

Ultrasound Characteristics of Breast Changes in Albanian Postmenopausal Women Who use Hormonal Replacement Therapy

Albana SHAHINI Ph.D, Erinda KOSTURI M.D.

Abstract: Background: HRT has been widely used in Albania, but it seems its importance has been raising lately. Many women are opting for this treatment as soon as menopause onset is diagnosed. It wasn't until late though, that gynecologist started referring women for regular breast ultrasound after hormonal replacement therapy began. The aim of this study was identifying changes in breasts of postmenopausal women who had been under HRT, using sonography. Materials: This is a retrospective study, based on datas gathered from women who were referred to us by gynecologist. All women were under cyclic regimen HRT. From all 165 women, only 150 patients are included in this report. The 15 women excluded from the study, had either insufficient records or had been diagnosed with suspicious lesions since the first visit and were sent for further investigation. Once a year, for 6 consecutive years, breast ultrasonography was performed, and lesions were described using BIRAD-S lexicon. Patient's datas were completed with careful anamnestic details time after time, and with hormonal and biochemical analysis. Results: After HRT, we noticed that breast glandular section thickness had increased while breast ducts had become smaller. We were able to identify solid breast lesion ex novo in 8.7% and cysts in 2%. Reported serum estradiol levels in the 3rd year were quite higher in women who had marked structural changes opposed to the ones who didn't experience such morphological change. These differences were significant in the 6th year of therapy. Conclusions: Starting HRT, leads to many changes in breast structure, which afterword need careful sonography assessment. An increasing percentage of the glandular tissue was reported from the first examinations until the 6th year. In subjects with such change we can also monitor a raising level of estrogen. The use of ultrasound, is after all successful in determining breast structure changes and early identification of breast solid lesions or cysts. Therefore, we recommend annual follow-ups in all women, specially if under HRT

Keywords: ultrasound, breast, postmenopausal, BIRAD-S4

1. Introduction

At approximately 45 y.o., women reach a phase known as climacteric or colloquially. Every change that characterised their organism, during childhood-puberty transition, when hormonal flow stimulated the sexual characteristics- in order to reach the peak of sexual capacity and fertility- will be reversed. But, as the first part of the physical features are found in all mammals, the cessation of female reproductive capability, is a feature that belongs to humans only. While climacteric is a time period, that lasts for years, the end of the fertility is a single event, known as menopause, or the last menstruation of a women's life.

Every single women, will face such biologically predetermined phase, around 45-55 y.o. Nowadays, gynecologists and many other doctors, have to deal with this condition, but it wasn't many years before, that this age did not attract such attention. During the Bronze age, for example, only about 7%, of women reached the climacteric age, meanwhile it is estimated that about 95% of women in the same countries, reach menopause. On average, women are likely to live 30 years beyond the moment menopause initiates. At this times, we are giving these women a mean life expectancy of around 80 years, which on the other hand, has brought with it a rising number of severe health problems, not a few of which are directly related to the natural decrease of female sex hormones. At this point securing a total physical and mental wellness, has become an imperative for doctors.

This need of such wellness, is why more and more women opt for hormonal replacement therapy. Under HRT, women

need careful screening of all biochemical parameters and mostly periodical breast sonographic assessment.

2. Materials and Methods

This is a retrospective study, of 165 women, referred to us for breast ultrasonography. All women were under hormonal replacement therapy, after menopause had been diagnosed. Careful and detailed anamnesis was provided for all women before the ultrasound was performed, including menarche age, menstrual cycles, number of pregnancies, abortions and miscarriages, breastfeeding period. For all women, for which there were available breast imaging from before the HRT initiation, the radiologist noticed if any changes were present.

From the group of 165 women, 13 were excluded from the final group because of lack of follow up documentation and 2 of them, because were classified as BIRAD-S 4 and were referred for mammo exam and histological examination. They were both found to be adenocarcinomas.

From the moment that HRT was prescribed, all 150 women, once a year for the next 6 years under treatment, were sonographically followed and underwent mammography as part of the recommended protocol when needed.

During ultrasound, datas regarding the breast were carefully gathered and described. When lesions were present, they were characterised using the BIRAD-S lexicon. In collaboration with gynecologist, records of patients, were completed with hormonal lab results and biochemical analysis. In addition, any other pain or tension felt in the breasts was documented.

3. Results

In the first sonographic assesment , at least a benign lesion was identified in 6.6% of the women screened. 8 of them, or 5.3% had fibroadenomas, which measured at maximum 20.4x13.6mm, mostly localised at the inferior lateral quadrant region. 2 of the patients, or 1.3% of the women screened had cysts at the begining of the treatment, which at maximum measure 8.7x4.4mm, which met sonographic criteria of benign cysts, liquid filled, posterior acoustic enhancement and well defined borders.

During follow up, in the second year of HRT, pre-existent fibroadenomas, had undergone an increase in diameters of about 9.9x4.9 mm whereas the cysts an increase in diameter of aproximately 8.5x4.3mm. In the third year of check-ups, 8.7% of the patients, or 13 women, had new solid lesions, and 2% or 3 women, had new cysts. Sonographic examinations, pointed a thickness of the glandular tissues, which showed that HRT delayed the normal physiological development of adipous tissue of breast

In collaboration with gynecologist who reffered these patients, charts were up dated, and laboratoric parameters were noted. High levels of estradiol were present mosly in women who had distinct changes in the breasts compared to those with mild changes, or no changes at all. The sixth year of treatment showed the highest levels of breast changes. Mastodynia was present and more severe in all women with increased levels of estradiol and therefore the ones with structural changes as well.

4. Conclusions

Sonography , is one the finest methods , easily accessible and low cost used to screen for and early diagnose breast disease. It's importance amplifies in women who undergo HRT. Literature, shows a moderate increase in risk of breast cancer developement in all women under HRT, which increases by 2.3% per every year of HRT use, which gradually decreases therapy cessation. Starting a HRT, as reported above, leads to important changes in the breast structure, which implies the need of careful sonographic assessment.

In this study, this potential risk, was shown by ex novo lesions : of which 8.7% were diagnosed as solid lesions , or fibroadenomas, and 2% cysts. Under sonographic guidance, we identified changes in the breast tissues during a 6 year follow-up. All patients, in which the changes in the glandular tissues was important, had a higher estrogen level. Both these changes, accompanied mastodynia. In conclusion, even though the study group represented above, was modest, our findings emphasise the importance of ultrasound examination in diagnosing early breast lesions in women receiving HRT, thus we firmly underline the importance of ultrasonography in diagnosis and follow-up of women under HRT especialy.

References

- [1] Chlebowski RT, Kuller LH, Prentice RL, et al. Breast cancer after use of estrogen plus progestin in postmenopausal women. *New England Journal of Medicine* 2009; 360(6):573–587. [PubMed Abstract]
- [2] Rossouw JE, Anderson GL, Prentice RL, et al. Risks and benefits of estrogen plus progestin in healthy postmenopausal women: principal results from the Women's Health Initiative randomized controlled trial. *JAMA* 2002; 288(3):321–333. [PubMed Abstract]
- [3] Chlebowski RT, Anderson GL, Gass M, et al. Estrogen plus progestin and breast cancer incidence and mortality in postmenopausal women. *JAMA* 2010; 304(15):1684–1692. [PubMed Abstract]
- [4] Batur P, Blixen CE, Moore HC, Thacker HL, Xu M. Menopausal hormone therapy (HT) in patients with breast cancer. *Maturitas* 2006; 53(2):123–132. [PubMed Abstract]
- [5] Cummings Sr, Kelsey JI, Nevitt Nc, O'Dowd KJ. Epidemiology of osteoporosis and osteoporotic fractures. *Epidemiol Rev* 1986; 7:178-208. PubMed
- [6] Stampfer Mj, Colditz Ga, Willet Wc, Manson Je, Rosner B., Speizer Fe. Postmenopausal estrogen therapy and cardiovascular disease: ten-year follow-up from Nurse's Health Study. *N Engl J Med* 1991; 325: 756-762. PubMed
- [7] DiSaia Pj. Hormone-replacement therapy in patients with breast cancer: a reappraisal. *Cancer* 1993; 71: 1490-1500. PubMed
- [8] Marchant Dj. Estrogen-replacement therapy after breast cancer: risks versus benefits. *Cancer* 1993; 71: 2169-2176. PubMed
- [9] Wile Ag, Opfell Rw, Margileth Da. Hormone replacement therapy in previously treated breast cancer patients. *Am J Surg* 1993;165: 372-375. PubMed 3109/13697137.2013.795683.
- [10] Sturdee DW, Panay N; Recommendations for the management of postmenopausal vaginal atrophy. *Climacteric*. 2010 Dec;13(6):509-22. doi: 10.3109/13697137.2010.522875. Epub 2010 Sep 30.
- [11] Tan O, Bradshaw K, Carr BR; Management of vulvovaginal atrophy-related sexual dysfunction in postmenopausal women: an up-to-date review. *Menopause*. 2012 Jan;19(1):109-17. doi: 10.1097/gme.0b013e31821f92df.
- [12] Goldstein I; Recognizing and treating urogenital atrophy in postmenopausal women. *J Womens Health (Larchmt)*. 2010 Mar;19(3):425-32. doi: 10.1089/jwh.2009.1384.
- [13] Stevenson JC; HRT, osteoporosis and regulatory authorities Quis custodiet ipsos custodes? *Hum Reprod*. 2006 Jul;21(7):1668-71. Epub 2006 Mar 23.
- [14] Marjoribanks J, Farquhar C, Roberts H, et al; Long term hormone therapy for perimenopausal and postmenopausal women. *Cochrane Database Syst Rev*. 2012 Jul 11;7:CD004143. doi: 10.1002/14651858.CD004143.pub4.
- [15] Bagger YZ, Tanko LB, Alexandersen P, et al; Two to three years of hormone replacement treatment in healthy women have long-term preventive effects on bone mass and osteoporotic fractures: the PERF study. *Bone*. 2004 Apr;34(4):728-35.

- [16] Rossouw JE, Anderson GL, Prentice RL, et al; Risks and benefits of estrogen plus progestin in healthy postmenopausal women: principal results From the Women's Health Initiative randomized controlled trial. *JAMA*. 2002 Jul 17;288(3):321-33.
- [17] Schierbeck LL, Rejnmark L, Tofteng CL, et al; Effect of hormone replacement therapy on cardiovascular events in recently postmenopausal women: randomised trial. *BMJ*. 2012 Oct 9;345:e6409. doi: 10.1136/bmj.e6409.
- [18] Harman SM, Brinton EA, Cedars M, et al; KEEPS: The Kronos Early Estrogen Prevention Study. *Climacteric*. 2005 Mar;8(1):3-12.
- [19] Calleja-Agius J, Muscat-Baron Y, Brincat MP; Estrogens and the intervertebral disc. *Menopause Int*. 2009 Sep;15(3):127-30. doi: 10.1258/mi.2009.009016.
- [20] Lethaby A, Hogervorst E, Richards M, et al; Hormone replacement therapy for cognitive function in postmenopausal women. *Cochrane Database Syst Rev*. 2008 Jan 23;(1):CD003122.
- [21] Maki PM, Henderson VW; Hormone therapy, dementia, and cognition: the Women's Health Initiative 10 years on. *Climacteric*. 2012 Jun;15(3):256-62. doi: 10.3109/13697137.2012.660613.
- [22] Beral V; Breast cancer and hormone-replacement therapy in the Million Women Study. *Lancet*. 2003 Aug 9;362(9382):419-27.
- [23] Langer RD, Manson JE, Allison MA; Have we come full circle - or moved forward? The Women's Health Initiative 10 years on. *Climacteric*. 2012 Jun;15(3):206-12. doi: 10.3109/13697137.2012.666916
- [24] Santen RJ, Allred DC, Ardoin SP, et al; Postmenopausal hormone therapy: an Endocrine Society scientific statement. *J Clin Endocrinol Metab*. 2010 Jul;95(7 Suppl 1):s1-s66. doi: 10.1210/jc.2009-2509. Epub 2010 Jun
- [25] Chlebowski RT, Hendrix SL, Langer RD, et al; Influence of estrogen plus progestin on breast cancer and mammography in healthy postmenopausal women: the Women's Health Initiative Randomized Trial. *JAMA*. 2003 Jun 25;289(24):3243-53.

Author Profile

Albana SHAHINI Ph.D, Born in Vlora, Albania on September 11th 1973. 1998-1999 General physician. 1999-2000 Medical specialist in Public Health Department in Dibra. 2000-2004 Post graduate specialization in trades imaging in the Department of Radiology at University Hospital Center "Mother Teresa", Tirana, Albania June 2003 – present Radiologist in many private practices and Hospitals in Tirana. 2009 – Present, active in breast diseases diagnosis, through different radiological modalities Currently on doctorate process. Dissertation theme "Early diagnosis of breast disease".

Erinda KOSTURI M.D., Born in Tirana, Albania on June 24th 1985. Graduated from Medical Faculty in Tirana, Albania in July 2010. Specialisation on Family Medicine, graduated in April 2013. Microspecialisation on Abdominal Ultrasound on June 2013. 2011-present active on female health and screening procedures. Current position: Internal Medicine consultant at Bylykbashi Private Practice.