

The Pink Ribbon and the Season of Hope

When women take care of their health, they become their best friend.
Maya Angelou, American poet

What is health? Clearly, it is much more than the absence of pain or disability. According to the World Health Organization, it is a state of complete physical, mental, and social well-being and as one of the fundamental human rights (1). These three elements are interconnected, and we all have experienced or witnessed the negative influence of a physical health issue on the emotional or social aspects of our lives.

Overcoming the Fears

The most impacting diagnosis is, most probably, cancer. In a survey conducted in the United States, 40% of the respondents mentioned cancer as the condition they are most afraid of getting, while the second-ranked, dementia, was feared by only 17.5%.

According to the Center for Disease Control and Prevention, cancer is the first cause of mortality for women aged 45 to 84 and the second cause outside this age range (2). Breast cancer is the most frequent type of cancer diagnosed in women, except for skin cancers. The risk for a woman of being diagnosed with breast cancer at one point in her life is estimated to be 13%, meaning that approximately 1 in 8 women will be in this situation (3). There has been a long and heated debate about the benefit of mammograms screening for breast cancer. Breast cancer in women 50 and older is much more common than breast cancer in women younger than 50 and women ages 50-69 get the most overall benefit. Women ages 50-69 have a 17-33 percent lower risk of dying from breast cancer compared to women who didn't get mammograms as opposed to women ages 39-49 where the benefit is small (0-5 percent) (4, 5). According to a study on Swedish national registries, the overall risk of dying from breast cancer within ten years of diagnosis was 41% lower for women who participated in mammography screening (6). The study included women 40 years or older and did not report differences in mortality in different age groups.

Vaccines – a New Frontier

Following an imaginary time-lapse, if we go one step backward from early diagnosis, we find ourselves in the prevention stage. We would wish to stop cancer from developing, not only to catch it early.

Family history or aging cannot be changed, but avoiding being overweight or alcohol, being physically active and breastfeeding decreases the risk of breast cancer. Hormone replacement therapy or birth control pills should be used upon medical recommendation, in order to balance personal risks and benefits.

A promising prevention modality currently under study is vaccination. There are over 200 clinical trials in different phases, testing vaccines for breast cancer. Cancer cells develop into malignant tumors due to multiple mechanisms that allow them to escape our immune system. Various strategies target tumor neoantigens and various intracellular processes that lead to cancer. Peptides, proteins, carbohydrate antigens, DNA sequences, dendritic cells, modified tumor cells, or parts of them are incorporated in vaccines, mixed with adjuvants, which enhance the immunogenic response. The administration route is adapted to the type of vaccine. The vaccines can be administered intradermally, subcutaneously, intramuscular or intranodal,

according to their composition (7). Before being used for cancer prevention, they must be proven safe and useful. In general, in order to prove their lack of toxicity and evaluate their efficacy, vaccines are initially used in the metastatic setting - to evaluate if they induce a response, or in the adjuvant setting - to study the decrease of the risk of relapse. A promising phase 1 study is currently evaluating the safety and the most effective dose of a vaccine targeting the α -lactalbumin, a protein found in most triple-negative breast cancers. The vaccine is given to non-metastatic patients and a group of cancer-free women at high risk of developing breast cancer (8). The search for the best vaccine continues, and each suboptimal result represents a clue for a future improved vaccine version.

Precise and Personalized Therapy

In the setting of clinical breast cancer, new treatments aim to decrease the risk of relapse, decrease the symptoms, and increase the survival or the time lived disease free. As an example, significant progress has been made recently by using trastuzumab deruxtecan for metastatic HER-2-low tumors and various antibody-drug conjugates for metastatic hormone receptor-positive breast cancers resistant to endocrine treatments (9).

Advances in molecular biology has broaden our knowledge of breast cancer biology, and this knowledge has been translated into novel therapeutic approaches. A recent phase 3 randomized trial evaluated the omission of radiotherapy for patients over 65 years, diagnosed with early-stage hormone receptor-positive breast cancer and treated with breast-conserving surgery and adjuvant endocrine therapy. After a median follow-up of 9 years, overall survival and distant recurrence were almost identical in the two groups. However, the local recurrence rate was ten times lower in the group who received radiotherapy compared to the group who did not (0.9% vs 9.5%) (10). These results support the idea that for some patients, the treatment can be de-escalated by using only one type of postoperative therapy (either endocrine or radiation). At present, it is unclear who the patients that would benefit from this approach are. The ongoing EUROPA trial is expected to address a similar question. This study compares radiation only (partial or whole breast) to endocrine therapy alone, assessing the health-related quality of life and the time to ipsilateral breast tumor recurrence (11). The results might show that for some patients, a five-day radiotherapy treatment might have the same protective effect and fewer side effects than the five-year endocrine therapy, leading to a better quality of life. Since the frequency and type of side effects associated with different treatments are perceived differently, this information may help both physicians and patients in decision making.

Personalized therapies require proper biomarkers for identifying the best therapeutic option for a certain patient: both in terms of indication, planning and delivery of the treatment and also for the follow-up. Currently, the biomarker field is evolving rapidly and a wide variety of tests are becoming available that will hopefully improve the therapeutic results.

Epilogue

Currently, more than 60% of breast cancer patients receive radiotherapy as part of their treatment. In the near future the use of radiotherapy might decrease for some patients with low risk of recurrence but, on the other hand, it might increase in the oligo-metastatic setting, offering the chance of cure to some patients considered until recently incurable.

The season of hope - spring - is here - not only in the calendars!

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