Investigation of *BRCA1, BRCA2,* and *RAD51* Gene Expression Levels in Patients with Non-metastatic Prostate Cancer Undergoing Radical Prostatectomy

Authors: *Binnaz Özcan,[1] Selçuk Erdem,[2] Gözde Öztan,[1] Meltem Savran Karadeniz,[3] Yasemin Özlük,[4] Özge Hürdogan,[4] Emre Şentürk,[3] Öner Şanlı,[2] Faruk Özcan,[2] Fatma Savran Oğuz,[1] Hayriye Şentürk Çiftçi[1]

1. Department of Medical Biology, Istanbul Faculty of Medicine, Istanbul University, Türkiye
2. Division of Urologic Oncology, Department of Urology, Istanbul Faculty of Medicine, Istanbul University, Türkiye
3. Department of Anesthesiology and Reanimation, Istanbul Faculty of Medicine, Istanbul University, Türkiye
4. Department of Pathology, Istanbul Faculty of Medicine, Istanbul University, Türkiye

*Correspondence to binnazozcan364@gmail.com

Disclosure: The authors have delcared no conflicts of interest. The authors received approval from the local ethics committee (Clinical Research Ethics Committee of Istanbul University Medical Faculty; approval number: E-29624016-050.99-1672458; date: 8th March 2023).

Acknowledgements: The authors would like to express their gratitude to the Research Fund of Istanbul University for supporting this work. Project No: 39753.

Keywords: Expression, genes, molecular mechanism, prostate cancer (PCa), regulation.

Citation: EMJ Urol. 2025;13[Suppl 2]:14-17. https://doi.org/10.33590/emjurol/EWUY7965

BACKGROUND AND AIMS

Prostate cancer (PCa) is one of the most common malignancies in men and a major cause of cancer-related death worldwide.[1] PCa has a heterogeneous clinical course, with some cases exhibiting low-risk disease, while others exhibit aggressive phenotypes that quickly develop metastasis and treatment resistance. While androgen deprivation therapy is the standard treatment for metastatic cases, castration-resistant PCa is common.[2] The *BRCA1*, *BRCA2*, and *RAD51* genes, which are involved in the repair of DNA double-strand breaks, play a critical role in maintaining genomic stability through homologous recombination.[3] Mutations or changes in expression in these genes are associated with poor prognosis and treatment resistance in many cancers, including PCa.[4] The aim of this study was to determine *BRCA1*, *BRCA2*, and *RAD51* gene expression levels in patients with non-metastatic PCa and to evaluate their association with clinicopathological parameters such as biochemical recurrence (BCR), Gleason score, and age.[5]

METHODS

Fifty patients with non-metastatic PCa who underwent radical prostatectomy between January 2020–March 2023, as well as 20 healthy controls, were included. RNA isolated from peripheral blood was converted to complementary DNA, and *BRCA1*, *BRCA2*, and *RAD51* expression was measured by quantitative reverse transcription PCR using the *GAPDH* reference gene. Statistical analyses used parametric and non-parametric tests, Pearson correlation, and receiver operating characteristic analysis ($p<0.05$ was significant).

RESULTS

BRCA1 and *RAD51* expressions were decreased, and *BRCA2* was increased in patients with PCa compared to controls; the decrease in *BRCA1* was significant ($p<0.001$; Table 1 and Figure 1).

BRCA1 and *RAD51* were increased in patients with BCR, with the *BRCA1* increase demonstrating high significance ($p<0.001$; Table 2 and Figure 2). In patients with low Gleason scores (6–7), expression of all three genes was found to be elevated, with only the *RAD51* increase being significant ($p=0.019$). In patients aged 60 years and older, *BRCA1*, *BRCA2,* and *RAD51* levels

Table 1: Mean *BRCA1*, *BRCA2*, and *RAD51* expression and evaluation in the patient and control groups.

Genes	AVG Ct		AVG ΔCt		$2^{-AVG\ \Delta Ct}$		Fold change	Fold regulation	p
	Patient	Control	Patient	Control	Patient	Control			
BRCA1	33.61	29.72	3.74	1.03	0.074822	0.490220	0.15	−6.55	0.004561
BRCA2	31.79	33.79	2.25	4.82	0.210808	0.035390	5.96	5.96	0.222315
RAD51	27.88	26.70	−1.36	−1.99	2.572195	3.970994	0.65	−1.54	0.802367

$p<0.05$ was considered significant.

AVG: average; Ct: cycle threshold.

Figure 1: Fold change ratio and significance values of the genes examined in the patient (N=50) and control (N=20) groups.

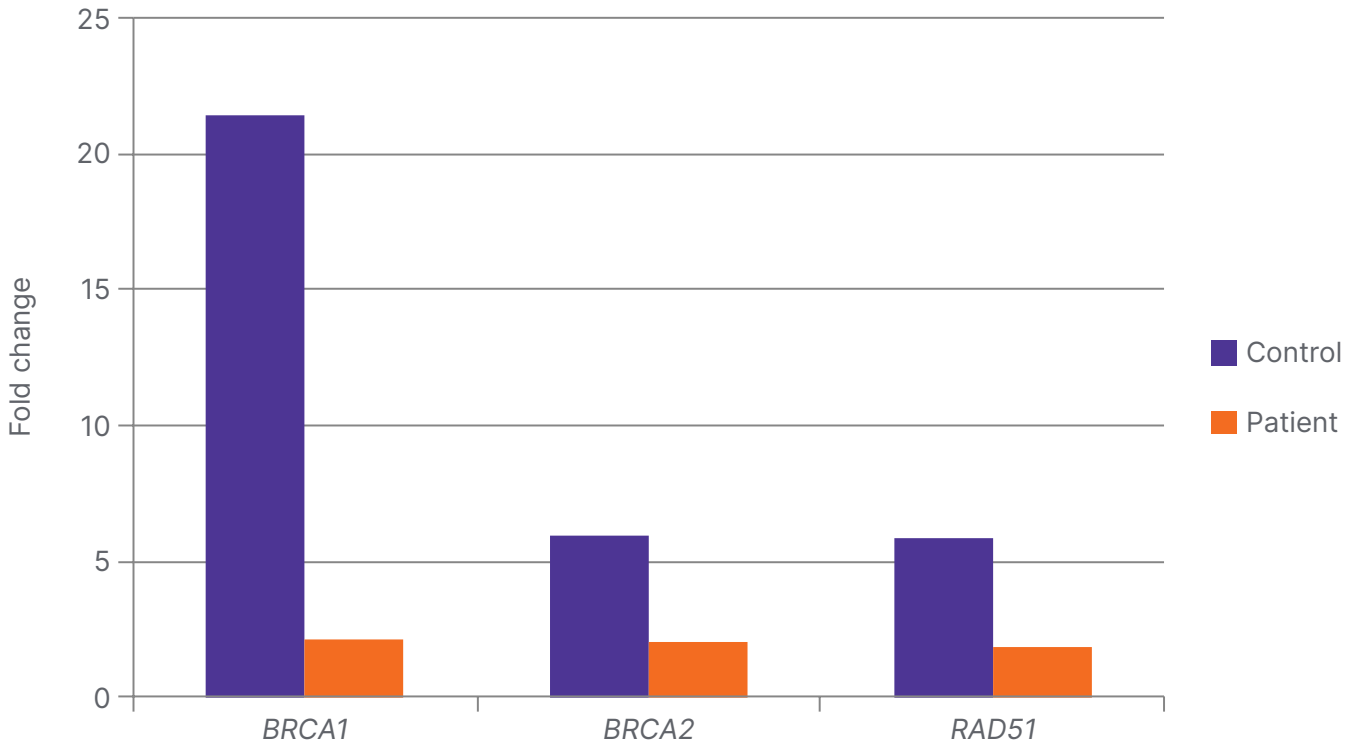


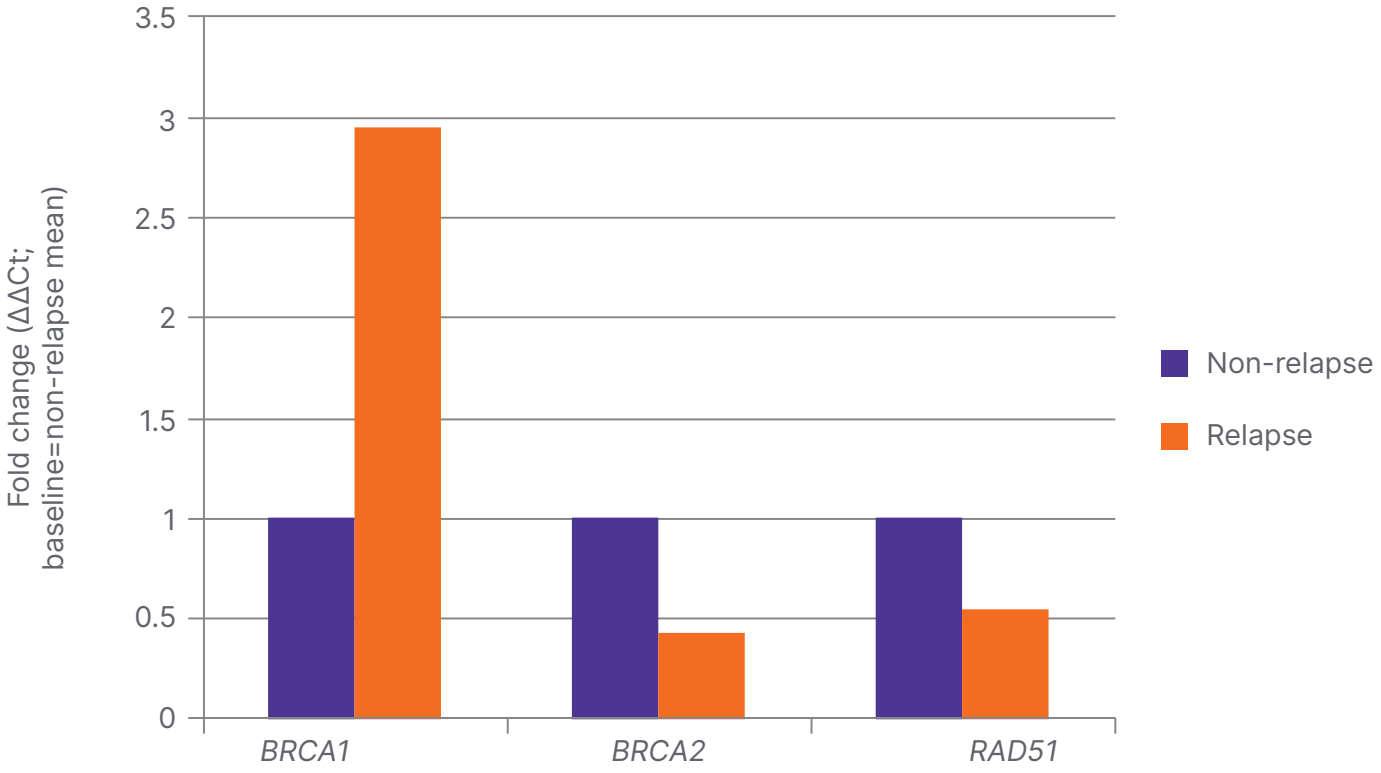
Table 2: Mean *BRCA1*, *BRCA2*, and *RAD51* expression and assessment in patients with and without relapse.

Genes	AVG Ct		AVG ΔCt		$2^{-AVG\ \Delta Ct}$		Fold change	Fold regulation	p
	Relapse group (n=4)	Non-relapse group (n=46)	Relapse group	Non-relapse group	Relapse group	Non-relapse group			
BRCA1	33.39	33.63	0.44	4.03	0.734584	0.061343	11.98	11.98	**0.000478**
BRCA2	31.95	31.78	−0.54	2.49	1.448942	0.178275	8.13	8.13	0.695177
RAD51	27.80	27.89	−4.40	−1.10	21.075574	2.142255	9.84	9.84	0.368219

The bolded p value indicates that it is significant.

AVG: average; Ct: cycle threshold.

Figure 2: Fold change rates and significance values of *BRCA1*, *BRCA2*, and *RAD51* genes in patient groups with and without relapse.



Ct: cycle threshold.

were significantly lower (p=0.012, p<0.001, and p<0.001, respectively). A positive correlation was found between *BRCA1* and *RAD51* (r=0.46; p<0.01). Receiver operating characteristic analysis indicated that the combination of *BRCA1* and *RAD51* exhibited a significant trend in predicting BCR.

DISCUSSION

The increase in *BRCA1* and *RAD51* in patients with BCR suggests that these genes may play a role in tumour aggressiveness and recurrence risk.[6,7] The high expression of *RAD51* in low-grade tumours suggests that DNA repair capacity may be more effective at an early stage, while the differential expression pattern of *BRCA2* may reflect its unique function in the homologous recombination mechanism.[6] The literature suggests that *BRCA2* mutations increase the risk of PCa by two-to-four-fold and are associated with aggressive histology and higher mortality.[8,9] This study is one of the few to demonstrate the association of *BRCA1* and *RAD51* with age, tumour grade, and BCR in non-metastatic PCa in the same cohort.

CONCLUSION

BRCA1, BRCA2, and *RAD51* genes exhibit clinically significant expression changes in non-metastatic PCa, with a strong association with age, Gleason score, and BCR. In particular, the increase in *BRCA1* and *RAD51* in BCR cases, and the decrease in all three genes with age, support the potential of these genes as diagnostic and prognostic biomarkers. Studies with larger series will provide valuable information for genetic screening strategies and personalised treatments.

References

1. Bray F et al. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2024;74(3):229-63.
2. Tilki D et al. EAU-EANM-ESTRO-ESUR-ISUP-SIOG guidelines on prostate cancer. Part II-2024 update: treatment of relapsing and metastatic prostate cancer. Eur Urol. 2024;86(2):164-82.
3. Chen CC et al. Homology-directed repair and the role of BRCA1, BRCA2, and related proteins in genome integrity and cancer. Annu Rev Cancer Biol. 2018;2:313-36.
4. Fan Y et al. Homologous recombination repair gene mutations in prostate cancer: prevalence and clinical value. Adv Ther. 2024;41(6):2196-216.
5. Özcan B et al. Investigation of BRCA1, BRCA2, and RAD51 gene expression levels in non-metastatic prostate cancer patients undergoing radical prostatectomy. Abstract 0124. IURES Congress, 6-9 November, 2025.
6. Zhang W et al. Role of the DNA damage response in prostate cancer formation, progression and treatment. Prostate Cancer Prostatic Dis. 2020;23(1):24-37.
7. Wang Z et al. The emerging roles of Rad51 in cancer and its potential as a therapeutic target. Front Oncol. 2022;12:935593.
8. Giri VN et al. Genetic testing in prostate cancer management: considerations informing primary care. CA Cancer J Clin. 2022;72(4):360-71.
9. Page EC et al. Interim results from the IMPACT study: evidence for prostate-specific antigen screening in BRCA2 mutation carriers. Eur Urol. 2019;76(6):831-42.