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Invited Commentary

WHO HAS TO UNDERGO CANCER GENETIC TESTING? A PERSPECTIVE.

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ABSTRACT

Genetic testing is a medical tool employed to screen changes in genes linked to cancer and other genetic diseases. Genetic tests are available for breast, ovarian, colon, thyroid, and some other cancers and they represent the main tool for early identification of the "risk" subjects.
The choice to undergo genetic testing by a healthy or affected cancer patient with family history of the cancer has to be the fruit of a careful and prudent assessment of the advantages and disadvantages discussed during oncogenetic counselling. The latter, in turn, in the case of a patient's positive and informed choice, must constantly affiliate the genetic testing, in order to preserve the prediction and information role of the test as much as possible.

1. Commentary

Genetic testing looks for specific inherited changes (mutations) in a person's chromosomes, genes, or proteins; is a medical tool employed to screen changes in genes linked to cancer and other genetic diseases. Genetic tests are available for breast, ovarian, colon, thyroid, and some other cancers and they represent the main tool for early identification of the "risk" subjects. The genetic mutations that cause many of the known hereditary cancer syndromes have been identified, and genetic testing can confirm whether a condition is, indeed, the result of an inherited syndrome.Therefore, all information obtained from the genetic tests should be appropriately interpreted and integrated along with the data obtained during oncogenetic counselling, and cannot be considered alone.
Although in the case of a positive outcome the test represents a powerful prevention toolable to implement a specific surveillance program, in case of an uncertain result, the genetic test has numerous limits due to unknown meaning variants for which functional studies are essential to establish the pathogenicity or neutrality of the variant[1,4]. This aspect is complicated by the possibility that it is the combination of multiple variants and not the single variant to determine predisposition to malignancy.
On the other hand, also the negative outcome requires special attention. The negative result could provide a sense of excessive security, as this does not mean there is no risk, but having a risk to develop the neoplasia equal to that of the general population.
In addition, the main limitation of the genetic test is that a negative result is likely to be a false negative, as the patient may be a carrier of disease-causing mutations in known genes possibly involved in the predisposition to cancer, but not yet considered in the field of genetic testing. For example, it is well known, that the cases of breast cancer characterized by the presence of germline pathogenetic mutations in *BRCA1* and *BRCA2* are human genes that produce oncosoppressor genes, these proteins help repair damaged DNA, Together, *BRCA1* and *BRCA2* mutations account for about 20 to 25 percent of hereditary breast cancers (1) and about 5 to 10 percent of *all* breast cancers [2,3], constitute only a small percentage, equal to 15%, of all of breast cancer familial cases [3,4].
About the 5% of susceptibility to hereditary breast cancer cases are related to the mutation of high-penetrance genes such as: *PALB2,TP53, STK11, CDH1* and in particular *PTEN*, acting like as a negative regulator of the cell cycle and concomitant down-regulator of cyclin D1[5]. Others genes such as *CHEK2, ATM, NBN, MRE11A, RAD50* and *BRIP1*instead present

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a low frequency [5].Variants in high and low penetrance genes are clearly attributable to breast cancer, but can be found in other type of neoplasia, including rectal colon cancer, thyroid cancer, ovarian cancer and lung cancer. At the same time, other tumors, such as thyroid and prostate ones, may present similar variants in other genes (i.e., *BRAF* and *Galectin*) [6,7] Considering these observations and the apparent complexity of the analysed disease, it is clear that the choice to undergo genetic testing by a healthy or affected cancer patient with family history of the cancer has to be the fruit of a careful and prudent assessment of the advantages and disadvantages discussed during oncogenetic counselling. The latter, in turn, in the case of a patient's positive and informed choice, must constantly affiliate the genetic testing, in order to preserve the prediction and information role of the test as much as possible.

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