pISSN 1598-2998, eISSN 2005-9256

Cancer Res Treat. 2015;47(2):208-214

http://dx.doi.org/10.4143/crt.2013.223

Original Article

Open Access

The Clinical Impact of 21-Gene Recurrence Score on Treatment Decisions for Patients with Hormone Receptor-Positive Early Breast Cancer in Korea

Moo Hyun Lee, MD[1]
Wonshik Han, MD, PhD[2]
Jeong Eon Lee, MD, PhD[3]
Ku Sang Kim, MD, PhD[4]
Heeseung Park, MD[5]
Jongjin Kim, MD[2]
Soo Youn Bae, MD[3]
Hyun Joo Shin, MD[4]
Jong Won Lee, MD[5]
Eun Sook Lee, MD, PhD[1]

[1]*Center for Breast Cancer, National Cancer Center, Goyang,*
[2]*Department of Surgery, Seoul National University College of Medicine, Seoul,*
[3]*Department of Surgery, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul,*
[4]*Department of Surgery, Ajou University School of Medicine, Suwon,*
[5]*Department of Surgery, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea*

Correspondence: Eun Sook Lee, MD, PhD
Center for Breast Cancer, National Cancer Center, 323 Ilsan-ro, Ilsandong-gu, Goyang 410-769, Korea
Tel: 82-31-920-2011
Fax: 82-31-920-1511
E-mail: eslee@ncc.re.kr

Co-correspondence: Jong Won Lee, MD
Department of Surgery, Asan Medical Center, University of Ulsan College of Medicine, 88 Olympic-ro 43-gil, Songpa-gu, Seoul 138-736, Korea
Tel: 82-2-3010-5603
Fax: 82-2-474-9027
E-mail: asanbreastcenter@gmail.com

Received October 31, 2013
Accepted January 27, 2014
Published online September 11, 2014

Purpose

The 21-gene (Oncotype DX) recurrence score (RS) assay is useful in predicting the benefits of adjuvant chemotherapy for early breast cancer patients and is widely used in Western countries. However, to date, it has not gained much popularity in East Asia. We analyzed the results from five institutions' experience from using the 21-gene assay and examined the impact of assay results on decision making of chemotherapy in Korean breast cancer patients and the associations between RS and clinicopathologic characteristics.

Materials and Methods

The 21-gene assay was performed on 212 patients with estrogen receptor-positive early breast cancer in five institutions. Each center made systemic treatment decisions both before and after the knowledge of assay results.

Results

Among the 212 patients, 132 (62.3%) had a low RS of < 18, 60 (28.3%) had an intermediate RS of 18-30, and 20 (9.4%) had a high RS of ≥ 31. Histologic grade, presence of micrometastases, Ki-67, and presence of lymphatic invasion were statistically associated with the RS results. Treatment decisions were changed in 115 of 212 patients (54.2%) in 109 of 212 (51.4%) from chemotherapy plus hormone therapy to hormone therapy, and in six of 212 (2.8%) from hormone therapy to chemotherapy plus hormone therapy.

Conclusion

The 21-gene breast cancer assay proved to have a significant impact on treatment decision-making. The test reduces chemotherapy use in more than 50% of Korean estrogen receptor-positive, early breast cancer patients.

Key words
Breast neoplasms, Oncotype DX, Adjuvant chemotherapy

Copyright ⓒ 2015 by the Korean Cancer Association
This is an Open-Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (http://creativecommons.org/licenses/by-nc/3.0/) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

Introduction

Breast cancer is the second-most common cancer among Korean women and the mortality rate associated with it is increasing in Korea. The incidence of newly diagnosed breast cancer patients was 14,277, and a total of 1,868 patients died from breast cancer in 2010 [1].

Development of systemic treatment in management of breast cancer has improved the prognosis of breast cancer patients. A proper combination of adjuvant with local therapy is essential in improving survival. However, only 4%-5% of estrogen receptor (ER)-positive patients with node negative early breast cancer will benefit from adjuvant chemotherapy, and many patients are exposed to the adverse effects of adjuvant chemotherapy without significant benefits [2].

Gene expression profiles have provided information on the prognosis and benefit prediction of adjuvant chemotherapy in early breast cancer patients. Among them, the 21-gene Oncotype DX breast cancer assay has been the most widely used. The quantitative recurrence score (RS) result from this assay ranges from 0 to 100, with stratification into low (RS < 18), intermediate (RS, 18 to 30), or high (RS > 30) risk groups, based on the estimated risk of recurrence. The assay was validated for prognostic and therapeutic significance in patients with node-negative, ER-positive early breast cancer [2,3]. The use of RS in guiding clinical treatment decisions has been incorporated within clinical guidelines, such as American Society of Clinical Oncology (ASCO) [4], National Comprehensive Cancer Network (NCCN) [5], European Society of Medical Oncology (ESMO) [6], and the St Gallen Consensus Guidelines [7].

Although the 21-gene breast cancer assay has been widely used in Western countries, to date, it has been less popular in East Asia. In Korea, the primarily reason is because it is not covered by the national health insurance system. Benefits for cancer treatments in Korea depend on the treatment guidelines devised by the Health Insurance Review and Assessment Service (HIRA). While the current NCCN guideline incorporates the 21-gene assay for the management of ER-positive early stage breast cancer patients with node-negative or micrometastatic nodal disease and tumor size > 0.5 cm, the current Korean national treatment guideline is based on the previous version of NCCN guidelines, which recommends adjuvant chemotherapy for node-negative ER-positive breast cancer patients with tumor size > 1 cm. Many ER-positive, node-negative early breast cancer patients are reluctant to undergo chemotherapy and are willing to avoid it if possible. For these patients, the 21-gene assay may assist in the decision process by providing information on the likelihood of benefit from chemotherapy.

The impact of the 21-gene assay on clinical practice has been evaluated in several studies in node-negative ER-positive breast cancer patients [8-18]. These studies showed changes in the treatment recommendations in 19%-44% of early breast cancer cases. After knowledge of the assay results, many patients who had initial recommendations for chemoendocrine treatment were advised to have endocrine treatment only. The use of the assay has also been found to be cost-effective in different national health care systems [16,19].

We evaluated the impact of the 21-gene assay on adjuvant decision-making and the associations between RS results and clinicopathologic characteristics in Korean clinical practice for patients with ER-positive, node-negative early breast cancer.

Materials and Methods

Patients were selected via an initial record review of all ER-positive node-negative (pN0, pN0i+) or micrometastatic (pN1mi) breast cancer patients with tumor tissue analyzed by the 21-gene assay between August 2010 and July 2013 at 5 institutions in Korea (Asan Medical Center, National Cancer Center, Seoul National University College of Medicine, Samsung Medical Center, Ajou University School of Medicine). From this initial review, a total of 212 patients, who had available medical records and tumor slides, were included in this study.

The Oncotype DX assay was performed on fixed paraffin-embedded tissues by Genomic Health (Redwood City, CA). After a review of hematoxylin and eosin-stained slides to determine whether sufficient invasive breast cancer was present and whether manual microdissection was indicated, RNA was extracted from the unstained sections. Cases with no cancer (depleted by prior tissue studies) or with cancer cells occupying < 5% of the section area were excluded from the assay [3]. The analyses of all tissues from patients of our study were successful.

A retrospective chart review was completed on all patients in the participating five institutions for whom Oncotype DX was performed. An anonymized database was created where patients' age, tumor size, hormone receptor status, histologic type, histologic grade, nodal status, presence of lymphatic invasion, Ki-67 status, RS and treatment decision without and with knowledge of RS were registered. Pre-assay adjuvant therapy decisions were made in accordance to the institutions' guidelines, based on clinicopathologic characteristics from retrospective collected data. Although institutions'

guidelines vary slightly, they were largely based on the national health insurance guidelines. Post-assay treatment recommendations were decided based on the review of Oncotype DX by each institution. However, the actual adjuvant treatment administered to each patient may differ from the recommendation, as 10 patients did not follow the entire treatment plan.

Two types of analyses were performed to determine the association of RS and clinicopathologic characteristics, as defined in the study: with RS as a continuous variable or as a discrete variable defined by low (RS, < 18), intermediate (RS, 18-30), and high (RS, ≥ 31) RS groups. RS results between clinicopathologic characteristics were compared using the one-way analysis of variance and Kruskal-Wallis test, when appropriate. The prognostic factors between the RS category were compared using the χ^2 test and the Fisher exact test, when appropriate. The differences in the pathologic characteristics between the patients whose treatment decisions remained unchanged and those whose treatment decisions were changed were compared using the Student's t test, Mann-Whitney test, χ^2 test, and the Fisher exact test, when appropriate. Statistical significance was determined if the two-sided p-value was < 0.05.

Table 1. Clinicopathologic characteristics

	No. (%)
Age (yr)	46.07 (29-67)
Tumor size (cm)	1.86 (0.6-5.5)
< 1	19 (9)
≥ 1 and < 2	114 (53.8)
≥ 2	79 (37.3)
Pathologic type	
Ductal	187 (88.2)
Lobular	7 (3.3)
Others	18 (8.5)
Nodal status	
N0	192 (90.6)
N1mi	20 (9.4)
Histologic grade	
1	39 (18.8)
2	136 (65.4)
3	33 (15.9)
Lymphatic invasion	
No	140 (74.5)
Yes	48 (25.5)
Ki-67 (%)	
< 14	135 (69.6)
≥ 14	59 (30.4)
Radiotherapy	
No	37 (17.5)
Yes	175 (82.5)

Values are presented as mean (range) or number (%).

Table 2. Association between clinicopathologic characteristics and recurrence score (RS) results

Prognostic factor	Mean RS (range)	p-value
Tumor size (cm)		
< 1	18.05 (6-41)	0.182
≥ 1 and < 2	16.48 (1-62)	
≥ 2	18.39 (0-67)	
Histologic type		
Ductal	17.14 (0-67)	0.930
Lobular	16 (9-22)	
Others	19.89 (6-62)	
Histologic grade		
1	13.1 (5-28)	< 0.001
2	16.66 (0-62)	
3	25.64 (1-67)	
Nodal status		
N0	16.91 (0-67)	0.057
N1mi	21.4 (8-42)	
Lymphatic invasion		
No	16.4 (1-67)	0.024
Yes	20.35 (0-47)	
Ki-67 (%)		
< 14	15.54 (1-41)	0.002
≥ 14	20.22 (0-47)	

Results

The average age of subjects was 46 (range, 29 to 67 years), and all patients were women. The average tumor size was 1.9 cm (range, 0.6 to 5.5 cm). One hundred eighty-seven cases are invasive ductal, seven were invasive lobular, and 18 exhibited other features. Lymph-node metastasis were absent in 192 cases and present as micrometastases in 20 cases. Lymphatic invasion was absent in 140 cases and present in 48 cases. Her2 status was negative in all cases. Ki-67 was less than 14 in 135 cases and more than 14 in 59 cases. Oncotype DX assay results showed low RS of < 18 in 132 cases, intermediate RS of 18-30 in 60 cases, and high RS of ≥ 31 in 20 cases. Table 1 shows the clinicopathologic characteristics.

The associations of clinicopathologic prognostic factors and RS results are summarized in Table 2. Histologic grade, presence of lymphatic invasion, and Ki-67 showed significant correlations with the RS values; however, no statistical associations were noted between the tumor size, histologic type, and presence of micrometastasis with RS results. Table 3 shows the associations of the clinicopathologic characteristics and RS risk groups. Histologic grade, presence of lymphatic invasion, Ki-67, and presence of micrometastatsis had statistical associations with the RS risk categories; however, tumor size and histologic type did not.

Changes in treatment decisions from the assay results are summarized in Table 4. Before knowledge of assay results, adjuvant chemohormonal therapy (CHT) would have been recommended to 150 of the 212 women (70.8%) and hormone therapy alone (HT) to the remaining 62 women (29.2%), based solely on the classical clinicopathologic factors.

Treatment decisions were changed in 115 patients (54.2%) after individual assay results were available. For 109 patients (51.4%), the initial decision was revised from CHT to HT, and for 6 individuals (2.8%), from HT to CHT. In the low RS group, treatment decisions changed for 88 of 132 patients (66.7%), all of whom changed from CHT to HT. Among the 20 patients with high RS, two (10%) had a change in the treatment plan, both from HT to CHT. A total of 25 of the 61 women (41.7%) with intermediate RS had a change in the treatment decision (21 from CHT to HT [84% of changes], and four from HT to CHT [16% of changes]).

We analyzed the differences in the pathologic characteristics between patients whose treatment decisions remained unchanged and those whose treatment decisions were changed (Table 5). For patients whose pre-assay treatment

Table 3. Distribution of clinicopathologic characteristics according to recurrence score risk group

	Recurrence score risk group			p-value
	Low	Intermediate	High	
Tumor size (cm)				
< 1	12	4	3	0.311
≥ 1 and < 2	77	29	8	
≥ 2	43	27	9	
Histologic type				
Ductal	116	53	18	0.415
Lobular	3	4	0	
Others	13	3	2	
Histologic grade				
1	32	7	0	< 0.001
2	85	42	9	
3	12	10	11	
Nodal status				
N0	122	56	14	0.004
N1mi	10	4	6	
Lymphatic invasion				
No	90	43	7	0.012
Yes	25	14	9	
Ki-67 (%)				
< 14	93	36	6	0.002
≥ 14	29	19	11	

Table 4. Treatment decisions before and after knowledge of the recurrence score

Recurrence score	Pre-ODX	Post-ODX	No. (%)
Low	CHT	HT	88 (66.7)
	HT	CHT	0
	CHT	CHT	0
	HT	HT	44 (33.3)
	Any change		88 (66.7)
	Total		132 (100)
Intermediate	CHT	HT	21 (35)
	HT	CHT	4 (6.7)
	CHT	CHT	23 (38.3)
	HT	HT	12 (20)
	Any change		25 (41.7)
	Total		60 (100)
High	CHT	HT	0
	HT	CHT	2 (10)
	CHT	CHT	18 (90)
	HT	HT	0
	Any change		2 (10)
	Total		20 (100)
Total	CHT	HT	109 (51.4)
	HT	CHT	6 (2.8)
	CHT	CHT	41 (19.3)
	HT	HT	56 (26.4)
	Any change		115 (54.2)
	Total		212 (100)

ODX, Oncotype DX; CHT, adjuvant chemohormonal therapy; HT, hormone therapy alone.

Table 5. Comparative pathologic characteristics between patients whose treatment decisions remained unchanged and those whose treatment decisions were changed

	HT to HT (n=56)	HT to CHT (n=6)	p-value	CHT to CHT (n=41)	CHT to HT (n=109)	p-value
Tumor size (cm)	1.51±0.75	1.35±0.69	0.566	2.15±0.81	1.96±0.85	0.206
Histologic type						
Ductal	51 (91.1)	5 (83.3)	0.472	37 (90.2)	94 (86.2)	0.683
Lobular	1 (1.8)	0		2 (4.9)	4 (3.7)	
Others	4 (7.1)	1 (16.7)		2 (4.9)	11 (10.1)	
Histologic grade						
I	16 (28.6)	1 (16.7)	0.032	1 (2.5)	21 (19.8)	< 0.001
II	39 (69.6)	3 (50)		23 (57.5)	71 (67)	
III	1 (1.8)	2 (33.3)		16 (40)	14 (13.2)	
Nodal status						
N0	55 (98.2)	6 (100)	1.000	34 (82.9)	97 (89)	0.408
N1mi	1 (1.8)	0		7 (17.1)	12 (11)	
Lymphatic invasion						
No	37 (88.1)	3 (60)	0.154	21 (56.8)	79 (76)	0.035
Yes	5 (11.9)	2 (40)		16 (43.2)	25 (24)	
Ki-67 (%)	11.54±10.51	25.08±20.76	0.090	14.33±12.29	9.69±10.77	0.031

Values are presented as mean±standard deviation or number (%). HT, hormone therapy alone; CHT, adjuvant chemohormonal therapy.

decision was HT, there was a statistically higher number of histologic grade I tumors in patients whose treatment decision remained the same, when compared to the group whose treatment decisions were changed to CHT. For patients whose pre-assay treatment decisions was CHT, there were statistically higher numbers of histologic grade III tumors and lymphatic invasion, and higher Ki-67 levels in patients whose treatment decisions remained the same, than the group whose treatment decisions were changed to HT.

Discussion

To date, the experience of using Oncotype DX for Korean breast cancer patients has not been reported. Our study is the first report on the impact of this assay on treatment decision for early breast cancer patients in Korea.

Our result showed that treatment decisions changed for 54.2% of patients after the assay results were known. The most common change was from CHT to HT in 51.4% of cases. In the low RS group, all post-Oncotype DX treatment decisions were HT only. In the high RS group, all post-Oncotype DX treatment decisions were CHT. In the intermediate RS group, treatment decisions were HT only in 55% and CHT in 45% of the cases. There are several prospective and retrospective studies regarding the assay's impact on treatment decision of early breast cancer patients [8-18]. The studies showed that changes in treatment recommendations were in 19%-44% of early breast cancer cases. Our analysis demonstrated that treatment decisions were changed in more than half of the cases, and most of them were CHT to HT. This may have been the case because Korean oncologists had to make a treatment decision on the basis of the national treatment guideline by HIRA and tended to over-treat the patients in treatment decision making for ER-positive, node-negative breast cancer than other countries.

In Korea, neither the national health insurance nor private health insurance covers the Oncotype DX test because the assay is performed abroad. Therefore, the cost of the test for breast cancer patients is burdensome, whether they have private health insurance or not. Although the effective antiemetic and growth factor support medications have contributed to improved tolerability of regimens, chemotherapy still has the potential short-term and long-term toxicities. In addition, empirical use of adjuvant chemotherapy in early breast cancer can also lead to substantially increased costs for patient and the health care system. The result of the present study showed that more than 50% of early breast cancer patients were able to avoid the unnecessary adjuvant cytotoxic chemotherapy.

Histologic grade, presence of micrometastases, Ki-67, and presence of lymphatic invasion were statistically associated with the categorized RS groups in this study. Several recent studies showed that specific pathologic features, such as histologic features, mitotic count, and receptor expression, correlate with the assay results [13,20-23]. Despite these correlations, the assay more accurately predicted the risk of recurrence than clinicopathologic characteristics alone [24]. Furthermore, the 21-gene signature has been the only factor to date that has shown prospective validation evidence of predicting chemotherapy benefits [2]. However, if Oncotype DX assay is not available, treatment decision can be based on these pathologic features.

One of the limitations of our study is that we used retrospectively collected data. Furthermore, all treatment decisions were made by each institute independently, and the decisions were not cross-checked by others. In addition, the data was collected from multiple centers and pathologic results were not reviewed by a central pathologist. Additional confounding factors include one patient with history of contralateral breast cancer. Finally, the clinical significance of intermediate RS tumors has not proven yet. The prospective Trial Assigning IndividuaLized Options for Treatment (TAILORx) study was designed in efforts to evaluate the chemotherapy benefits in patients with intermediate RS. The results of this study will provide more information on the benefit of adjuvant chemotherapy in patients with intermediate RS [25].

Conclusion

Our study is the first study showing the impact of the Oncotype DX assay on treatment decisions for early breast cancer patients in Korea. The assay has a significant impact on treatment decision-making, resulting in HT for all low RS patients and CHT for those with high recurrence score results. The test reduces chemotherapy use in more than half of ER-positive, early breast cancer patients, an effect that ultimately may have favorable health-economic implications if the assay becomes more broadly available in Korea.

Conflicts of Interest

Conflict of interest relevant to this article was not reported.

References

1. Jung KW, Won YJ, Kong HJ, Oh CM, Seo HG, Lee JS. Cancer statistics in Korea: incidence, mortality, survival and prevalence in 2010. Cancer Res Treat. 2013;45:1-14.
2. Paik S, Tang G, Shak S, Kim C, Baker J, Kim W, et al. Gene expression and benefit of chemotherapy in women with node-negative, estrogen receptor-positive breast cancer. J Clin Oncol. 2006;24:3726-34.
3. Paik S, Shak S, Tang G, Kim C, Baker J, Cronin M, et al. A multigene assay to predict recurrence of tamoxifen-treated, node-negative breast cancer. N Engl J Med. 2004;351:2817-26.
4. Harris L, Fritsche H, Mennel R, Norton L, Ravdin P, Taube S, et al. American Society of Clinical Oncology 2007 update of recommendations for the use of tumor markers in breast cancer. J Clin Oncol. 2007;25:5287-312.
5. National Comprehensive Cancer Network Practice Guidelines in Oncology. Breast Cancer (version v3, 2013) [Internet]. Fort Washington: National Comprehensive Cancer Network; 2013 [cited 2013 Aug 1]. Available from: http://www.NCCN.org.
6. Aebi S, Davidson T, Gruber G, Cardoso F; ESMO Guidelines Working Group. Primary breastcancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol. 2011;22 Suppl 6:vi12-24.
7. Goldhirsch A, Wood WC, Coates AS, Gelber RD, Thurlimann B, Senn HJ, et al. Strategies for subtypes: dealing with the diversity of breast cancer: highlights of the St. Gallen International Expert Consensus on the Primary Therapy of Early Breast Cancer 2011. Ann Oncol. 2011;22:1736-47.
8. Lo SS, Mumby PB, Norton J, Rychlik K, Smerage J, Kash J, et al. Prospective multicenter study of the impact of the 21-gene recurrence score assay on medical oncologist and patient adjuvant breast cancer treatment selection. J Clin Oncol. 2010;28:1671-6.
9. Geffen DB, Abu-Ghanem S, Sion-Vardy N, Braunstein R, Tokar M, Ariad S, et al. The impact of the 21-gene recurrence score assay on decision making about adjuvant chemotherapy in early-stage estrogen-receptor-positive breast cancer in an oncology practice with a unified treatment policy. Ann Oncol. 2011;22:2381-6.
10. Albanell J, Gonzalez A, Ruiz-Borrego M, Alba E, Garcia-Saenz JA, Corominas JM, et al. Prospective transGEICAM study of the impact of the 21-gene Recurrence Score assay and traditional clinicopathological factors on adjuvant clinical decision making in women with estrogen receptor-positive (ER+) node-negative breast cancer. Ann Oncol. 2012;23:625-31.
11. Ademuyiwa FO, Miller A, O'Connor T, Edge SB, Thorat MA, Sledge GW, et al. The effects of oncotype DX recurrence scores on chemotherapy utilization in a multi-institutional breast cancer cohort. Breast Cancer Res Treat. 2011;126:797-802.
12. Kamal AH, Loprinzi CL, Reynolds C, Dueck AC, Geiger XJ, Ingle JN, et al. Breast medical oncologists' use of standard prognostic factors to predict a 21-gene recurrence score. Oncologist. 2011;16:1359-66.
13. Asad J, Jacobson AF, Estabrook A, Smith SR, Boolbol SK, Feldman SM, et al. Does oncotype DX recurrence score affect the management of patients with early-stage breast cancer? Am J Surg. 2008;196:527-9.
14. Eiermann W, Rezai M, Kummel S, Kuhn T, Warm M, Friedrichs K, et al. The 21-gene recurrence score assay impacts adjuvant therapy recommendations for ER-positive, node-negative and node-positive early breast cancer resulting in a risk-adapted change in chemotherapy use. Ann Oncol. 2013;24:618-24.
15. Joh JE, Esposito NN, Kiluk JV, Laronga C, Lee MC, Loftus L, et al. The effect of Oncotype DX recurrence score on treatment recommendations for patients with estrogen receptor-positive early stage breast cancer and correlation with estimation of recurrence risk by breast cancer specialists. Oncologist. 2011;16:1520-6.
16. Hornberger J, Cosler LE, Lyman GH. Economic analysis of targeting chemotherapy using a 21-gene RT-PCR assay in lymph-node-negative, estrogen-receptor-positive, early-stage breast cancer. Am J Manag Care. 2005;11:313-24.
17. de Boer RH, Baker C, Speakman D, Chao CY, Yoshizawa C, Mann GB. The impact of a genomic assay (Oncotype DX) on adjuvant treatment recommendations in early breast cancer. Med J Aust. 2013;199:205-8.
18. Biroschak JR, Schwartz GF, Palazzo JP, Toll AD, Brill KL, Jaslow RJ, et al. Impact of Oncotype DX on treatment decisions in ER-positive, node-negative breast cancer with histologic correlation. Breast J. 2013;19:269-75.
19. Tsoi DT, Inoue M, Kelly CM, Verma S, Pritchard KI. Cost-effectiveness analysis of recurrence score-guided treatment using a 21-gene assay in early breast cancer. Oncologist. 2010;15:457-65.
20. Flanagan MB, Dabbs DJ, Brufsky AM, Beriwal S, Bhargava R. Histopathologic variables predict Oncotype DX recurrence score. Mod Pathol. 2008;21:1255-61.
21. Wolf I, Ben-Baruch N, Shapira-Frommer R, Rizel S, Goldberg H, Yaal-Hahoshen N, et al. Association between standard clinical and pathologic characteristics and the 21-gene recurrence score in breast cancer patients: a population-based study. Cancer. 2008;112:731-6.
22. Auerbach J, Kim M, Fineberg S. Can features evaluated in the routine pathologic assessment of lymph node-negative estrogen receptor-positive stage I or II invasive breast cancer be used to predict the Oncotype DX recurrence score? Arch Pathol Lab Med. 2010;134:1697-701.
23. Geradts J, Bean SM, Bentley RC, Barry WT. The oncotype DX recurrence score is correlated with a composite index including routinely reported pathobiologic features. Cancer Invest. 2010;28:969-77.
24. Goldstein LJ, Gray R, Badve S, Childs BH, Yoshizawa C, Rowley S, et al. Prognostic utility of the 21-gene assay in hormone receptor-positive operable breast cancer compared with classical clinicopathologic features. J Clin Oncol. 2008;26:4063-71.
25. Sparano JA. TAILORx: trial assigning individualized options for treatment (Rx). Clin Breast Cancer. 2006;7:347-50.