MEDICAL SCIENCE MONITOR

META-ANALYSIS

e-ISSN 1643-3750
© Med Sci Monit, 2016; 22: 1939-1945
DOI: 10.12659/MSM.896260

Received: 2015.10.13
Accepted: 2015.11.23
Published: 2016.06.08

Association Between BRCA Status and P53 Status in Breast Cancer: A Meta-Analysis

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

ABCDE 1 Lin Peng*
ABCDE 2 Tao Xu*
AEF 3 Ting Long
AFG 1 Huaiquan Zuo

1 Department of Breast Surgery, Affiliated Hospital of Luzhpu Medical College, Luzhou, Sichuan, P.R. China
2 Department of Neurosurgery, The Traditional Chinese Medicine (TCM) Hospital Affiliated with Sichuan Medical University, Luzhou, Sichuan, P.R. China
3 Department of Internal Medicine-Neurology, Affiliated Hospital of Luzhou Medical College, Luzhou, Sichuan, P.R. China

* These authors contributed equally to this work

Corresponding Author: Huaiquan Zuo, e-mail: 512994887@qq.com
Source of support: Departmental sources

Background: Research on BRCA mutation has meaningful clinical implications, such as identifying risk of second primary cancers and risk of hereditary cancers. This study seeks to summarize available data to investigate the association between BRCA status and P53 status by meta-analysis.

Material/Methods: We searched PubMed, Embase, and Cochrane library databases for relevant studies. Meta-analysis was conducted using STATA software. We summarized odds ratios by fixed-effects or random-effects models.

Results: This study included a total of 4288 cases from 16 articles, which including 681 BRCA1 mutation carriers ($BRCA1^{Mut}$), 366 carriers of BRCA2 mutation ($BRCA2^{Mut}$), and 3241 carriers of normal versions of these genes. $BRCA1^{Mut}$ was significantly associated with P53 over-expression compared with $BRCA2^{Mut}$ (OR 1.851, 95% CI=1.393–2.458) or non-carriers (OR=2.503, 95% CI=1.493–4.198). No difference was found between p53 protein expression in $BRCA2^{Mut}$ carriers and non-carriers (OR=0.881, 95% CI=0.670–1.158).

Conclusions: Our meta-analysis suggests that $BRCA1^{Mut}$ breast cancer patients are more likely to have P53 overexpression compared with $BRCA2^{Mut}$ and non-carriers. This information provides valuable information for clinicians who perform related studies in the future.

MeSH Keywords: Genes, BRCA1 • Genes, BRCA2 • Tumor Suppressor Protein p53

Full-text PDF: http://www.medscimonit.com/abstract/index/idArt/896260

1944 1 6 39

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS] [Index Copernicus]

Background

Approximately 5–10% of all breast cancers are hereditary, and germline mutations in at least 10 genes linked to DNA repair have been found to be associated with an increased risk for breast cancer [1,2]. Six genes confer a high risk for hereditary breast cancer: BRCA1, BRCA2, TP53, PTEN, CDH1, and STK11. Germline mutations in BRCA1, *BRCA2*, and P53 are the most common known causes of hereditary breast cancer. BRCA1 and BRCA2 are involved in DNA damage repair and recombination, cell cycle checkpoint control, apoptosis, and transcriptional regulation [3]. P53 is a tumor suppressor that plays a pivotal role in the cellular response to DNA damage by inducing pathways involved in apoptosis, cell cycle arrest, and DNA repair [4,5]. The occurrence of TP53 somatic mutation in breast cancer is well known. Mutations and genetic polymorphisms can alter P53 function and activity, thereby impairing the cellular response to DNA damage [5].

Previous studies of the relationship between BRCA status and p53 status have reported inconsistent results. Several investigations have demonstrated that p53 over-expression is more common in breast tumors associated with BRCA1 mutation than with BRCA2 mutation or non-carriers [6–9]. Others have identified p53 over-expression in tumors with BRCA2 mutation in comparison with non-carriers [10,11]. Conversely, several reports have found no association between p53 over-expression and BRCA status [12,13]. Greater insights into the specific DNA repair mechanism in BRCA mutations and P53 status in breast cancer create more opportunities for effective treatment of patients.

We sought to clarify the relationship between BRCA mutation status and p53 expression status by performing a meta-analysis.

Material and Methods

Publication search

The PubMed, Embase, and Cochrane Library databases were searched for suitable studies published before June 2015. Publications with the following search terms in the title, abstract, or key words were included: TP53, p53, p53 expression, BRCA, BRCA1, BRCA1 mutation, BRCA2, BRCA2 mutation, and breast cancer. We also used these search terms for manual examination of referenced studies. When multiple studies were identified, we evaluated their potential eligibility for inclusion by scanning abstracts and full texts.

Selection and exclusion criteria

The inclusion criteria were: 1) original investigation with evaluation of p53 status in 3 groups (*BRCA1Mut*, *BRCA2Mut*, and non-carriers); 2) included sufficient data to determine odds ratio (OR) and 95% confidence interval (CI); 3) published as an original article in English; 4) breast cancer patients including both hereditary and sporadic; and 5) being a high-quality case-control study (Newcastle-Ottawa Scale (NOS) ≥7 points. The exclusion criteria were: 1) data obtained from animal models; 2) *BRCA1Mut* and *BRCA2Mut* not examined individually; 3) review article or letter; 4) lacking essential data (e.g., number of P53-positive and -negative individuals in each group not separately indicated); and 5) use of duplicate data.

Data extraction

For each of the eligible manuscripts, 2 investigators (PL and XT) independently extracted the following data: first author name; year of publication; country; numbers of *BRCA1Mut* patients with p53(+), *BRCA1Mut* patients with p53(-), *BRCA2Mut* patients with p53(+), *BRCA2Mut* patients with p53(-), non-carrier patients with p53(+), and non-carrier patients with p53(-); method of BRCA testing; and method of p53 testing. Any disagreements were resolved by a third author.

Statistical analysis

Statistical analyses were conducted using STATA software (version 12.0, Stata Corporation). We evaluated the association between P53 status and BRCA status using OR and 95% CI. The χ^2 and I^2 test methods were used to evaluate data heterogeneity in the studies. The fixed-effects model was used when I^2 <50% and p>0.05 for χ^2; otherwise, the random-effects model was used [14].

Results

Study characteristics

A total of 718 articles were identified by initial database searches. After excluding duplicates, laboratory studies, reviews, and other irrelevant studies, 58 reports remained. We then excluded 11 studies that provided only *BRCA1Mut* and P53 data, 6 studies that provided only *BRCA2Mut* and P53 data, 11 studies that contained insufficient data, 9 studies that evaluated *BRCA1* and *2* together, and 5 studies that used animal models. The 16 remaining eligible articles [12,15–29] were subsequently included in the meta-analysis (Figure 1).

Table 1 provides the main parameters of the meta-analysis. The 16 eligible studies were published between 1999 and 2015 and all were case-control studies. A total of 4288 patients were included in this meta-analysis, with 681 *BRCA1Mut* carriers, 366 *BRCA2Mut* carriers, and 3241 non-carriers. All patients came from 1 of 10 countries (Japan, China, Finland,

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS] [Index Copernicus]

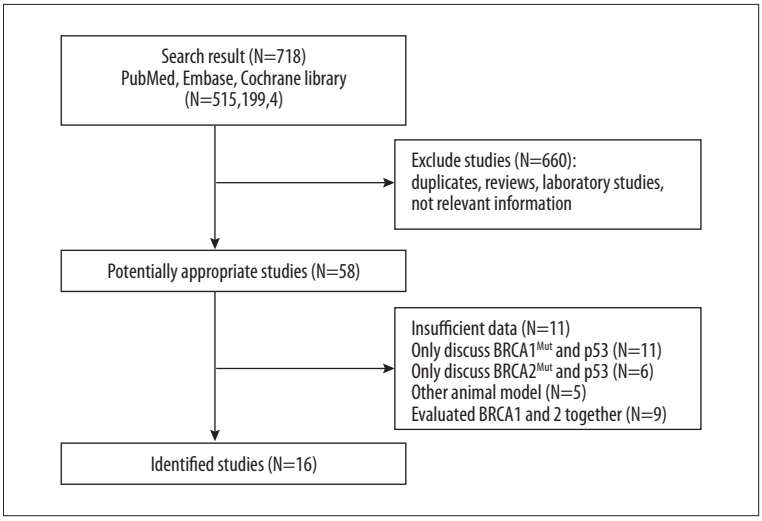

Figure 1. Flow chart used to identify relevant studies. $BRCA1^{Mut}$ – BRCA1 mutation; $BRCA2^{Mut}$ – BRCA2 mutation.

Table 1. Main Characteristics of eligible studies.

Author	Country	Year	BRCA-1		BRCA-2		Noncarries		NOS	Method of BRCA test	Method of P53 test
			P53(+)	P53(–)	P53(+)	P53(–)	P53(+)	P53(–)			
Gretarsdottir S	USA	1998	NA	NA	10	24	62	306	7	FISH	Not mentioned
Lynch BJ	USA	1998	8	14	5	8	2	18	8	Not mentioned	Immunohistochemistry
Noguchi S	Japan	1999	14	5	6	8	29	59	7	SSCP	Immunohistochemistry
Armes JE	Australia	1999	7	3	1	8	9	11	8	PTT	Cycle sequencing, SSCP, sub-cloning
Freneaux P	France	2000	9	7	0	4	13	21	8	Not mentioned	Immunohistochemistry
Lakhani SR	UK	2002	188	137	59	48	126	80	8	Not mentioned	Immunohistochemistry
Kim S	USA	2003	5	1	1	4	19	45	9	Not mentioned	Immunohistochemistry
Palacios	Spain	2003	10	9	2	11	1	26	8	PTT and SSCP	Immunohistochemistry
Berns EM	Netherlands	2003	27	14	7	7	0	0	7	Enzyme-immunoassay	Immunohistochemistry
Sensi E	Italy	2003	6	4	0	9	25	47	7	PTT and SSCP	Immunohistochemistry
Eerola H	Finland	2005	16	27	9	42	32	118	8	Not mentioned	Not mentioned
Musolino A	Italy	2006	7	1	1	4	13	26	7	FISH	FISH
Colombo M	Italy	2008	10	12	1	15	2	31	8	DHLPC	Not mentioned
Lagos-Jaramillo VI	USA	2011	24	19	11	10	33	37	8	Not mentioned	Immunohistochemistry
Xu J	China	2011	18	34	6	22	98	182	7	HRM	Immunohistochemistry
Aleskandarany M	UK	2015	12	33	4	19	492	1278	8	Not mentioned	Immunohistochemistry

SSCP – single strand conformation polymorphism; DHLPC – denaturing high-performance liquid chromatography; PTT – protein truncation test; HRM – high resolution melting; FISH – fluorescence *in situ* hybridization.

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS] [Index Copernicus]

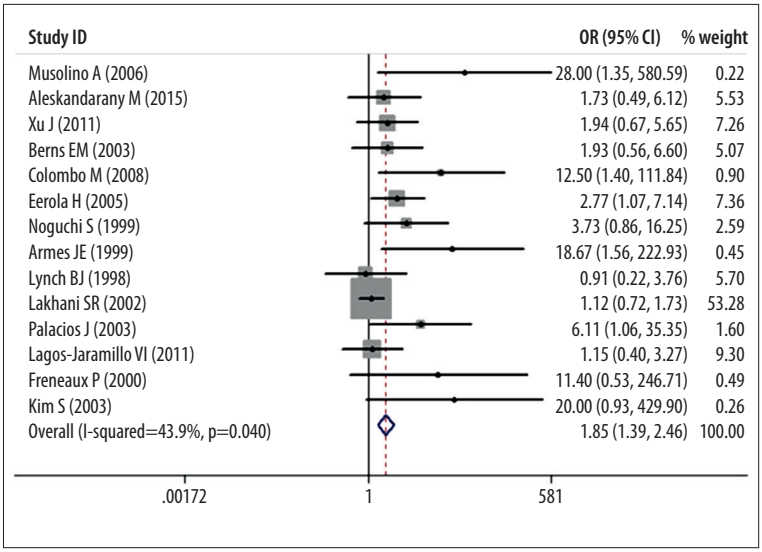

Figure 2. Forest plot of odds ratio for P53 mutations: BRCA1 mutations versus BRCA2 mutations.

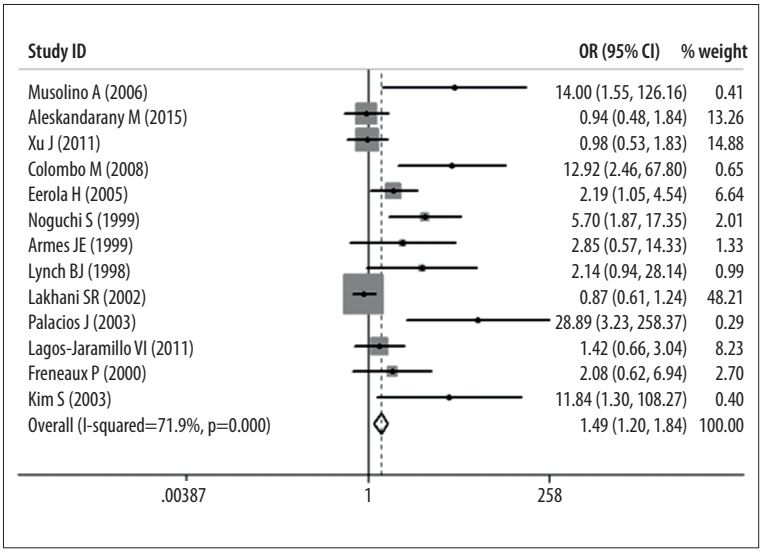

Figure 3. Forest plot of odds ratio for P53 mutations: BRCA1 mutations versus non-carriers.

Spain, The Netherlands, Italy, France, Australia, USA, and the UK). Methods used to assess *BRCA* mutation were fluorescence *in situ* hybridization (FISH), denaturing high-performance liquid chromatography (DHLPC), single-strand conformation polymorphism (SSCP), protein truncation test (PTT), horseradish peroxidase (HRP), and high-resolution melting (HRM). Immunohistochemistry (IHC), SSCP, and FISH were the methods used for p53 detection.

Study results and meta-analysis

We found that BRCA1^{Mut} was significantly associated with p53 overexpression compared with BRCA2^{Mut} (OR=1.929; 95% CI=1.457–2.554; p<0.001 using the random-effects model; Figure 2). There was no obvious evidence of heterogeneity (I^2=46.8%, p=0.024). Compared with the non-carrier group, P53 overexpression was more common in BRCA1^{Mut} carriers (OR=1.509; 95% CI=1.221–1.864; p<0.001 using the random-effects model; Figure 3). Moderate heterogeneity was present for risk difference studies (I^2=70.2%, p<0.001). We found no difference in P53 protein expression between BRCA2^{Mut} carriers and non-carriers (OR=0.842; 95% CI=0.642–1.13; p=0.211 using the fixed-effects model; Figure 4), with no obvious evidence of heterogeneity.

Sensitivity analysis and publication bias

Sensitivity analyses was used to verify the influence of each single study on the overall results in each comparison. The results indicated that 1 study, Lakhani et al. [20], had the most significant impact on the total effect (Figure 5) and it had the most cases of all included studies. However, when the study was removed, the ORs were not substantially changed. The OR was 1.882 (95% CI=1.486–2.427) for excluding the study, and

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS] [Index Copernicus]

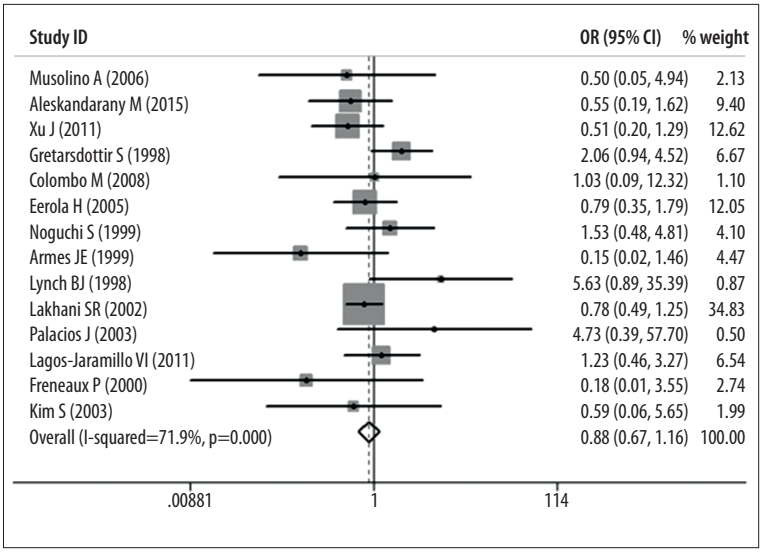

Figure 4. Forest plot of odds ratio for P53 mutations: BRCA2 mutations versus non-carriers.

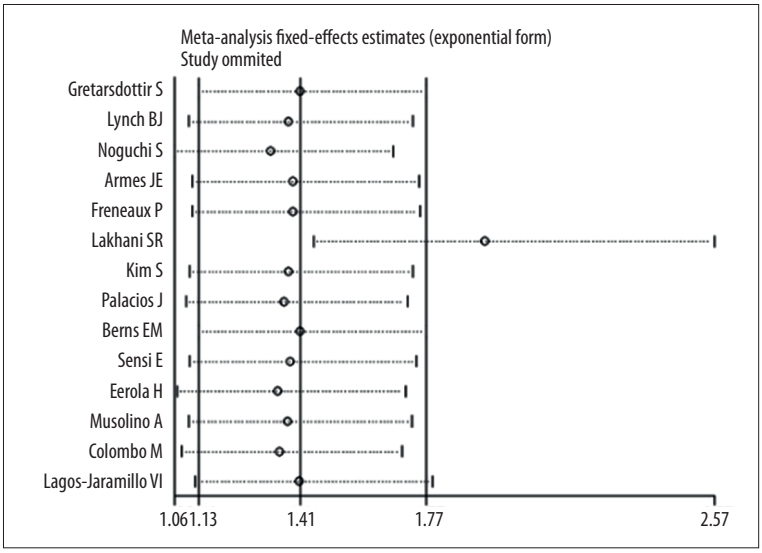

Figure 5. Sensitivity analysis for each individual study.

the previous OR was 1.929 (95% CI=1.457–2.554). Moreover, the heterogeneity was not significantly changed. I^2 was 46.8%, and dropped to 45.6% when the study was removed. The impact of the total combined effect was the largest.

Begg's funnel plot was used to test for potential publication bias. Potential publication biases were found in funnel plot analysis (Figure 6).

Discussion

Our meta-analysis suggests an intimate link between $BRCA1^{Mut}$ and P53 overexpression. $BRCA1^{Mut}$ was significantly associated with P53 overexpression compared with $BRCA2^{Mut}$ and non-carrier genotypes.

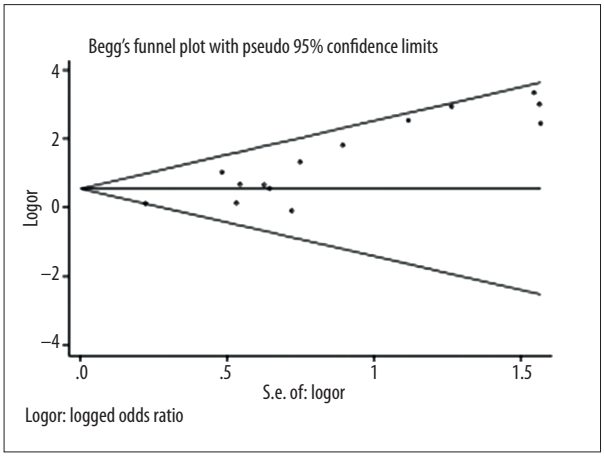

Figure 6. Begg's funnel plot on effectinevess to evaluated the publication bias of the studies.

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS] [Index Copernicus]

P53 mutation is frequently identified in high-grade estrogen receptor-negative, progesterone receptor-negative, basal-like breast cancer with increased genomic instability and poor prognosis [30,31]. Additionally, BRCA1^{Mut} breast cancer typically behaves in a manner similar to that described above [12,28]. Several explanations for these similarities are possible. First, both P53 and BRCA1 are tumor suppressors involved in many cellular processes ranging from DNA double-strand repair to cell-cycle arrest, cells apoptosis, and transcriptional control [32,33]. Second, both P53 and BRCA1 are located on chromosome 17, and simultaneous loss of heterozygosity (LOH) at P53 and BRCA1 may occur via misregulation of chromosome 17. This could result in protein-truncating P53 mutations occurring in cis with the *BRCA1* germline mutation [34]. Finally, LOH at the P53 locus might occur more efficiently in BRCA1-deficient cells because BRCA1 is also involved in the G2-M and spindle assembly checkpoints [35].

Cells possess numerous DNA repair pathways in which several proteins interact with each other in response to damage detection. The spectrum of P53 mutations identified in BRCA1^{Mut}-associated tumors is highly heterogeneous. This may be because of reduced efficiency of DNA repair activity in BRCA1^{Mut} cells. Dong et al. [36] revealed that P53 mediates homologous recombination during DNA repair by inhibiting excessive BRCA1 function via a mechanism of transcriptional regulation. Consistent with this, we found that *BRCA1Mut* was significantly associated with P53 overexpression compared with BRCA2^{Mut} or non-carriers.

BRCA2 and P53 have been extensively studied through genetic tests by some medical centers. However, the relationship between P53 expression and BRCA2^{Mut} is less clear than that for BRCA1^{Mut}. Biesma et al. [37] identified P53 overexpression in approximately 50% of BRCA2^{Mut}, whereas others reported that less than 20% of such tumors had elevated P53 [38]. Additionally, P53 overexpression was not found in BRCA2^{Mut} tumors in 1 report [39]. Our meta-analysis found no difference in P53 protein expression in BRCA2^{Mut} carriers and non-carriers.

- At present, the methods for detection of site-directed mutation of p53 gene include direct method, indirect method, and biosense technique. Direct method is a technique for the detection of pathogenic gene mutations. The premise of direct method is that the normal sequence and structure of the detected genes have been elucidated. Direct sequencing (DS), PCR restriction fragment length polymorphism analysis (PCR-RFLP), single-strand conformation polymorphism analysis (SSCP), and high-resolution melting (HRM) are used in the direct method. Although these methods are used in clinical practice, it is common to have some problems: it is complicated and time-consuming, generates false-positive results, and requires expensive equipment. The indirect method is based on the expression of p53 protein and determines whether there is a point mutation of p53 gene. The indirect method includes immunohistochemistry (IHC), tissue microarray, flow cytometry, and enzyme-linked immunosorbent assay. IHC is widely used in clinical applications, but there are false-positive and false-negative results. Biosense technology has the advantages of good selectivity, high sensitivity, high speed, low cost, high automation, miniaturization, and integration. It provides a fast and simple method for basic medical research and clinical diagnosis.
- The relationship between gene mutation and protein expression has long been controversial. Although there is a certain consistency, there are some differences. Gene mutations were detected in tissues of partial protein-negative expression, while the expression of protein-positive tissue showed no gene changes. The following types of mutations are predicted to escape detection: mutations in noncoding regions, which are estimated to account for a minimum of 10% of pathogenetic BRCA1 and BRCA2 mutations; large deletions undetectable by PCR-based assays; and mutations within the first and last 180 nucleotides of the amplicons analyzed by PTT.

Moderate heterogeneity was found in this study, which is reasonable considering the various races, ages, and different detection methods. The method of BRCA testing – asymmetrical funnel plots – indicated publication bias, perhaps due to diverse reasons (e.g., studies with favorable results are more likely to be published, poor methodological quality of small studies, inclusion of numerous studies without registration, true heterogeneity, artifactual results, and other causes).

There are several limitations to the current study. First, the eligible studies examined were conducted in different populations and were case-control studies; therefore, recall bias and selection bias were inevitable. Second, as only English articles were selected, language bias may be a factor. Third, positive results are more likely to be published than negative findings, and this may also be a source of bias. Fourth, various methods for assessing BRCA1^{Mut} and BRCA2^{Mut} were used in different eligible studies, and different standards were used to define positivity. Fourth, while detection of P53 was predominately via IHC, the antibody source, dilution rate, and cut-off value varied in different studies. Finally, in view of the relationship between protein expression and gene mutation, the present results should be regarded as an approximation.

BRCA1^{Mut} and P53^{Mut} are associated with poor prognosis in breast cancer, and P53 loss rescues the proliferative deficiency of BRCA1^{Mut} cells. Assessing the presence of both mutations could serve as a potential auxiliary biomarker for breast cancer prognosis. The biological characteristics of BRCA1^{Mut} or BRCA2^{Mut} in breast cancers are distinctly different. Our findings suggest that the homologous recombination-deficient-targeting

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS] [Index Copernicus]

therapeutics used in treating p53-deficient tumors might be most effective in those tumors also carrying *BRCA1* mutations.

Conclusions

Our meta-analysis suggests that *BRCA1Mut* breast cancer patients were more likely to have P53 overexpression compared with *BRCA2Mut* and non-carriers. This information may provide valuable guidance for clinicians performing related studies in the future.

Competing interests

The authors declare that they have no competing interests.

References:

1. Walsh T, Casadei S, Coats KH et al: Spectrum of mutations in BRCA1, BRCA2, CHEK2, and TP53 in families at high risk of breast cancer. JAMA, 2006; 295: 1379–88
2. Venkitaraman AR: Cancer susceptibility and the functions of BRCA1 and BRCA2. Cell, 2002; 108(2): 171–82
3. Venkitaraman AR: Cancer suppression by the chromosome custodians, BRCA1 and BRCA2. Science, 2014; 343(6178): 1470–75
4. Brosh R, Rotter V et al: When mutants gain new powers: news from the mutant p53 field. Nat Rev Cancer, 2009; 9: 701–13
5. Isik A, Peker K, Firat D et al: Importance of metastatic lymph node ratio in non-metastatic, lymph node-invaded colon cancer: a clinical trial. Med Sci Monit, 2014; 20: 1369–75
6. Choi DH, Lee MH et al: Incidence of BRCA1 and BRCA2 mutations in young Korean breast cancer patients. J Clin Oncol, 2004; 22(9): 1638–45
7. Valenti F, Ganci F, Fontemaggi G et al: Gain of function mutant p53 proteins cooperate with E2F4 to transcriptionally downregulate RAD17 and BRCA1 gene expression. Oncotarget, 2015; 6(8): 5547–66
8. Lakhani SR, Van De Vijver MJ, Jacquemier J et al: The pathology of familial breast cancer: predictive value of immunohistochemical markers estrogen receptor, progesteronereceptor, HER-2, and p53 in patients with mutations in BRCA1 and BRCA2. J Clin Onco, 2002; 20: 2310–18
9. Palacios J, Honrado E, Osorio A et al: Phenotypic characterization of BRCA1 and BRCA2 tumors based in a tissue microarray study with 37 immunohistochemical markers. Breast Cancer Res Treat, 2005; 90: 5–14
10. Manoukian S, Peissel B, Pensotti V et al: Germline mutations of TP53 and cBRCA2 genes in breast cancer/sarcoma families. Eur J Cancer, 2007; 43(3): 601–6
11. Lynch BJ, Holden JA, Buys SS et al: Pathobiologic characteristics of hereditary breast cancer. Hum Pathol, 1998; 29: 1140–44
12. Aleskandarany M, Caracappa D, Nolan CC et al: DNA damage response markers are differentially expressed in BRCA-mutated breast cancers. Breast Cancer Res Treat, 2015; 150(1): 81–90
13. Xu J, Wang B, Zhang Y et al: Clinical implications for BRCA gene mutation in breast cancer. Mol Biol Rep, 2012; 39(3): 3097–102
14. Egger M, Smith GD, Schneider M, Minder C: Bias in meta-analysis detected by a simple, graphical test. BMJ, 1997; 315: 629–34
15. Gretarsdottir S, Thorlacius S, Valgardsdottir R et al: BRCA2 and p53 mutations in primary breast cancer in relation to geneticinstability. Cancer Res, 1998; 58(5): 859–62
16. Lynch BJ, Holden JA, Buys SS et al: Pathobiologic characteristics of hereditary breast cancer. Hum Pathol, 1998; 29(10): 1140–44
17. Noguchi S, Kasugai T, Miki Y et al: Clinicopathologic analysis of BRCA1- or BRCA2-associated hereditary breast carcinoma in Japanese women. Cancer, 1999; 85: 2200–5
18. Armes JE, Trute L, White D et al: Distinct molecular pathogeneses of early-onset breast cancers in BRCA1 and BRCA2 mutation carriers: a population-based study. Cancer Res, 1999; 59(8): 2011–17
19. Freneaux P, Stoppa-Lyonnet D, Mouret E et al: Low expression of bcl-2 in Brca1-associated breast cancers. Br J Cancer, 2000; 83(10): 1318–22
20. Lakhani SR, Van De, Vijver MJ et al: The pathology of familial breast cancer: predictive value of immunohistochemical markers estrogen receptor, progesteronereceptor, HER-2, and p53 in patients with mutations in BRCA1 and BRCA2. J Clin Oncol, 2002; 20(9): 2310–18
21. Berns EM, Dirkzwager-Kiel MJ, Kuenen-Boumeester V et al: Androgen pathway dysregulation in BRCA1-mutated breast tumors. Breast Cancer Res Treat, 2003; 79(1): 121–27
22. Palacios J, Honrado E, Osorio A et al: Immunohistochemical characteristics defined by tissue microarray of hereditary breast cancer not attributable to BRCA1 or BRCA2mutations: Differences from breast carcinomas arising in BRCA1 and BRCA2 mutation carriers. Clin Cancer Res, 2003; 9(10 Pt 1): 3606–14
23. Kim S, Rimm D, Carter D et al: BRCA status, molecular markers, and clinical variables in early, conservatively managed breast cancer. Breast J, 2003; 9(3): 167–74
24. Sensi E, Tancredi M, Aretini P et al: P53 inactivationis a rare event in familial breast tumors negative for BRCA1and BRCA2 mutations. Breast Cancer Res Treat, 2003; 82(1): 1–9
25. Eerola H, Heikkia P, Tamminen A et al: Relationship of breast tumours in BRCA1 and BRCA2 and mutation-negative breast cancer families. Breast Cancer Res, 2005; 7(4): R465–69
26. Musolino A, Bella MA, Bortesi B et al: BRCA mutations,molecular markers, and clinical variables in early-onset breast cancer: A population-based study. Breast, 2007; 16(3): 280–92
27. Colombo M, Giarola M, Mariani L et al: Cyclin D1 expression analysis in familial breast cancers may discriminateBRCAX from BRCA2-linked cases. Mod Pathol, 2008; 21(10): 1262–70
28. Xu J, Wang B, Zhang Y et al: Clinical implications for BRCA gene mutation in breast cancer. Mol Biol Rep, 2012; 39(3): 3097–102
29. Lagos-Jaramillo VI, Press MF, Ricker CN et al: Pathological characteristics of BRCA-associated breast cancers in Hispanics. Breast Cancer Res Treat, 2011; 130(1): 281–89
30. Rybárová S, Vecanová J, Hodorová I et al: Association between polymorphisms of XRCC1, p53 and MDR1 genes, the expression of their protein products and prognostic significance in human breast cancer. Med Sci Monit, 2011; 17(12): BR354–63
31. Kim HW, Lee HM, Hwang SH et al: Patterns and biologic features of p53 mutation types in Korean breast cancer patients. J Breast Cancer, 2014; 17(1): 1–7
32. Xu B, Kim S, Kastan MB: Involvement of Brca1 in S-phase and G(2)-phase checkpoints after ionizing irradiation. Mol Cell Biol, 2001; 21: 3445–50
33. Seagle BL, Eng KH, Dandapani M et al: Survival of patients with structurally-grouped TP53 mutations in ovarian and breast cancers. Oncotarget, 2015; 6(21): 18641–52
34. Holstege H, Joosse SA, vanOostrom CT et al: High incidence of protein-truncating TP53 mutations in BRCA1-related breast cancer. Cancer Res, 2009; 69(8): 3625–33
35. Deng CX: BRCA1: cell cycle checkpoint, genetic instability, DNA damage response and cancer evolution. Nucleic Acids Res, 2006; 34: 1416–26
36. Dong C, Zhang F, Luo Y et al: p53 suppresses hyper-recombination by modulating BRCA1 function. DNA Repair (Amst), 2015; 33: 60–69
37. Biesma HD, Schouten PC, Lacle MM et al: Copy number profiling by array comparative genomic hybridization identifies frequently occurring BRCA2-like male breast cancer. Genes Chromosomes Cancer, 2015; 54(12): 734–44
38. Lagos-Jaramillo VI, Press MF, Ricker CN et al: Pathological characteristics of BRCA-associated breast cancers in Hispanics. Breast Cancer Res Treat, 2011; 130(1): 281–89
39. Ramalho EA, Silva-Filho JL, Cartaxo MF et al: Assessment of changes in the BRCA2 and P53 genes in breast invasive ductal carcinoma in northeast Brazil. Biol Res, 2014; 47: 3

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS] [Index Copernicus]