of tamoxifen on endometrial pathology.

European Journal of Cancer, Vol. 34, Suppl. 4, pp. S34–S35, 1998

Printed in Great Britain
0959-8049/98$—see front matter

PII: S0959-8049(98)00102-6

III.4 Tamoxifen and the Uterus: Potential Uterine Risks of Anti-oestrogens. The Approach of the European Institute of Oncology

D. Franchi,[1] N.N. Colombo,[1] L. Bocciolone,[1] A. Maggioni,[1] A. Costa[2] and V. Sacchini[2]

[1]Department of Gynecological Surgery; and [2]Department of Senology, European Institute of Oncology, Milan, Italy

Tamoxifen has been widely used as adjunctive therapy for women with breast cancer because it acts as an excellent anti-oestrogen for breast tissue. However, tamoxifen has been found to be associated with various endometrial pathologies, such as endometrial hyperplasia, endometrial polyps and endometrial carcinoma [De Muylder and colleagues. *Int J Gynecol Pathol* 1991, 36, 127–129]. Transvaginal ultrasonography has been found to be an accurate diagnostic method in assessing endometrial thickness in correlation with various physiological and pathological endometrial conditions. Consistently, an endometrial thickness less than 4–5 mm has been associated with inactive endometrium on biopsy [Granberg S and colleagues. *Am J Obstet Gynecol* 1991, 164, 47–52]. However, transvaginal ultrasonography has limited use in the diagnosis of specific abnormalities because of many false positive monographic findings in patients receiving tamoxifen. Some patients taking tamoxifen show heterogeneous centrally located uterine changes when initially viewed with vaginal probe ultrasound. When such patients are viewed with a technique of fluid enhancement (sonohysterography), some changes thought to be in the endometrium were actually in the proximal myometrium, probably due to reactivation of adenomyosal foci in the form of microcysts [Goldstein SR. *Am J Obstet Gynecol* 1994, 170, 447–451]. The aim of this study is to assess the clinical value of sonohysterography in identifying endometrial diseases among asymptomatic, postmenopausal breast cancer patients treated with tamoxifen 20 mg/day, and to compare its accuracy with that of transvaginal ultrasonography, hysteroscopy and endometrial sampling. © **1998 Elsevier Science Ltd. All rights reserved.**

THE ENDOMETRIUM of 75 tamoxifen-treated patients was scanned by transvaginal ultrasound to evaluate thickness and morphology. Endometrial thickness was measured in the antero-posterior dimension and was considered normal when less than 8 mm. Those patients with endometrial thickness ≥ 8 mm were prospectively evaluated by sonohysterography and subsequently evaluated within 4 weeks by hysteroscopy

Correspondence to D. Franchi.

and endometrial sampling. All patients were treated with 20 mg of tamoxifen daily.

Transvaginal ultrasonography and hysterosonography were performed with a 6.5 MHz endovaginal transducer attached to a Hitachi Spazio.

Before starting the procedure a bimanual pelvic examination was performed to verify the accessibility and safety of the procedure. Then the transvaginal probe was inserted and the uterus was scanned both sagitally and coronally to determine the regularity of the endometrium. An antero-posterior measurement of endometrial thickness was recorded at the widest point observed. After the vaginal scanning was completed, a number 5.3 F catheter (Goldstein SHG catheter, Cook Ob/Gyn) was introduced into the uterine cervix and a 10-ml syringe containing sterile saline solution was attached to the catheter.

Under sonographic vision, physiologic saline was injected into the uterus through the catheter. A range between 3 and 10 ml was usually sufficient to define the endometrial cavity. The transducer was moved in the long and transverse section without missing any portion of the uterine cavity.

The mean duration of tamoxifen treatment was 12.8 ± 6.8 months (range 6–40) and mean patient age was 58.2 ± 9.6 years (range 42–74). Forty-eight examinations (64%) showed endometrial thickness less than 8 (negative group) and 27 (36%) showed endometrial thickness of 8 mm or more (positive group). Transvaginal sonography showed an inhomogeneous and thickened endometrium in 17 patients of the positive group, in the remaining 10 patients the sonographic appearance was suggestive for endometrial polyps.

The uterine cavity of the 27 patients was immediately evaluated by sonohysterography. In the 10 patients (37%) in whom transvaginal sonography had revealed an echogenic mass suggestive for a polyp, sonohysterography identified an endocavitary polyp surrounded by regular, thin endometrium, which were all confirmed at operative hysteroscopy and at histological assessment. 9 of the 17 patients (63%) in whom transvaginal sonography had shown only a thickened endometrium, were identified by sonohysterography to have one or more endometrial polyps confirmed at operative hysteroscopy and histology. Overall, 19 patients (70%) were diagnosed to have endometrial polyps.

Of the remaining 8 patients, 5 were identified at sonohysterography to have a normal thin endometrium with typical subendometrial microcysts induced by tamoxifen; 3 patients had an irregular thickened endometrium. Hysteroscopy and histologic assessment confirmed atrophy in the first 5 patients, 1 simple hyperplasia and 2 cases of endometrial adenocarcinoma. Overall sonohysterography accurately diagnosed endometrial disease in 100% of these patients. There was no false-negative diagnosis.

Sonohysterography is more accurate than transvaginal sonography alone, and less invasive than hysteroscopy, which sometimes requires general anaesthesia to obtain adequate information. Sonohysterography can be a useful diagnostic tool for the assessment of endometrial diseases in asymptomatic postmenopausal breast cancer patients treated with tamoxifen, who were diagnosed by transvaginal sonography to have a thickened endometrium.

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European Journal of Cancer, Vol. 34, Suppl. 4, pp. S35–S36, 1998

Printed in Great Britain
0959-8049/98$—see front matter

PII: S0959-8049(98)00103-8

III.5 Saline Infusion Sonohysterography is a Good Approach for Additional Assessment of the Endometrium

S.J.M. Neele,[1] W.M. van Baal,[2] M.J. van der Mooren,[2] P. Kenemans[2] and J.C. Netelenbos[1]

[1]Division of Endocrinology, Department of Internal Medicine; and [2]Department of Obstetrics and Gynecology, Academic Hospital Vrije Universiteit Amsterdam, The Netherlands

We describe the results of endometrial assessment with transvaginal ultrasound (TVU) and saline infusion sonohysterography (SIS) in healthy, asymptomatic early postmenopausal women. We used cross-sectional data obtained from women who were screened prior to participation in a clinical trial for prevention of osteoporosis, with either hormone replacement therapy, placebo or a selective oestrogen receptor modulator. © **1998 Elsevier Science Ltd. All rights reserved.**