Reviewer's report

Title: Genotype-phenotype correlations among BRCA1 c.4034delA (4153delA) and c.5266dupC (5382insC) mutations carriers from Latvia

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Reviewer: Khalil Helou

Reviewer's report:

The statistical analysis in the manuscript is appropriate, however a tad too simplistic. The authors should work more on formulation, to make it easier for the reader to understand what they did. There are some red flags in the text.

1. I would recommend that the authors remove the confidence intervals form the first paragraph of the results. If you observed 96 patients with mutations of 2546, that is 96. In this section no inference is made you just summarize the study population, hence no need for confidence interval. The observed number and percentages are sufficient.

2. The second paragraph of the result section on the other hand requires a test statistic. Please present both the raw data and the associated P-value, or confidence interval

“The proportion of BRCA1 founder mutation carriers among breast (X%) and ovarian (Y%) cancer cases tested in 2006-2009 does not differ significantly from the whole population (test statistic and P-vale or X%-Y% and 95% CI).

3. Very long sentence, it is difficult to follow. Additionally, I'm unsure if here odds ratios proper. If I understood correctly the authors compare the prevalence of different mutation among breast and ovarian cancer. I would suggest that the authors present the prevalence (maybe as percentages) and test the difference. You could do the same as in point 2.

However, in our population-based series we observed significant difference in prevalence of c.4034delA and c.5266dupC mutation carriers among breast and ovarian cancer patients with higher prevalence of c.5266dupC carriers among breast cancer patients (Odds Ratio (OR) = 2.76, 95%CI = 1.74 to 4.38, P < 0.0001) and almost equal prevalence of carriers of both described above mutations among ovarian cancer patients (OR = 0.93, 95% CI = 0.59 to 1.46, P = 0.8), which point out the genotype-phenotype correlation of BRCA1 mutations located in different parts of BRCA1 gene.


Analysis of these linear trends has revealed a significant correlation between a specific BRCA1 mutation and age at diagnosis of breast cancers with tendency to younger age of onset for c.5266dupC mutation carriers in comparison with
c.4034delA mutation carriers (#2# = 4.39, with 1 degree of freedom, P = 0.03). I would recommend against using the “correlation”. Maybe indicating that the cumulative incidence differs among the three mutational types is better. The Log Rank should refer to the difference in cumulative incidence and not tendency for younger age at onset. This is an understandable typo, just move test statics and P value.

“We observed significant difference in cumulative incidence of breast cancer (#2= 4.39,df=1, P = 0.03)…. ”

Were you excluded the comparison with patient with no mutation, while the figure plots the incidence rate even for that. This has to be specified as readers might think otherwise.

5. The same as mentioned above.

As a last point I would suggest to try a Cox-regression analysis and perhaps adjust for other clinical characteristics as well.

**Level of interest:** An article of importance in its field

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

I declare that I have no competing interests