BRCA 1-2 Full gene sequence + large rearrangements or panel genetic testing ? Clinica Alemana Breast cancer risk evaluation unit initial experience.

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Introduction

Since the appearance of genetic panel testing and more affordable prices there is a continuous debate in which should be used when testing a patient at risk of being a deleterious genetic mutation carrier
Panel testing offers the opportunity to have more information, with a higher possibility to have a VUS or a " newly described " mutation in which information may be scarce and by that no clear indications on prevention/risk reduction or management.
In a country in which genetic testing haves no legislation or insurance coverage the patient may ask for what he thinks is better, sometime not as the physician asked for.
Working with a genetic counselor may help by doing a thorough pedigree – select the panel to use-, analyzing the family history and educate the patient prior to the testing preparing for the possible results

Hypothesis

If there are more genetic panel testing there should be more VUS and potential misleading information about management of these detected mutations

Methods

Information from genetic testing was analyzed and compared the results among BRCA 1-2 Full gene sequence + large rearrangements and panel testing in our oncological risk assessment unit.
Genetic testing criteria is the one suggested in 2014- 2015 NCCN guidelines
All panel testing were performed in INVITAE

Results

We started the oncological risk evaluation on year 2009; on 2012 we create a decentralized oncological risk evaluation program. On 2014 we incorporated the panel testing as an option.
We have 80 patients tested, 28 BRCA 1-2 Full gene sequence + large rearrangements, 52 panel testing

On full gene sequence 1 VUS (BRCA1 c.179A>G (p.Q60R)), on panel testing 7 VUS (PTEN c. 132C>T (p. Gly44Gly) , BRCA1c.5473G>A(p.Gly1825Arg), CDH1c.2359G>A (p.Val787Ile), MLH1 c.2060G>A (p.Arg687Gln) & MSH6 c.3740C>G (p.Thr1247Ser, BRCA2 c.6000T>C (Silent), BRCA 2 c.6901G>C (p.Glu2301Gln))
Among VUS or non-conventional high-risk genes 4 patients have expressed doubts about their safety and 2 have asked for surgical reduction options. One of them having a PAL B 2 opted for a risk reduction Salpingoophorectomy along with a bilateral risk reduction mastectomy

Conclusions

Panel testing offers the opportunity to have more information when analyzing a patient DNA. Even though this appears to be more attractive than full gene sequence testing one should be cautious about what should we seek for. The genetic counseling is crucial in terms of explaining the benefits and limitations of genetic testing and that a VUS mutation doesn´t means that the person is sick.
Physicians should be cautious applying risk reduction strategies on recently described high-risk mutations
Since we have few cases we cant draw conclusion related to VUS yet.
One palb2 patient opted for risk reduction salpingoophorectomy (performed outside our program), which is not a standard procedure for that mutation so we need to encourage the information given to patients and referral physicians.
We suggest to our patients to choose for the test that gives us the information we need to plan her risk reduction and tailored screening strategies.