

## Garlic (*Allium Sativum*) diet might influence overall survival for metastatic triple-negative breast cancer patients

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### Abstract

Many in vitro and animal studies have reported a relation between garlic intake supplementation and risk cancer prevention. Several studies in humans also reported an inverse association in humans. The protective effect appears to be related to the presence of organosulfur compounds and mainly allyl derivatives from allicin and a nonsulfur compound called allixin. The objective of this study is to test the capacity of garlic to prolong the life of metastatic triple negative breast cancer patients, a type of breast cancer with a bad prognostic whose treatment varies less (lowers the chances of biases) because of the lack of receptors for cancer therapy. The treatment of breast cancer has undergone some major changes over the past few years, ranging away from a mutilating Halsted radical mastectomy, towards breast-conserving procedures. The therapeutic objective in breast cancer is improving the quality of health care through standardized treatment and guidance for the physician in taking an optimal therapeutic decision, but also by providing access to all the potentially relevant information. Nutrition was considered, because giving to body the nutrients it needs, is important for everyone. As a conclusion, radical surgery removes cancerous tumors, but increased immunity and a optimal diet may also contribute to the healing of cancer.

**Keywords:** garlic, metastatic, cancer

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### 1. Introduction

Breast cancer in women is a major health burden worldwide [1], being the primary cause of cancer death among women globally, responsible for 23% of the total new cancer cases and 14% of the total cancer deaths [2]. Prognosis and survival rates for breast cancer vary greatly depending on the cancer type, stage, treatment. There are 4 stages of breast cancer judging by the spread of disease, the metastatic stage being the last, meaning that cancer has spread to distant metastases in different organs [3]. As an initial presentation metastatic breast cancer is uncommon in the industrialised countries occurring in about 6-10% of newly diagnosed cases [4,5] while in Romania, because of the lack of screening and medical education the percentage raises over 60% [6]. This stage is treated with radiation therapy or surgery only for palliative purposes [7].

Triple-negative breast cancers account for 15-25% [8] of all types of breast cancers and are more prevalent in premenopausal women [9,10]. They refer to any breast cancer that does not express the genes for estrogen receptor, progesterone receptor, or do not overexpress Her2/neu [11]. They have a poor prognosis, likely a combination of limited treatment options and inherent aggressiveness, and are characterized by shorter relapse-free survival times, a tendency to develop visceral metastases [12,13,14] and a higher rate of mortality (42.2% vs 28.0%) [11,15]. Because of the lack of genes for receptors early-stage of triple-negative breast cancer is treated only with a combination of surgery, radiation, and neoadjuvant/adjuvant chemotherapy, which can often lead to a good prognosis. However, compared with other breast cancers, patients experience a higher proportion of distant recurrence [15,16]. For advanced stages (metastatic cancer) treatment options are being limited, they vary from sequential single

agent chemotherapy to combination therapy especially for rapidly progressing visceral disease [17,18,19]. Bone metastasis limit survival to about 16 months, liver and brain metastases usually shorten it to no more than 8 respectively 5 months [20,21].

*Allium sativum*, commonly known as garlic, is a species in the onion genus, *Allium* [22]. It is unique because of its high sulfur content. In addition to sulfur, garlic also contains arginine, oligosaccharides, flavonoids, and selenium, all of which may be beneficial to health [23].

A phytoalexin (allixin) first isolated and characterized in 1989, a nonsulfur compound with a  $\gamma$ -pyrone skeleton structure with antioxidant effects, antimicrobial effects [24], antitumor promoting effects, inhibition of aflatoxin B2 DNA binding, inhibitory effect on aflatoxin B1-induced mutagenesis [25]. Allixin showed an antitumor promoting effect in vivo, inhibiting skin tumor formation by the two powerful specific carcinogens, 12-O-tetradecanoylphorbol-13-acetate and 7,12-dimethylbenz (a)anthracene initiated mice [26]. Analogs of this compound have exhibited antitumor promoting effects in vitro experimental conditions.

A sulfur compound alliin (S-allyl-L-cysteine sulfoxide) produces allicin (diallyl thiosulfinate) via the enzyme allinase. Allicin has a thiosulfinate functional group, R-S(O)-S-R and occurs in garlic only in the presence of tissue damage [27]. Ingestion of allicin causes instability and metabolites in the blood like diallyl sulfide, allyl methyl sulfoxide, diallyl disulfide [28,29,30]. Organosulfur compounds have been shown to modulate the activity of glutathione S transferases [31], a family of enzymes important in detoxification of carcinogens, and cytochromes P450 [32], a family of enzymes that activate many chemical carcinogens in experimental animals. Chemical constituents containing allyl groups (allyl methyl trisulfide, allyl methyl disulfide, diallyl trisulfide, and diallyl sulfide) have demonstrated strong inhibition of cancer development in the presence of known tumor promoters including 12-O-tetradecanoylphorbol-13-acetate [33,34] and 7,12-dimethylbenzanthracene [35], and phorbol-myristate-acetate [36], as well as tumor inducers such as 7,12-dimethylbenzanthracene [34] and 1,2-dimethylhydrazine [37,38].

Research has provided evidence of anti-proliferative effects of garlic on human cancer cell lines [39], including induction of apoptosis [40,41,42,43,44], regulation of cell cycle progression [45], and signal transduction modification. Both cellular proliferation [46,47] and immune function appear to be affected [48-49].

## 2. Materials and methods

We have made a prospective study enrolling 20 female patients with metastatic triple negative breast cancer. The criteria were: histologically confirmed breast cancer, incurable, metastatic breast cancer documented by CT, bone scan, MRI, brain metastases only if neurological asymptomatic, life expectancy at least 12 weeks, hepatic ALT, AST <3 times upper limit of normal, creatinine clearance > 60ml/min, no symptomatic congestive heart failure or angina pectoris, no persistent diarrhea, no uncontrolled diabetes mellitus, no active infection and able to ingest food. The minimum age was 43 and the maximum was 79. Each of them gave the agreement in participating the study. At presentation 66% had more than one documented visceral metastases, 75% had multiple metastases (hepatic, bone, lung).

They were split in two groups, a 12 women group with a median age of 52 years, which was given the recommendation of eating 4 regular cloves of raw garlic (4 grams) daily with no time limit, for as long as oral ingestion of garlic could be tolerated (1 in the morning, 2 in the afternoon, one in the evening), and a 8 women group with a median age of 49 which had garlic intolerance or who entirely refused garlic. The metastatic tumors ranged between few millimeters to 5 cm (the latter from the garlic group). All patients received combination chemotherapy doxorubicin and cyclophosphamide every two weeks for four cycles followed by paclitaxel every two weeks for four cycles. All patients followed a normal chemotherapy-specific and cancer-specific diet all their life.

## 3. Results and Discussions

Each patient's survival time are as follows: figure 1 and 2.

The median survival time for all patients was 11,65 months. The median survival time for the garlic diet group was 11,8 while for the non garlic group was 11,45. The mean survival time for all patients was 11,17; the mean survival time for the garlic group was 11,2 while for the non garlic group was 11,125. One major source of bias might be due to the low number

of patients(n=20),another because of the placebo effect. We cannot be certain about every patient's diet. The median garlic group was higher with 4 years than the control group, knowing that this type of cancer is more aggressive as age decreases, we have another bias source.

The patients selection was not random an aspect that might too influence our results

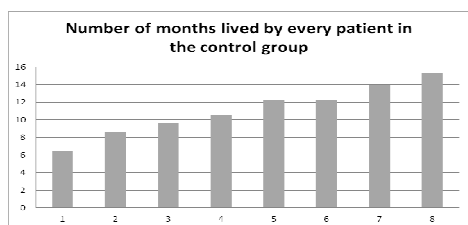


Figure 1. The non garlic group

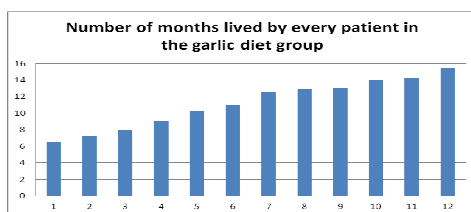


Figure 2. The garlic group

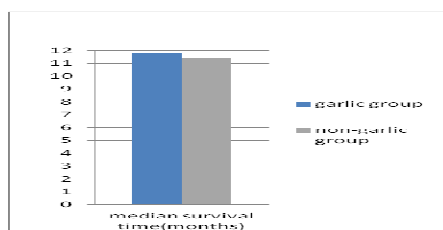


Figure 3. Median survival time per group in months

#### 4. Conclusions

- Radical surgery removes cancerous tumors, but increased immunity and a optimal diet may also contribute to the healing of cancer.
- Results of our study have a small statistical significance but seems that garlic supplementation might slightly delay the final prognostic of these patients. The delay as a median value is less than half a month, while as a mean value is even less than that. A wider and better controlled study is needed to confirm these results.

#### Compliance with Ethics Requirements

Authors declare that they respect the journal's ethics requirements. Authors declare that they have no conflict of interest and all procedures involving human and/or animal subjects (if exists) respect the specific regulations and standards.

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