Investigating The Impact of Polysomy 17 in Breast Cancer Patients Without Amplification Through Meta-Analysis

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ABSTRACT

Since studies regarding the effect of polysomy 17 (P17) in breast cancer cases in some clinical findings are few in number and are in small sample sizes, during the meta-analysis the effects of P17 in patients without amplification on lymph node involvement, estrogen receptor, progesterone receptor and immunohistochemistry were examined. With the aim of researching into the effects of P17 in breast cancer patients, by using the keywords "polysomy 17 breast cancer", the Pubmed literature database was scanned up to June 2017 and 141 studies were accessed. For research into the impact of P17 on immunohistochemistry, lymph node involvement, estrogen receptor, progesterone receptor in breast cancer patients through meta-analysis, 14 of the publications examined were found to be suitable. In cases of publication bias, the trim and fill method was applied. In cases where heterogeneity was determined in the publications the DerSimonian-Laird method was carried out using the random effects model, while when there was homogeneity in the publications, the Mantel Haenszel method was applied using the fixed effects model. As a result of this study, it was observed that in lymph node involvement, P17 was a risk factor in patients without amplification(OR= 1.84, p= 0.001). P17 wasn't a risk factor on estrogen and progesterone receptor in patients without amplification (OR=0.94, p=0.875; OR=0.83, p=0.387). In terms of immunohistochemistry (IHC) levels, it was observed that P17 was a risk factor for immunohistochemistry increase in patients without amplification (IHC[2+, 3+]/IHC[1+,2+,3+] OR=6.15, p< 0.001; IHC[2+]/IHC[1+,2+] OR= 3.06, p= 0.002; IHC[3+]/IHC[1+,3+] OR= 19.92, p< 0.001; IHC[3+]/IHC[2+,3+] OR= 8.29, p< 0.001).

Keywords: Meta Analysis, Polysomy 17, Breast Cancer, HER2, Amplification

ÖZET

Meta-Analiz ile Amplifikasyon Olmayan Meme Kanseri Hastalarında Polizomi 17'nin Etkisinin Aratılması

Meme kanserli olgularda polizomi 17(P17)'nin bazı klinik bulgulardaki etkisine yönelik az sayıda ve küçük örneklem büyüklüklerinde çalışmalar olması nedeniyle meta analizi kapsamında P17'nin amplifikasyon olmayan hastalarda lenf nodu tutulumuna, östrojen reseptör, progesteron reseptör ve immünohistokimya üzerine etkileri incelenmiştir. P17'nin meme kanserli hastalar üzerine etkisinin meta analizi ile araştırılması amacı doğrultusunda "polysomy 17 breast cancer" anahtar sözcükleri kullanılarak, Haziran 2017 tarihine kadar, Pubmed literatür erişim sistemi taranmış ve 141 çalışmaya ulaşılmıştır. P17'nin meme kanserli hastalar üzerine immünohistokimya, lenf nodu tutulumu, östrojen reseptör, progesteron reseptör, üzerine etkisinin meta analizi ile araştırılması için incelenen yayınlardan 14 tanesi uygun bulunmuştur. Yayın yanlılığının olması durumunda trim fill yöntemi uygulandı. Heterojenlik olduğuna karar verilmesi durumunda rastgele etkiler modeli kullanılarak DerSimonian Laird yöntemi uygulanırken, yayınlarda homojenlik olması durumunda sabit etkiler modeli kullanılarak Mantel Haenszel yöntemi uygulandı. Bu çalışma sonucunda, lenf nodu tutulumunda P17'nin amplifikasyon olmayan hastalarda bir risk faktörü olduğu görülmüştür (OR= 1.84, p=0.001). P17'nin amplifikasyon olmayan hastalarda östrojen ve progesteron reseptörleri üzerinde risk faktörü olmadığı görülmüştür (OR= 0.94, p= 0.875; OR= 0.83, p= 0.387). İmmunohistochemistry (IHC) düzeyleri bakımından ise amplifikasyon olmayanlarda P17 immünohistokimyanın artışı yönünde bir risk faktörü olduğu görülmüştür (IHC[2+, 3+]/IHC[1+,2+,3+] OR= 6.15, p< 0.001; IHC[2+]/IHC[1+,2+] OR= 3.06, p= 0.002; IHC[3+]/IHC[1+,3+] OR= 19.92, p< 0.001; IHC[3+]/IHC[2+,3+] OR= 8.29, p< 0.001).

Anahtar Kelimeler: Meta Analiz, , Polizomi 17, Meme kanseri, HER2, Amplifikasyon

INTRODUCTION

Breast cancer is the most frequently diagnosed cancer and the leading cause of cancer death among females, accounting for 23% of the total cancer cases and 14% of the cancer deaths.[1] Worldwide, the ratio of mortality to incidence is about 36%. Because of this relatively favourable prognosis, breast cancer ranks fifth as a cause of death from cancer overall.[2]

Approximately half of all deaths in breast cancer patients in the world occur in low- and middle-income families. Distribution of incidence of breast cancer varies according to geographic, economic, social and cultural factors.[3]

Numerous anomalies including chromosome 17 are seen in breast cancer. Amplification or overexpression of HER-2/neu oncogene is associated with poor prognosis. Moreover, increased CEP17 count in "polysomy 17" (P17) invasive breast cancer series is a frequent finding.[4]

In cases of uncommon illnesses and their related features, meta-analysis applications are frequently-consulted systematic methods of evaluation. Studies regarding the effect of P17 in breast cancer cases in some clinical findings are few in number and are in small sample sizes. For this reason, too, in our study, the effects of P17 in patients without amplification on lymph node involvement, estrogen receptor, progesterone receptor and immunohistochemistry have been examined.

HER2 is a member of the human epidermal growth factor receptor family encoded by a gene located on the long arm of chromosome 17 (17q12–21.32).[4] Amplification of the human epidermal growth factor receptor 2 gene (HER2, official name ERBB2) in chromosome 17q, which indicates poor prognosis but which shows positive activity in anti-HER2 treatments (trastuzumab, pertuzumab, lapatinib), is reported in 15-20% of breast cancer cases.[5] Gene amplification refers to an increase in the copy number of a specific chromosomal region and is commonly linked to overexpression of the affected genes. Well over 90% of HER2-overexpressing breast tumors show focal gains involving the HER2 locus. In contrast, polysomy is defined by the presence of extra copies of one or more whole chromosomes. Although polysomy of chromosome 17 provides an alternative mechanism for increasing HER2 gene dosage, its effect on HER2 expression, other clinicopathologic variables, prognosis, and treatment response is not well established. CEP17 count ('polysomy') is frequently reported in breast cancer. Defined by the relevant authors as an elevated CEP17 count, "polysomy 17" is a common finding in invasive breast cancer series. Using the definition of ≥ 3 CEP17 copies per cell, reported prevalence rates range between 3% and 46%. Despite numerous inconsistencies between the studies, these data provide some indications that elevated CEP17 count ('polysomy') may be associated with unfavorable clinicopathologic variables and poorer prognosis, albeit to a lesser extent than HER2 amplification.[4]

Immunohistochemistry (IHC) and fluorescence in situ hybridization (FISH), are testing methods for HER2. While IHC identifies excessive expression of HER2 protein on the cell surface, FISH determines levels of the HER2 gene. Four scores from 0 to 3+ (0, 1+, 2+ and 3+) are given for results obtained from the IHC test. Only samples with scores of 3+ are considered HER2-positive. While samples with scores of 0 or 1+ are interpreted as HER2-negative, tumours with IHC 2+ are considered as having indefinite (suspect) status and are generally subjected to a confirmatory test such as FISH or chromogenic in situ hybridization (CISH).[6,7]

Estrogen receptor (ER) and progesterone receptor (PR) statuses are also well known prognostic and predictive factors and play a key role in breast cancer outcome and treatment.[8]

MATERIALS AND METHODS

With the aim of researching into the effects of polysomy 17 on lymph node involvement, estrogen receptor, progesterone receptor and immunohistochemistry in breast cancer patients, by using the keywords "polysomy 17 breast cancer", the Pubmed literature database was scanned up to June 2017 and 141 studies were accessed. For research into the impact of polysomy 17 on immunohistochemistry, lymph node involvement, estrogen receptor, progesterone receptor in breast cancer patients through meta-analysis, 14 of the publications examined were found to be suitable for the purpose of our research.

Among these studies, the lymph node involvement, estrogen receptor, progesterone receptor, im-

Table 1. Relevant statistics for meta-analysis in examining the effect of polysomy 17 on lymph node involvement in those without amplification

Study	Polysomy 17*	Her 2 Neg*	Odds ratio	%95 C.I.	z	p	Weights (%)SEM
Orsaria et al- 2015	15/34	49/155	1.708	0.801-3.641			24.68
Huiyong Jiang et al- 2014	27/37	26/72	4.777	2.000-11.407			18.66
Vanden Bempt et al- 2008	27/62	26/67	1.216	0.603-2.456			28.65
Takehisa et al- 2007	9/15	5/16	3.300	0.753-14.469			6.47
Dal Lago et al- 2006	23/37	42/73	1.213	0.539-2.727			21.53
Fixed Effects	101/185	148/383	1.841	1.272-2.663	3.239	0.001	100

*a/n: (number of lymph node involvement positive)/(total number of cases)

munohistochemistry factors having findings without HER2 amplification were included in the study.

While the impact of polysomy 17 was being researched, lymph node involvement, estrogen receptors and progesterone receptors were analysed as having "+" and lacking "-".

While the impact of polysomy 17 on immunohistochemistry was being researched, meta-analysis was carried out by separation into sub-categories as follows: impact of polysomy 17 on cases with immunohistochemistry 3+ or 2+ and those with 1+, impact on cases with immunohistochemistry 2+ and those with 1+, impact on cases with immunohistochemistry 3+ and those with 1+, and impact on cases with immunohistochemistry 3+ and those with 2+.

Prior to meta-analysis, publication bias of the studies was examined with Begg and Egger tests. In cases of publication bias, the trim and fill method was applied. Heterogeneity of the studies was evaluated according to the Cochran Q test, while to determine degree of statistic was employed. In the meta-analyses, the lowest number of studies taken for analysis was 3. In the studies, the value of α was taken as 0.10 for the homogeneity and publication bias tests.

In cases where heterogeneity was determined in the publications following Cochran's Q test, the DerSimonian-Laird method was carried out using the random effects model, while when there was homogeneity in the publications, the Mantel Haenszel method was applied using the fixed effects model.[9] In the statistical analyses, the MedCalc version 16.4 and Stata/SE 14.0 programs were used.

RESULTS

Examination of Impact of Polysomy 17 on Lymph Node Involvement in Patients without Amplification

With the aim of examining the impact of polysomy 17 on lymph node involvement, following the literature review of studies on patients with polysomy 17 and without amplification, 5 studies were found. As a result of the Egger test (p= 0.375) and Begg's test (p= 0.142), it was determined that there was no publication bias. Cochran's Q test revealed that there was no heterogeneity (p= 0.107; I^2= 47.38%).. The results of the meta-analysis carried out to examine the impact of polysomy 17 on lymph node involvement are given in Table 1 and the forest graph is presented in Figure 1(a).

Examination of Impact of Polysomy 17 on Estrogen Receptor in Patients without Amplification

With the aim of examining the impact of polysomy 17 on estrogen receptor, following the literature review of studies on patients with polysomy 17 and without amplification, 5 studies were found. As a result of the Egger test (p= 0.067) and Begg's test (p= 0.142), it was determined that there was publication bias. Due to this publication bias, the trim and fill method was applied. Cochran's Q test revealed that there was heterogeneity (p= 0.021; I^2=57.36%).). The results of the meta-analysis carried out to examine the impact of polysomy 17 on estrogen receptor are given in Table 2 and the forest graph is presented in Figure 1(b).

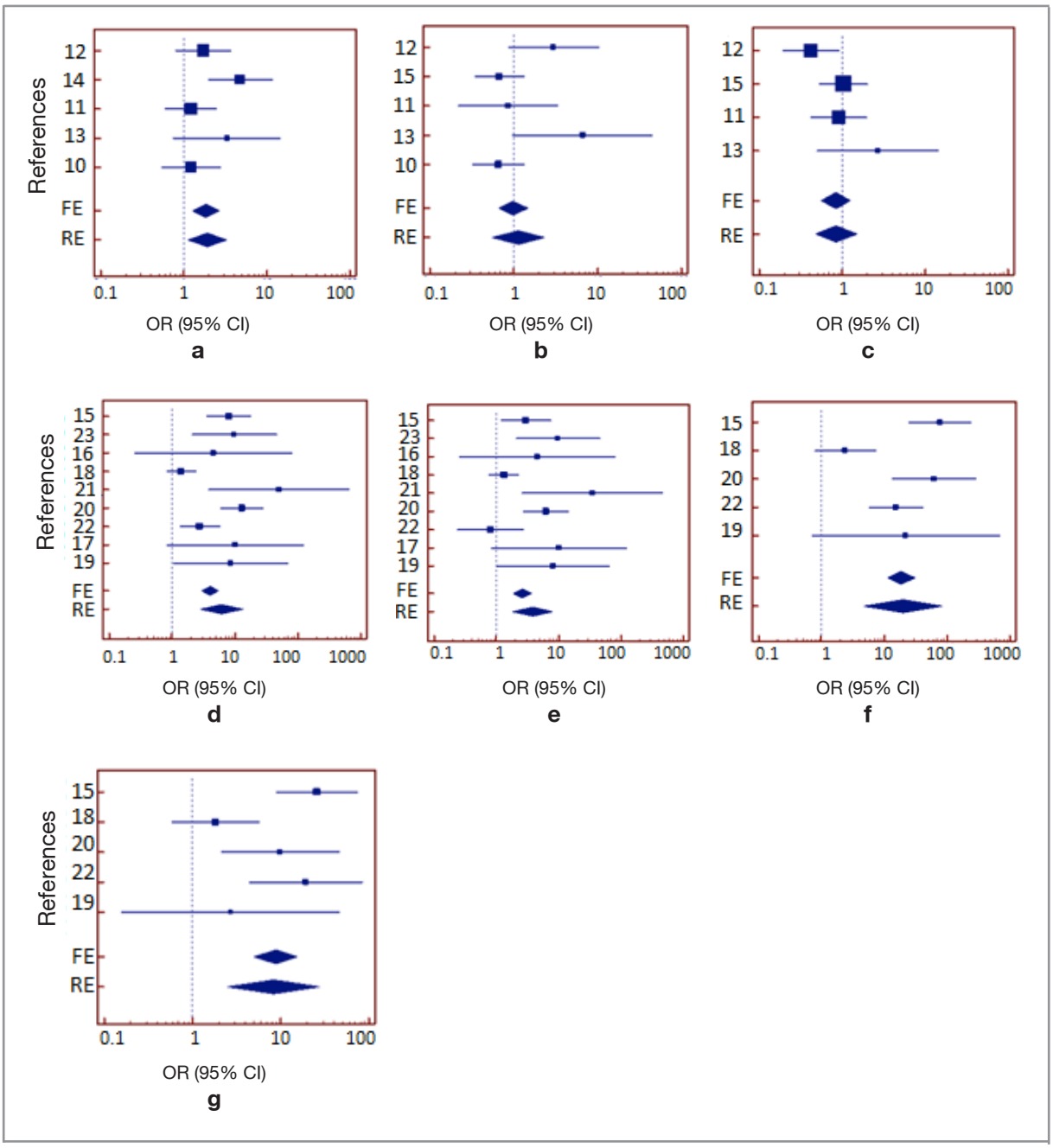

Figure 1. Forest graph **(a)** in examining the effect of polysomy 17 on lymph node involvement, **(b)** in examining the effect of polysomy 17 on estrogen receptor, **(c)** in examining the effect of polysomy 17 on progesterone receptor, **(d)** in examining the effect of polysomy 17 on immunohistochemistry (IHC[2+,3+]/IHC[1+,2+,3+]) in those without amplification, **(e)** in examining the effect of polysomy 17 on immunohistochemistry (IHC[2+]/IHC[1+,2+]) in those without amplification, **(f)** in examining the effect of polysomy 17 on immunohistochemistry (IHC[3+]/IHC[1+,3+]) in those without amplification, **(g)** in examining the effect of polysomy 17 on immunohistochemistry (IHC[3+]/IHC[2+,3+]) in those without amplification

Examination of Impact of Polysomy 17 on Progesterone Receptor in Patients without Amplification

With the aim of examining the impact of polysomy 17 on progesterone receptor, following the literature review of studies on patients with polysomy 17 and without amplification, 4 studies were found. As a result of the Egger test (p= 0.518) and Begg's test (p= 1.00), it was determined that there was no publication bias. Cochran's Q test revealed that there was no heterogeneity (p= 0.148; I^2= 43.76%). The results of the meta-analysis carried out to ex-

Table 2. Relevant statistics for meta-analysis in examining the effect of polysomy 17 on estrogen receptor in those without amplification

Study	Polysomy 17*	Her 2 Neg*	Odds ratio	%95 C.I.	z	p	Weights (%) REM
Orsaria et al- 2015	41/44	142/173	2.984	0.868-10.259			17.75
Liu et al- 2014	32/48	172/230	0.674	0.345-1.318			28.42
Vanden Bempt et al- 2008	4/62	5/67	0.855	0.219-3.341			15.91
Takehisa et al- 2007	6/11	2/13	6.600	0.970-44.927			10.14
Dal Lago et al- 2006	36/54	91/121	0.659	0.327-1.328			27.77
Random Effects (Trim fill was applied)	119/219	412/604	0.940	-0.816-0.695	-0.157	0.875	100

*a/n: (the number of estrogen receptor positive)/(total number of cases)

amine the impact of polysomy 17 on progesterone receptor are given in Table 3 and the forest graph is presented in Figure 1(c).

Examination of Impact of Polysomy 17 on Immunohistochemistry in Patients without Amplification

Although 11 studies were accessed in the literature review carried out to determine polysomy 17 for cases with 3+, 2+ or 1+, in some studies no cases were observed with cells having 2+ or 3+, therefore, in our evaluation, impact of cases with 2+ and above were evaluated according to cases with 1+. 9 studies were found as a result of the literature review conducted. As a result of the Egger test (p= 0.120) and Begg's test (p= 0.677), it was determined that there was no publication bias. Cochran's Q test revealed that there was heterogeneity (p< 0.0001; I^2=76.49%). The results of the meta-analysis carried out to examine the impact of polysomy 17 on immunohistochemistry are given in Table 4 and the forest graph is presented in Figure 1(d).

With the aim of evaluating the effect of polysomy 17 in cases with 2+ according to cases with 1+, 9 studies were found following the literature review carried out with regard to patients with polysomy 17 and no amplification. As a result of the Egger test (p= 0.081) and Begg's test (p= 0.532), it was determined that there was publication bias. Due to this publication bias, the trim and fill method was applied. Cochran's Q test revealed that there was heterogeneity (p= 0.002; I^2=65.75%). The results of the meta-analysis carried out to examine the impact of polysomy 17 on immunohistochemistry are given in Table 5 and the forest graph is presented in Figure 1(e).

With the aim of evaluating the effect of polysomy 17 in cases with 3+ according to cases with 1+, 5 studies were found following the literature review carried out with regard to patients with polysomy

Table 3. Relevant statistics for meta-analysis in examining the effect of polysomy 17 on progesterone receptor in those without amplification

Study	Polysomy 17*	Her 2 Neg*	Odds ratio	%95 C.I.	z	p	Weights (%) SEM
Orsaria et al- 2015	32/45	141/165	0.419	0.193-0.911			27.62
Liu et al- 2014	32/48	152/230	1.026	0.531-1.984			38.31
Vanden Bempt et al- 2008	44/62	49/67	0.898	0.416-1.939			28.11
Takehisa et al- 2007	6/11	4/13	2.700	0.507-14.373			5.96
Fixed Effects	114/166	346/475	0.836	0.557-1.255	-0.864	0.387	100

*a/n: (the number of progesteron receptor positive)/(total number of cases)

Table 4. Relevant statistics for meta-analysis in examining the effect of polysomy 17 on immunohistochemistry (IHC[2+,3+]/IHC[1+,2+,3+]) in those without amplification

Study	Polysomy 17*	Her 2 Neg*	Odds ratio	%95 C.I.	z	p	Weights (%)REM
Liu et al- 2014	40/48	89/230	7.921	3.545-17.703			15.25
Cuadros et al- 2010	6/12	4/43	9.750	2.112-45.006			10.75
Corzo et al- 2007	1/10	1/42	4.556	0.260-79.883			5.32
Torrisia et al- 2007	34/68	139/335	1.140	0.836-2.378			16.80
Yakut et al- 2006	10/12	1/11	50.000	3.83-643.904			6.21
Downs-Kelly et al- 2005	95/112	17/56	12.820	5.944-27.652			15.46
Varshney et al- 2004	12/41	74/568	2.762	1.350-5.651			15.77
Kunitomo et al- 2002	2/13	1/57	10.182	0.848-122.316			6.44
Bose et al- 2001	17/18	44/66	8.500	1.061-68.089			7.98
Random Effects	217/334	370/1408	6.154	2.805-13.499	4.534	<0.001	100

*a/n: (Total number of cases with IHC 2+ and 3+)/(Total number of cases with IHC 1+ and 2+ and 3+)

17 and no amplification. As a result of the Egger test (p= 0.755) and Begg's test (p= 0.624), it was determined that there was no publication bias. Cochran's Q test revealed that there was heterogeneity (p= 0.0002; I^2=81.53%). The results of the meta-analysis carried out to examine the impact of polysomy 17 on immunohistochemistry are given in Table 6 and the forest graph is presented in Figure 1(f).

With the aim of evaluating the effect of polysomy 17 in cases with 3+ according to cases with 2+, 5 studies were found following the literature review carried out with regard to patients with polysomy 17 and no amplification. As a result of the Egger test (p=0.824) and Begg's test (p= 0.327), it was determined that there was no publication bias. Cochran's Q test revealed that there was heterogeneity (p= 0.009; I^2=70.06%). The results of the meta-analysis carried out to examine the impact of polysomy 17 on immunohistochemistry are given in Table 7 and the forest graph is presented in Figure 1(g).

Table 5. Relevant statistics for meta-analysis in examining the effect of polysomy 17 on immunohistochemistry (IHC[2+]/IHC[1+,2+]) in those without amplification

Study	Polysomy 17*	Her 2 Neg*	Odds ratio	%95 C.I.	z	p	Weights (%) REM
Liu et al- 2014	14/22	83/224	2.973	1.197-7.386			15.76
Cuadros et al- 2010	6/12	4/43	9.750	2.112-45.006			10.97
Corzo et al- 2007	1/10	1/42	4.556	0.260-79.883			5.04
Torrisia et al- 2007	29/63	127/323	1.316	0.764-2.267			18.62
Yakut et al- 2006	7/9	1/11	35.000	2.632-465.395			5.85
Downs-Kelly et al- 2005	41/58	15/54	6.271	2.759-14.254			16.49
Varshney et al- 2004	3/32	64/558	0.798	0.236-2.696			13.26
Kunitomo et al- 2002	2/13	1/57	10.182	0.848-122.316			6.20
Bose et al- 2001	16/17	43/65	8.186	1.018-65.829			7.82
Random Effects	119/236	339/1377	3.812	1.820-7.984	3.548	<0.001	100
Random Effects (Trim fill was applied)	119/236	339/1377	3.064	0.416- 1.825	3.116	0.002	100

*a/n : (Number of cases with IHC 2+)/(Total number of cases with IHC 1+ and 2+)

Table 6. Relevant statistics for meta-analysis in examining the effect of polysomy 17 on immunohistochemistry (IHC[3+]/IHC[1+,3+]) in those without amplification

Study	Polysomy 17*	Her 2 Neg*	Odds ratio	%95 C.I.	z	p	Weights (%) REM
Liu et al- 2014	26/34	6/147	76.375	24.471-238.374			22.71
Torrisia et al- 2007	5/39	12/208	2.402	0.796-7.252			22.90
Downs-Kelly et al- 2005	54/71	2/41	61.941	13.520-283.770			20.35
Varshney et al- 2004	9/38	10/504	15.331	5.781-40.658			23.63
Bose et al- 2001	1/2	1/23	22.000	0.719-672.824			10.42
Random Effects	95/184	31/923	19.922	4.839-82.019	4.144	<0.001	100

*a/n : (Number of cases with IHC 3+)/(Total number of cases with IHC 1+ and 3+)

DISCUSSION

When planning and carrying out their studies, researchers come across many restricting factors. Due to these restricting factors, they are forced to work with small sample sizes and their studies may not have the required or adequate strength. The reason for this, besides the underlying factors related to time and cost, may be considered as the fact that the illness or related factor is rarely seen. Meta-analysis application is an approach which is preferred for this and for similar problems and which enables a more general and representative value with regard to population parameter to be achieved.

In this study, too, due to the fact that in the literature there are few studies related with polysomy 17 and that the studies were made with a small number of cases in terms of the subgroups without amplification on prognosis for breast cancer was examined through meta-analysis. In this study, the aim was to examine the impact of polysomy 17 on the lymph node involvement, estrogen receptor, progesterone receptor, immunohistochemistry. The related meta-analysis applications were conducted in categories, namely for those without amplification.

With the aim of examining the impact of polysomy 17 on lymph node involvement, following the literature review of studies on patients with polysomy 17 and without amplification, 5 studies were found. In the studies made by Dal Lago et al.[10], Vanden Bempt et al.[11], Orsaria et al.[12], Takehisa et al.[13], it was stated that polysomy 17 was not a significant risk factor for patients without amplification, whereas Jiang et al.[14] stated that it was a significant risk factor. As a result of the meta-analysis, it was revealed that in cases with positive lymph node involvement, polysomy 17 had a risk factor 1.8 times more significant than for cases with negative lymph node involvement.

For cases without amplification, the literature review carried out with regard to the impact of polysomy 17 on estrogen receptor revealed five studies, namely those by Vanden Bempt et al.[11], Orsaria et al.[12], Liu et al.[15], Takehisa et al.[13], Dal Lago et al.[10]. In each of these studies, it was determined that polysomy 17 was not a significant risk factor for estrogen receptor. As a result of the meta-analysis, it was revealed that in patients without amplification, polysomy 17 was not a significant risk factor in cases with positive estrogen receptor compared to those with negative estrogen receptor.

With the aim of examining the impact of polysomy 17 on progesterone receptor, following the literature review of studies on patients with polysomy 17 and without amplification, 4 studies were found. In the studies made by Vanden Bempt et al.[11], Liu et al.[15], Takehisa et al.[13], it was stated that polysomy 17 was not a significant risk factor for patients without amplification, whereas Orsaria et al.[12] stated that it was a significant risk factor. As a result of the meta-analysis, it was revealed that in patients without amplification, polysomy 17 was not a significant risk factor in cases with positive progesteron receptor compared to those with negative progesteron receptor.

In the research into the impact of polysomy 17 on immunohistochemistry in patients without amplification, in the literature review conducted with

Table 7. Relevant statistics for meta-analysis in examining the effect of polysomy 17 on immunohistochemistry (IHC[3+]/IHC[2+,3+]) in those without amplification

Study	Polysomy 17*	Her 2 Neg*	Odds ratio	%95 C.I.	z	p	Weights (%)REM
Liu et al- 2014	26/40	6/89	25.690	8.964-73.631			24.41
Torrisia et al- 2007	5/34	12/139	1.825	0.596-5.584			23.81
Downs-Kelly et al- 2005	54/95	2/17	9.878	2.138-45.631			20.08
Varshney et al- 2004	9/12	10/74	19.200	4.429-83.240			20.64
Bose et al- 2001	1/17	1/44	2.688	0.158-45.571			11.06
Random Effects	95/198	31/363	8.287	2.543-27.003	3.509	<0.001	100

*a/n : (Number of cases with IHC 3+)/(Total number of cases with IHC 2+ and 3+)

regard to its impact on patients with immunohistochemistry 2+ and above compared to those with immunohistochemistry 1+, 9 studies were accessed. In these studies, whilst those made by Corzo et al.[16], Kunitomo et al.[17], and Torrisia et al.[18] revealed that polysomy 17 was not a significant risk factor for patients without amplification, those made by Liu et al.[15], Bose et al.[19], Downs-Kelly et al.[20], Yakut et al.[21], Varshney et al.[22], and Cuadros et al.[23] stated that it was a significant risk factor. The meta-analysis revealed that in patients without amplification, polysomy 17 had a risk factor 6.1 times more significant for cases with immunohistochemistry 2+ and above in relation to those with immunohistochemistry 1+ in patients without amplification.

In the research into the impact of polysomy 17 on immunohistochemistry in patients without amplification, in the literature review conducted with regard to its impact on patients with immunohistochemistry 2+ compared to those with immunohistochemistry 1+, 9 studies were accessed. In these studies, whilst those made by Corzo et al.[16], Kunitomo et al.[17], Torrisia et al.[18] and Varshney et al.[22] revealed that polysomy 17 was not a significant risk factor for patients without amplification, those made by Liu et al.[15], Bose et al.[19], Downs-Kelly et al.[20], Yakut et al.[21] and Cuadros et al.[23] stated that it was a significant risk factor. The meta-analysis revealed that in patients without amplification, polysomy 17 had a risk factor 3.06 times more significant for cases with immunohistochemistry 2+ in relation to those with immunohistochemistry 1+ in patients without amplification.

In the research into the impact of polysomy 17 on immunohistochemistry in patients without amplification, in the literature review conducted with regard to its impact on patients with immunohistochemistry 3+ compared to those with immunohistochemistry 1+, 5 studies were accessed. In these studies, whilst those made by Torrisia et al.[18] and Bose et al.[19] revealed that polysomy 17 was not a significant risk factor for patients without amplification, those made by Liu et al.[15], Downs-Kelly et al.[20] and Varshney et al.[22] stated that it was a significant risk factor. The meta-analysis revealed that in patients without amplification, polysomy 17 had a risk factor 19.9 times more significant for cases with immunohistochemistry 3+ in relation to those with immunohistochemistry 1+ in patients without amplification.

In the research into the impact of polysomy 17 on immunohistochemistry in patients without amplification, in the literature review conducted with regard to its impact on patients with immunohistochemistry 3+ compared to those with immunohistochemistry 2+, 5 studies were accessed. In these studies, whilst those made by Torrisia et al.[18] and Bose et al.[19] revealed that polysomy 17 was not a significant risk factor for patients without amplification, those made by Liu et al.[15], Downs-Kelly et al.[20] and Varshney et al.[22] stated that it was a significant risk factor. The meta-analysis revealed that in patients without amplification, polysomy 17 had a risk factor 8.2 times more significant for cases with immunohistochemistry 3+ in relation to those with immunohistochemistry 2+ in patients without amplification.

Yakut et al.[21], in their study carried out in 2006, stressed that because the increase in HER-2/neu copy number dependent on numerical increase in chromosome 17 also causes an increase in protein expression, confirmation by a secondary method such as FISH analysis was therefore important in order to prevent false positivity in cases with polysomy 17. This study also shows that polysomy 17 has an effect on immunohistochemistry positivity in patients without amplification.

As a result of this study, when meta-analysis results are evaluated generally, it was observed that in lymph node involvement, polysomy 17 was a risk factor in patients without amplification. In terms of IHC levels, it was observed that polysomy 17 was a risk factor for immunohistochemistry increase in patients without amplification.

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