

Editorial – Beyond breast cancer care: exploring pleiotropic effects of nutritional treatment for breast cancer patients

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Breast cancer (BC) represents the most common neoplasia diagnosed worldwide in the general female population¹. It is estimated that, in developed countries, one out of eight women will develop BC during their lifetime^{2,3}. To avoid the diagnosis in an advanced stage, a secondary preventive screening, which consists in bilateral mammogram every two years for women from 50 to 70 years old, was designed by the National Health System⁴. The beneficial effects of BC screening program permit to detect a higher rate of early-stage diagnosis, leading to de-escalation of therapies⁵. In this context, it should be useful an innovative surgical protocol aimed at reducing surgical stress, to provide enhanced recovery after surgery and, in selected cases, to discharge the same day of the surgery^{6,7}. Despite the COVID-19 pandemic, BC specialists designed temporary measures to maintain as much as possible the beneficial effects of early diagnosis and treatment^{1,4,5}.

Thanks to innovations in BC diagnosis, treatments, and care, the BC clinical outcome had a steady improvement in the last 30 years, and it remained consistent even during the lockdown period⁴. Excellent clinical outcomes at early stages and even after far relapse, in a significant number of cases transformed BC in a chronic disease such as chronic kidney disease or metabolic syndrome^{8,9}. In light of these results, our opinion is that BC care research should shift its effort on target therapy, de-escalation therapy, and on the prevention of side effects thanks to a multidisciplinary clinical approach¹⁰.

From a nutritional point of view, the Mediterranean diet adherence in BC patients could promote a beneficial change in human gut microbiota, aiming at reducing the onset of other chronic non-communicable degenerative diseases^{11,12}. Although clinical data are limited, the obesity appears to negatively impact on the BC incidence, severity and mortality^{13,14}. Currently, the guidelines used by the international scientific community are those of the World Cancer Research Fund (WCRF) International but they have not been specifically processed for BC patients¹⁵.

Among nutritional approaches, the most encouraging results in terms of protection from BC development and of recurrences and mortality, were obtained in clinical trials, that used the “prudent” diet and the green-Mediterranean diet^{16,17}. The first nutritional approach is characterized by high intake of fruit, vegetables, whole grains and poultry, while the second one is particularly rich in polyphenols and presents a further restriction, in the consumption of red and processed meats, compared to the traditional Mediterranean diet¹⁸. In fact, nutritional habits, such as the regular consumption of extra-virgin olive oil, rich in polyphenols, can reduce the reactive oxygen species production and at the same time, counteract the low-grade chronic inflammatory status, a well-known risk factor for cancer development and recurrences^{19,20}. The polyphenols are a large family of organic compounds, derived from fruit and vegetables, with important healthy effects such as the anticancer one. Additional advantages of these compounds can be ascribed to their easily extraction from food and agricultural wastes, with a reduction on the environmental impact and with an empower of the circular economy processes²¹.

In estrogen-receptor positive (ER) BC, the obesity in postmenopausal women represents a high-risk factor to develop this cancer because the trunk adipose tissue is related to an increased production of pro-inflammatory cytokines and an alteration of lipid metabolism²². While in the premenopausal women, the obesity presents an inverse correlation with ERBC²³. Moreover, pre-obesity and obesity represent a risk factor to develop triple-negative BC (TNBC), namely a type of BC not dependent on estrogen, progesterone and human epidermal growth factor. In particular, pre-obesity and obesity women with TNBC show an increased death risk of 29% compared to normal weight women²⁴. In Table I, we reported selected studies that investigated the possible link between diet and BC.

Table I. Possible effects of dietary factors on BC risk.

Type of the Study	Ref.	Nutritional intervention focused on	Results
Meta-analysis (15 prospective studies)	31	Fruit, vegetables	RR = 0.89 (95% CI, 0.80-0.99, $p = 0.67$) fruit + vegetables; highest vs. lowest intake. RR = 0.92 (95% CI, 0.86-0.98, $p = 0.36$) fruit; highest vs. lowest intake. RR = 0.99 (95% CI, 0.92-1.06, $p = 0.26$) vegetables; highest vs. lowest intake.
Meta-analysis (13 cohort studies, 3 case-control studies, 2 clinical trials)	32	Red meat	RR = 1.06 (95% CI, 0.99-1.14) unprocessed red meat, highest vs. lowest intake. RR = 1.09 (95% CI, 1.03-1.16) processed red meat, highest vs. lowest intake.
Systematic review (18 studies)	33	Dietary fats	45-78% increased risk of death with enhanced intake of trans fats. HR = 1.20 (95% CI, 1.0-1.45, $p = 0.05$), highest vs. lowest quintile of total fat intake (ER+PR+ BC).
Meta-analysis (18 prospective cohort studies, $n = 1,063,471$)	34	Dairy products	RR = 0.91 (95% CI, 0.80-1.02, $p = 0.003$), milk consumption. RR = 0.85 (95% CI, 0.76-0.95, $p = 0.01$), highest vs. lowest total dairy food. RR = 0.90 (95% CI, 0.83-0.98, $p = 0.111$), highest vs. lowest dairy products.
Meta-analysis (19 prospective studies)	35	Carbohydrate, Glycemic Index	RR = 1.04 (95% CI, 1.00-1.07, $p = 0.19$), 10 units/d for glycemic index. RR = 1.01 (95% CI, 0.98-1.04, $p = 0.07$), 50 units/d for glycemic load. RR = 1.00 (95% CI, 0.96-1.05, $p = 0.01$), 50 g/d for carbohydrate intake.
Meta-analysis (18 prospective studies)	36	Isoflavones	RR = 0.89 (95% CI, 0.79-0.99, $p = 0.001$), highest vs. lowest isoflavone intake.

RR: Risk Reduction; HR: Hazard Ratio; CI: Confidence Interval; ER: Estrogen Receptor; PR: Progesteron Receptor.

Currently, BC represents the first diagnosed neoplasia in Italian population and up to a million of women with a previous diagnosis of BC present long-term side effects of its treatments⁴. In this perspective, low costs and green nutritional protocols could prove to be useful for primary and secondary prevention and to improve the long-term outcomes for BC onset and recurrences^{25,26}.

Nowadays, despite of BC represents the first diagnosed neoplasia in Italian population, in the last 20 years the treatment and the national screening program promoted a BC steady reduction in mortality with an increase of survivors⁴. It has been calculated that more than 50 000 women receive a diagnosis of BC yearly in Italy with currently up to a million of BC survivors²⁷. Although de-escalating therapy determined a reduction of side effects²⁸, thanks to outcome improvement, in the future a larger population will be at risk of recurrence and long-term side effects of its treatments²⁹. In BC survivors, nutritional support and healthy diet already demonstrated better survival rate (with low-fat diet), lower BC recurrence rate (with diet rich in phytoestrogens), and a reduction in cardiovascular risk³⁰⁻³⁶.

Conflict of Interest

The Authors declare that they have no conflict of interests.

Acknowledgments

We would like to thank Lazio Region and ARSIAL (Regional Agency for Development and Innovation of Lazio Agriculture)-Research project “Food culture well-being and natural cuisine”.

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