

INPLASY PROTOCOL

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Conflicts of interest:
None declared.

INTRODUCTION

Review question / Objective: Gene mutation has been identified as a considerable proportion of genetic factors related to prostate cancer. DNA damage response (DDR) is a signal cascade network aiming to maintain genomic

Prognostic role of DDR genes mutations and their association with the sensitivity of Olaparib in prostate cancer patients

Chen, X¹; Zhang, D²; Xu, X³; Wei, Y⁴; Li, Y⁵; Wu, X⁶; Li, G⁷; Lu, Z⁸; Zhang, X⁹; Ren, X¹⁰; Wang, S¹¹; Qin, C¹².

Review question / Objective: Gene mutation has been identified as a considerable proportion of genetic factors related to prostate cancer. DNA damage response (DDR) is a signal cascade network aiming to maintain genomic integrity in cells. This comprehensive analysis was performed to elucidate the relationship between different DDR gene mutations and prostate cancer.

Condition being studied: Prostate cancer: the relationship between different DDR gene mutations and prostate cancer

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METHODS

Participant or population: Human adult subjects (age >18) positive for any DDR gene mutations.

Intervention: Not applicable.

Comparator: Prostate cancer-affected patients vs general population, prostate cancer patients with DDR gene mutations vs those without DDR gene mutations

Study designs to be included: Observational studies, only prostate cancer were included, other cancers and other prostate diseases were excluded.

Eligibility criteria: To minimize the bias and improve reliability, four reviewers (Xinglin Chen, Xiaohan Ren, Xu Zhang, Yuang Wei) independently screened article titles and abstracts for eligibility.

Information sources: cBioPortal (cBio Cancer Genomics Portal, <https://www.cbioportal.org/>).

Main outcome(s): In total, 72 studies were included and the frequency of 13 DDR genes was analyzed in the research. According to 33 articles focusing on the risk estimates of DDR genes between normal people and PCa patients, DDR genes are more common in prostate cancer patients. (OR=3.6293 95% CI [2.4992; 5.2705]). Results also showed that patients in mutated group have a worse OS and DFS outcome than unmutated group (P<0.05). Among 13 DDR genes, The frequency of 9 DDR genes in prostate cancer is less than 1% and despite different races, the potential gene with the highest frequency is BRCA2 (REM Frequency=0.0426, 95%CI 0.0324 - 0.0541). Moreover, results indicate that the sensitivity of Olaparib, which is a PARB inhibitor, could be enhanced by mutations in genes like ATR, BLM and MLH1 in PCa patients.

Quality assessment / Risk of bias analysis: Four reviewers (Xinglin Chen, Xiaohan Ren, Xu Zhang, Guangyao Li) independently

assessed the quality of studies using the Newcastle-Ottawa Scale (NOS), which consists of eight items covering three domains: selection of study groups, ascertainment of the exposure and outcome, and comparability of groups. Ratings are based on a star system with a maximum score of nine. Studies with 1 to 3 stars are categorized as low quality, 4 to 6 stars as moderate quality and 7 to 9 stars as high quality.

Strategy of data synthesis: All statistical analyses were carried out in the R version 4.0.2 (R Foundation for Statistical Computing, Vienna, Austria; <http://www.R-project.org>) and RevMan v.5.0 software (Cochrane Collaboration, Oxford, UK). Both fixed effects models (FEMs) and random effects models (REMs) were fitted to assess the model types that were most suited to the data. Heterogeneity was evaluated using the Q test and the I² statistic. Statistical significance was set at a p value <0.05, Heterogeneity was evaluated using the Q test and the I² statistic. Statistical significance was set at a p value<0.05. Publication bias was assessed using funnel plots for direct comparisons with 10 or more studies, Sensitivity analysis was carried out to evaluate the influence of individual studies on the summary effect estimate.

Subgroup analysis: We conducted a subgroup analysis of the study and evaluated the frequency of DDR genes in different country PCa patients.

Sensitivity analysis: Sensitivity analysis was carried out to evaluate the influence of individual studies on the summary effect estimate.

Country(ies) involved: China.

Keywords: DDR, prostate cancer, gene mutations, frequency, prognosis.

Contributions of each author:

Author 1 - Xinglin Chen.

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