

IMPROVING THE QUALITY OF LIFE OF BREAST CANCER PATIENTS WITH INTEGRATED MEDICINE TECHNIQUES

ABSTRACT

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Context

As part of an integrated oncological treatment path, complementary medicines can provide support in mitigating the common side effects of conventional oncological treatments in breast cancer.

Objectives

The objective of this project was to involve patients undergoing oncology treatment through interventions specific to Complementary Medicine, to evaluate the impact on improving the quality of life of treated patients and controlling symptoms.

Materials and methods

After an interview to collect informed consent and a multidisciplinary clinical visit by doctors expert in Acupuncture, Phytotherapy and Homeopathy, 61 patients (60 women and one man) diagnosed with breast cancer were enrolled and underwent integrated and complementary medicine interventions including in the project entitled "Improving the quality of life of cancer patients, with the techniques of Complementary Medicine and Integrated Medicine", which was carried out at the hospital of Poggibonsi (SI) Local Health Authority of South-East Tuscany in the period April 2020-May 2021.

Some patients were treated for multiple symptoms. The effectiveness of the treatment was evaluated in patients treated with Complementary Medicines by administering the ESAS2 form (Edmonton Symptom Assessment Scale). Furthermore, a questionnaire on the perceived quality of the service was administered at the end of the treatment. The medical oncologist then re-evaluated the patient's state of health at the end of the treatment.

Results

Of 61 evaluable patients suffering from breast ETP in the observation period from April 2020 to May 2021, 72% of patients responded to the satisfaction questionnaire that the complementary therapies provided were very effective, while in 15% effective and in 13% not very effective. 92% of patients reported improvement in general well-being while for only 8% of patients well-being remained unchanged.

Furthermore, at the end of the therapeutic process, patients are encouraged to follow a lifestyle aimed at preventing the disease from returning.

Patients have released numerous written dedications thanking them for the benefit achieved.

Conclusions

This study demonstrates that Integrated Medicine can help reduce the side effects of conventional cancer treatments and can help patients improve their subjective quality of life. It therefore seems reasonable to offer an integrative approach as part of standard patient care.

KEY WORDS

BREAST CANCER, INTEGRATIVE MEDICINE, QUALITY OF LIFE

INTRODUCTION

Breast cancer remains the most common cancer among women worldwide. Due to the increase in studies and research to defeat this pathology, considerable progress has been achieved in the treatment of the disease. Survival rates for breast cancer are generally increasing worldwide, likely due to earlier diagnoses and improvements in treatment protocols, reaching 91% survival at 5 years and 80% at 15 years after diagnosis.

Local treatments and systemic anticancer therapies lead to improved patient survival outcomes, both disease-free survival and overall survival.³

With improvements in oncology treatment, many patients diagnosed with advanced cancer are now living longer with symptomatic disease and ongoing oncology treatment.⁴⁴

As survival after breast cancer increases, it is important to quantify the impact of a cancer diagnosis and its treatment on long-term health outcomes.^{4,5,43}

As disease diagnosis and treatment have improved dramatically over time, currently in addition to survival, quality of life has become an important outcome measure in breast cancer clinical investigations and survival studies.

Pain is one of the most common, disabling and feared symptoms experienced by patients diagnosed with cancer.^{1,2}

Many survivors, however, continue to experience chronic pain resulting from their cancer treatment that not only negatively impacts their quality of life, but also their daily functions.⁶

Chronic pain can also lead to non-adherence to cancer treatment such as hormone therapies.^{7,8}

Therefore, effective pain management is of fundamental importance throughout the treatment journey.

Cancer affects the whole person involving all dimensions of an individual: mind, body and spirit.

Health-specific quality of life was defined as breast cancer patients' perception of their physical, mental, and social health as influenced by diagnosis, treatment, post-treatment, and survival, assessed using well-validated tools.

Health-Related Quality of Life (HR QoL) is a key measure of patient-reported outcomes and is increasingly considered an important endpoint in cancer clinical trials, where it is used to inform care patient-centered, clinical decision-making and health policy.

Much research has shown that women with breast cancer may experience impaired physical and emotional functioning after cancer treatment due to having to deal with persistent symptoms.

The physical and psychological burden of these symptoms (pain, lymphedema, hair loss, constipation and diarrhea, hot flashes, vaginal dryness, neuropathy, sleep disturbances and fatigue) can negatively impact adherence to cancer treatments.

Some of these side effects are not fully assessed and adequately addressed during routine management of patients. These unmet needs are among the primary reasons patients seek complementary care approaches.

Integrated medicine, defined as the coordinated use of evidence-based complementary practices and conventional care treatments,⁹ includes interventions such as acupuncture, massage, phytotherapy, homeopathy which are increasingly available in oncology centers for management of symptoms and pain.^{10,11,29}

It is estimated that 40% of cancer patients use integrative medicine on an annual basis.¹²

The key guiding principle of integrative medicine is to use these interventions alongside conventional pain manage-

ment approaches (e.g., medications, radiation, injections, and physical therapies) and is not intended to replace conventional interventions.²⁴

In one of the largest studies evaluating quality of life among breast cancer survivors^{30,31,32} in the United States, found that negative predictors associated with lower HR QoL on average 5 years after cancer diagnosis are: a highest cancer stage at diagnosis, the presence of comorbidities, the presence of surgical complications, dissatisfaction with reconstructive breast surgery, and the experience of any recent recurrence, metastasis, or secondary malignancy.³³

Furthermore, it has been widely demonstrated that a prevalent diagnosis of anxiety and depression is associated with lower physical and mental HR QoL.

These studies reinforce the importance of supportive physical and psychological care for breast cancer survivors.^{40,41}

Many studies have reported that HR QoL is also a prognostic indicator for survival in breast cancer patients.

These data therefore confirm that prognostic factors, related to cancer treatment, are important predictors of HR QoL and together with comorbidity are associated with the risk of mortality in breast cancer survivors.

From these considerations we can deduce the need for further research in the field of complementary medicines in order to improve HR QoL in breast cancer survivors.

Several studies show that integrative medicine can help reduce the side effects of conventional cancer treatments and can help patients improve their quality of life.¹³⁻¹⁴

Acupuncture consists of the (non-painful) insertion of very thin needles (sterile and disposable) for therapeutic purposes into particular body sites, called acupuncture sites or acupoints, distributed over the entire body surface. After insertion, the needles can also be stimulated using various techniques: manual, electrostimulation, moxibustion...

The therapy is based on the idea that in the body there is a network of channels, called meridians, through which energy flows that is fundamental for health and life (Table 1). The patency of the channels allows the correct flow of this vital energy, on the contrary their obstruction alters the flow and this can determine the appearance of various kinds of problems. The objective of acupuncture treatment is to free the meridians, in case of obstruction, and re-establish correct flow. This is done by inserting specific needles into certain areas of the body.

The scientific rationale of acupuncture is based on the stimulus that acupuncture produces in the myofascial network at the level of the fibroblasts which activate a mechano-transduction process microtubules and integrins modifying histone modifications through an epigenetic contribution, DNA and non-coding RNA methylation, thus constituting a useful support for anti-inflammatory cytokines and in the regulation/inhibition of NF- κ B and other neurotransmitters that have a useful role in cancer prevention and treatment.^{56,57}

Phytotherapy is understood as the branch of pharmacotherapy that deals with preventing and treating various disorders and diseases through the use of medicinal plants and preparations obtained from them.^{25,26}

The term derives from the Greek $\phi\upsilon\tau\omicron\nu$ (plant) and $\theta\epsilon\rho\alpha\pi\epsilon\upsilon\omega$ (curo), therefore "to cure with plants".

Phytotherapy does not use the single active ingredient - as happens in "classic" or "synthetic" pharmacological therapy - but plants and products obtained from them which contain the phytocomplex which includes many substances.⁴⁵ To do this, phytotherapy uses specific treatments and suitable extraction technologies and creates products in well-defined pharmaceutical forms, purified and standardized in the

chemical constituents responsible for the pharmacological activity attributed to the plant itself and/or its preparations. With homeopathic medicine, substances similar to the agent that produces that type of disease are administered with

the aim of stimulating an adequate immune reaction which strengthens the body's defenses and promotes healing. It aims to treat not so much the pathology itself but the "terrain" on which the disease is acting.^{27,28}

The meridians of acupuncture

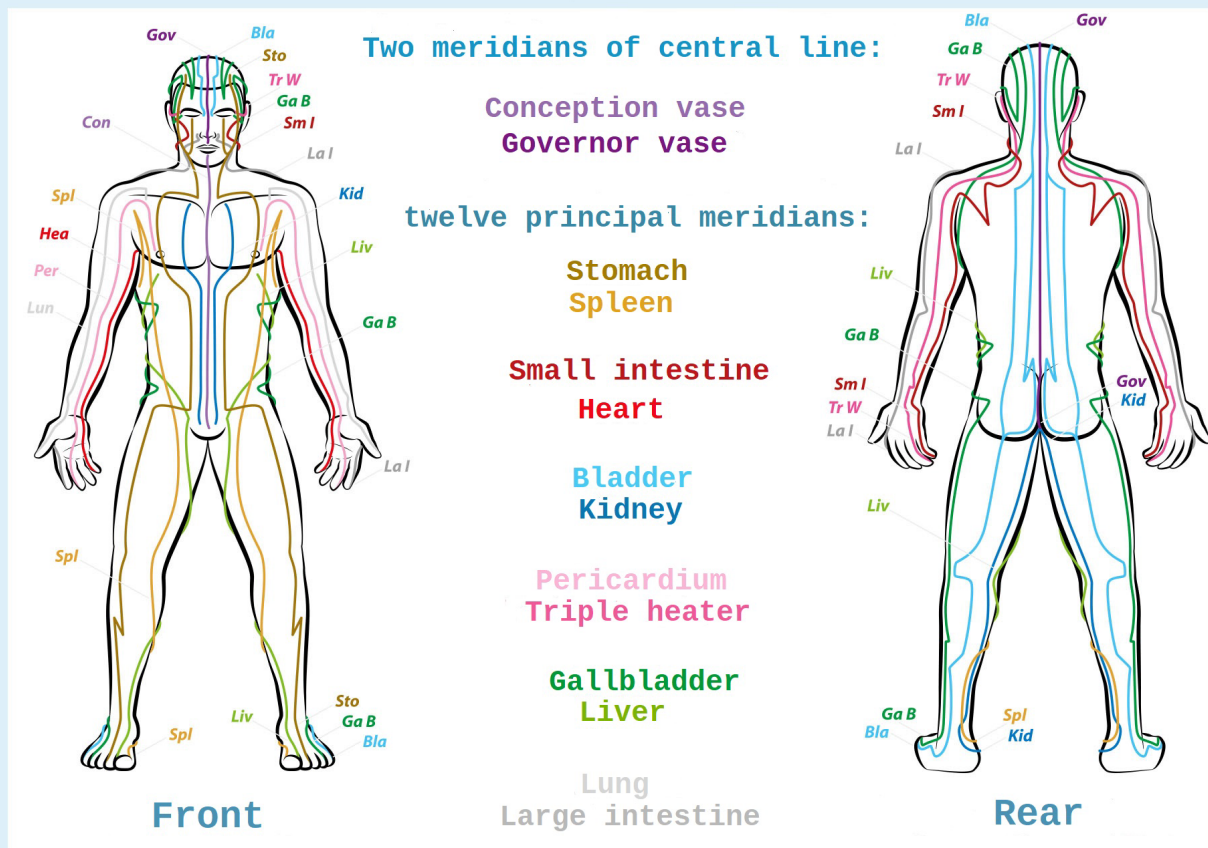


Table 1. The meridians of acupuncture.

PRIMARY OBJECTIVE

Improve the immune response and reduce:

1. inflammation;
2. pain;²⁰
3. gastrointestinal disorders (nausea, vomiting, gastritis);¹⁹
4. fatigue syndrome during chemotherapy (fatigue);^{21/42}
5. anxiety, depression and insomnia;^{15/16/17/22}
6. radiodermatitis (skin lesions resulting from radiotherapy treatment);
7. hot flashes from hormone therapy;^{18/23/34}
8. joint pain related to hormonal therapies

9. joint pain of inflammatory/degenerative origin
10. liver/bone marrow toxicity

MATERIALS AND METHODS

Acupuncture consists of the insertion of thin needles into specific acupoints and causes various effects, among which we remember:

- Analgesia with moderation of the reception and perception of pain;
- Regulation of the immune system through the increase in immune cells, decreasing the inflammatory state;

- Hormonal modulation, acting indirectly on the main hormones;^{52,53,54,55}
- Vasodilation: especially at the level of the skin, muscles and microcirculation, but also at the brain level;
- Modulation of the autonomic nervous system responsible for cardiovascular, respiratory and digestive functions;

Phytotherapy carries out a:

- Preventive, immunomodulatory, antioxidant, detoxifying action;
- Chemoprevention of tumors and recurrences;
- Direct onco-phytotherapeutic action of neoplasms and relapses;
- Chemopotiation and tolerability of conventional protocols;
- Chemoprotection from the jatrogenic effects of classical chemotherapy;⁵⁰
- Radiopotiation and tolerability of conventional treatments;
- Radioprotection from the jatrogenous effects of classical radiotherapy;
- Mycotherapy with anti-tumor and protective action on healthy cells;
- Prevention and support element therapy in anti-blastic treatments.^{35,36,37,38,39}

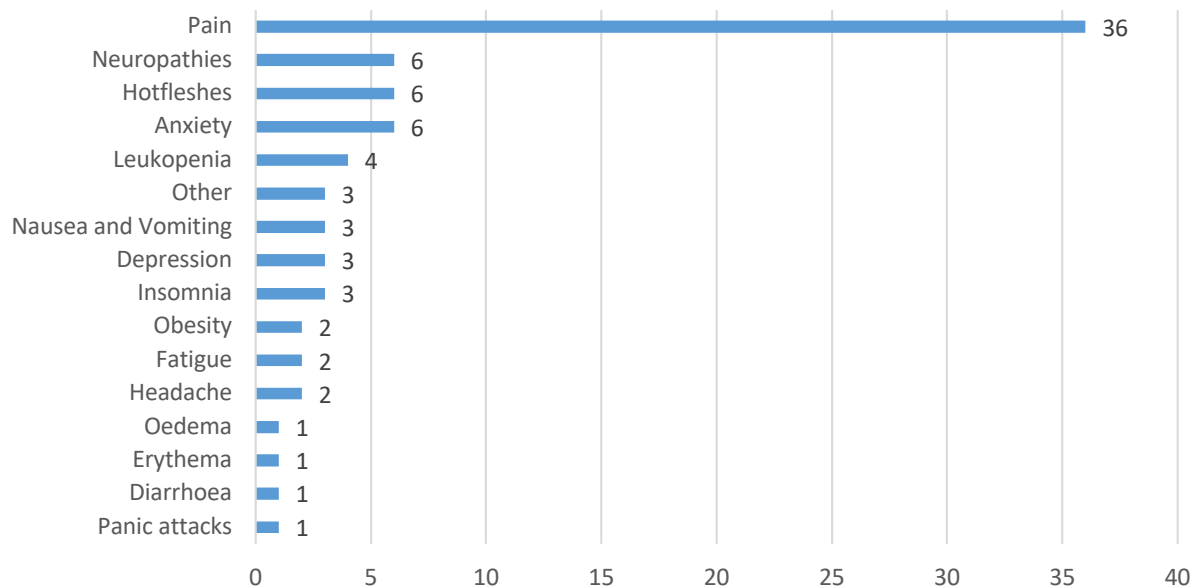
Homeopathy is a therapeutic method based on four fundamental principles:

- The law of similars
- Medicinal specificity
- The infinitesimal dose
- Hering's law ("All healing begins from the inside and proceeds outward, from the head downwards, and in reverse order from how the symptoms of the disease appeared").

There were 61 patients enrolled.

All patients involved sign an informed consent. A total of 16 different symptoms were treated, most of which side effects of cancer or conventional tumor therapies were reported by patients at the start of complementary therapy. By far, the greatest number of patients reported pain (n = 36, 59%), followed by neuropathy/caldane/anxiety (n = 18, 29.5%), leukopenia (n = 4, 6.5%), nausea and vomiting/depression/insomnia (n = 9, 14.7%) and miscellaneous symptoms (obesity/fatigue/migraine/edema/diarrhea/erythema/panic attacks) (n = 13, 21.3%). Some patients were treated for multiple symptoms (Graph 1). The effectiveness of the treatment was evaluated in patients treated with Complementary Medicines by administering the ESAS2 form (Edmonton Symptom Assessment Scale). Furthermore, a questionnaire on the perceived quality of the service was administered at the end of the treatment. The phytotherapeutic oncologist then re-evaluated the patient's state of health at the end of the treatment.

417 acupuncture treatments were carried out from a minimum of 4 to a maximum of 10 treatments per patient.



Graph 1. Symptoms prevalent in the population under study. Presenting symptoms in breast cancer patients.

RESULTS

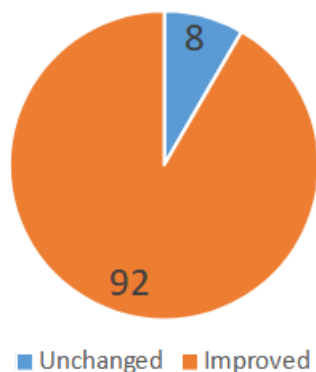
Follow-up of patients was carried out mainly by telepho-

ne and the intention was to occupy as little of the patients' time as possible and minimize inconvenience to them. The effectiveness of the protocol was evaluated through the following questionnaires: ESAS2 (Edmonton Symptom As-

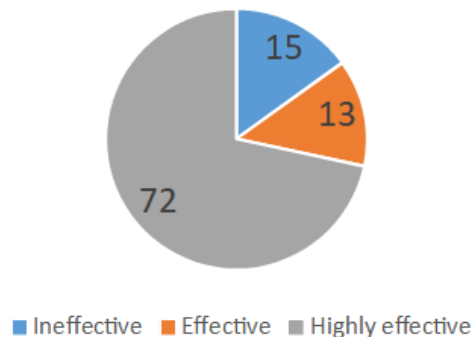
essment Scale 2) and satisfaction questionnaires, to evaluate the quality of life (Graph 2,3). Symptoms were assessed using the ESAS2, documented at the beginning and one month after the start of integrated

treatment on a 10-point scale. The result was recorded as the difference between the final score and the initial score (Graph 4).

Wellness in patients with Breast Cancer

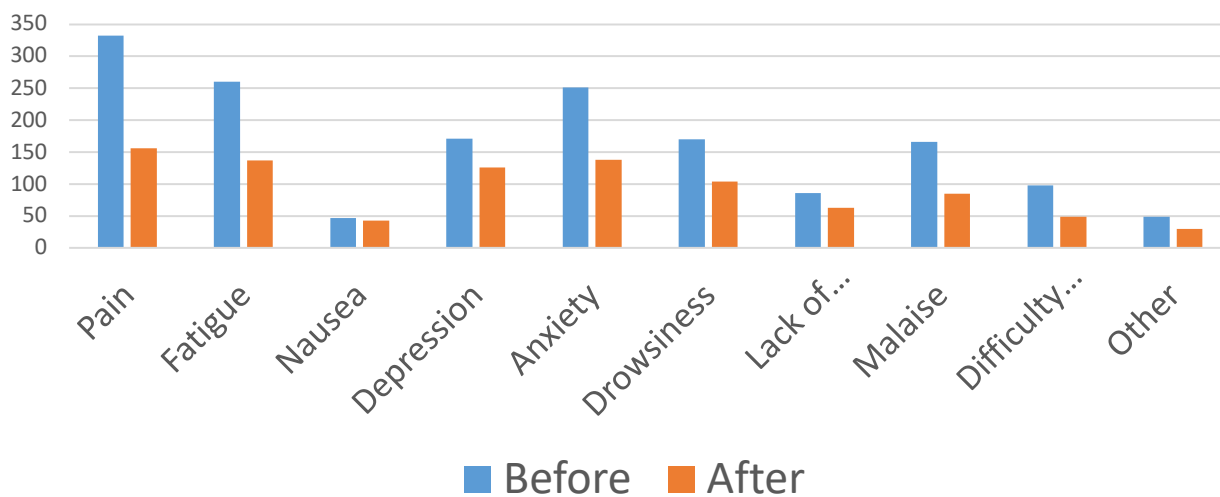


Effectiveness in patients with Breast Cancer



Graphs 2-3. Result of the Satisfaction Questionnaires carried out on 61 patients with breast cancer in the observation period April 2020-May 2021.

Treated symptoms in Breast Cancer



Graph 4. Improvement of symptoms after treatments.

DISCUSSION

Acupuncture can be used not only in the initial phase of the disease but also in the advanced phase, even in the presence of metastases. It is useless to reiterate here that the treatment supports but does not exclude traditional oncological therapy: by reducing the possibility of iatrogenic and side effects of the therapy, it contributes to making the patient "feel good" who can therefore better "adhere" to the necessary therapies, therefore strengthening the therapeutic compliance.

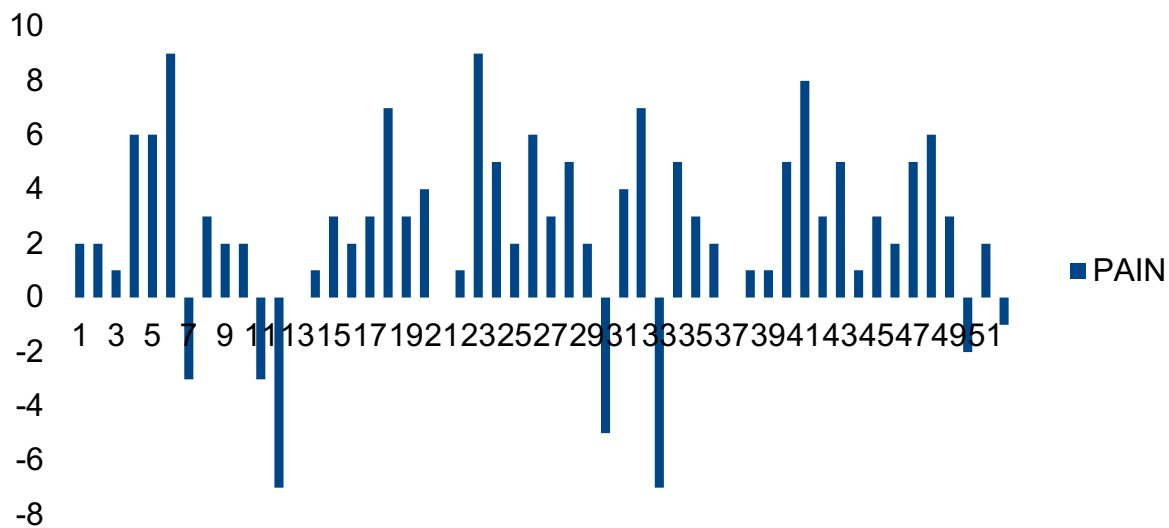
Acupuncture is therefore able to improve cancer pain (Graph 5), tiredness (Graph 6), headache, dry mouth, nausea and vomiting post-operatively or following chemotherapy and radiotherapy. In particular, with regard to the treatment of the side effects of chemotherapy, acupuncture cycles are able to reduce nausea and vomiting with an immediate effectiveness of 80-85% (Graph 7), with positive results also with regards to the state of well-being, asthenia, loss of appetite (Graph 11), insomnia and bowel disorders.⁴⁹ The results regarding nausea at the re-evaluation one month after the suspension of the acupuncture sessions were not satisfactory for 9 out of 21 patients who presented the symptom. It is also particularly useful in cases of anxiety (Graph 9) and depression (Graph 8) which patients are often afflicted with during the progression of the disease. It is also indicated in the nutritional support of patients with anorexia and neoplastic cachexia, also improving intestinal function. A further use of acupuncture is that of the treat-

ment of lymphedema, which often arises after mastectomy and lymphadenectomy in breast tumors with removal of the axillary lymph nodes. In the case of the 2 patients treated for this symptom we found objective improvement in the edema of the upper limb and referred pain with a 3-point decrease in the VAS scale of referred pain; this benefit was maintained for approximately 3 months.

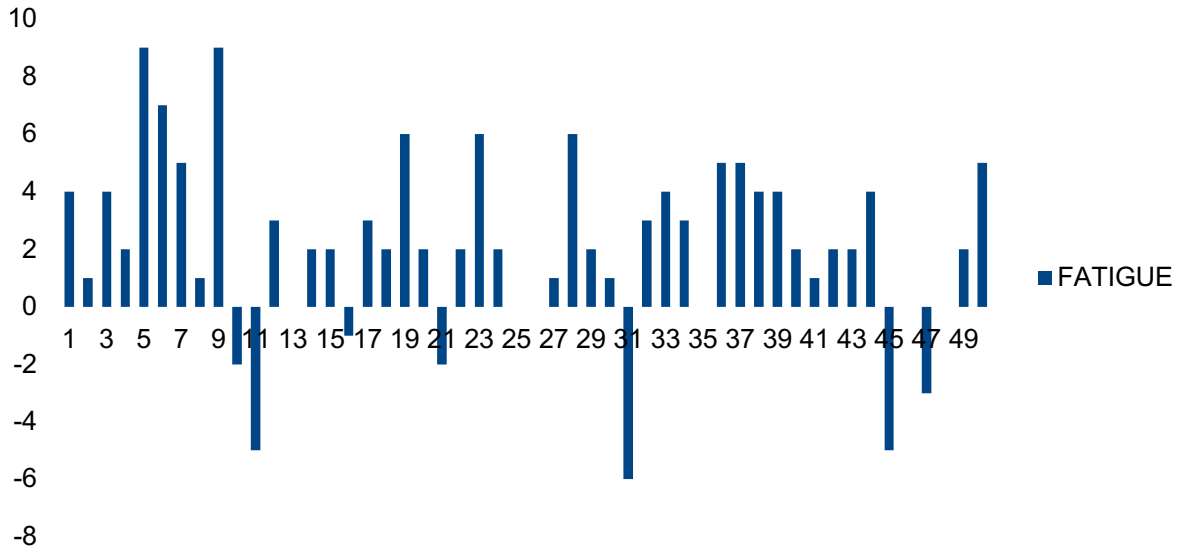
With integrated phytotherapeutic treatments it is possible to improve tolerance to the cytotoxicity of antineoplastic drugs, alleviate neoplastic symptoms, increase the effectiveness of chemotherapy and radiotherapy on tumor cells, inhibit the development of radio and chemoresistance.

The antimetastatic efficacy of herbal medicines was tested in five tumor types: lung, colorectal, stomach, liver and breast cancers. Phytotherapy in the context of TCM (Traditional Chinese Medicine) is widely used.

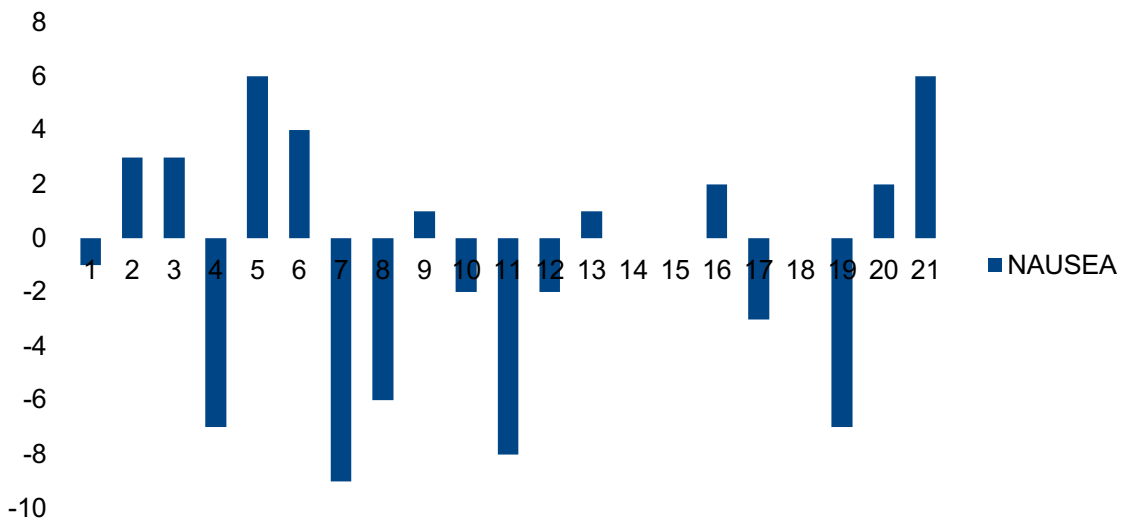
The most frequently reported outcome was improvement in clinical symptoms (63.6%) followed by quality of life (46.7%) and biomarker indices (40.9%). The choice of plants depends on: biological and molecular tumor targets, the pharmacological effect pursued (anti-inflammatory, analgesic, immunomodulatory, hormonal, antiangiogenic, antiproliferative, antimetastatic), integration with the chemotherapeutic agent in use (synergistic enhancement of the antitumor effect, synergy, reversal of chemoresistance, sensitization to radiotherapy, protective action against the adverse effects of the drug) the symptoms that are intended to be alleviated (nausea, fatigue, pain, cachexia, etc.) and neuro-psycho-endocrine-immune rebalancing. (Graph 10,12,13).



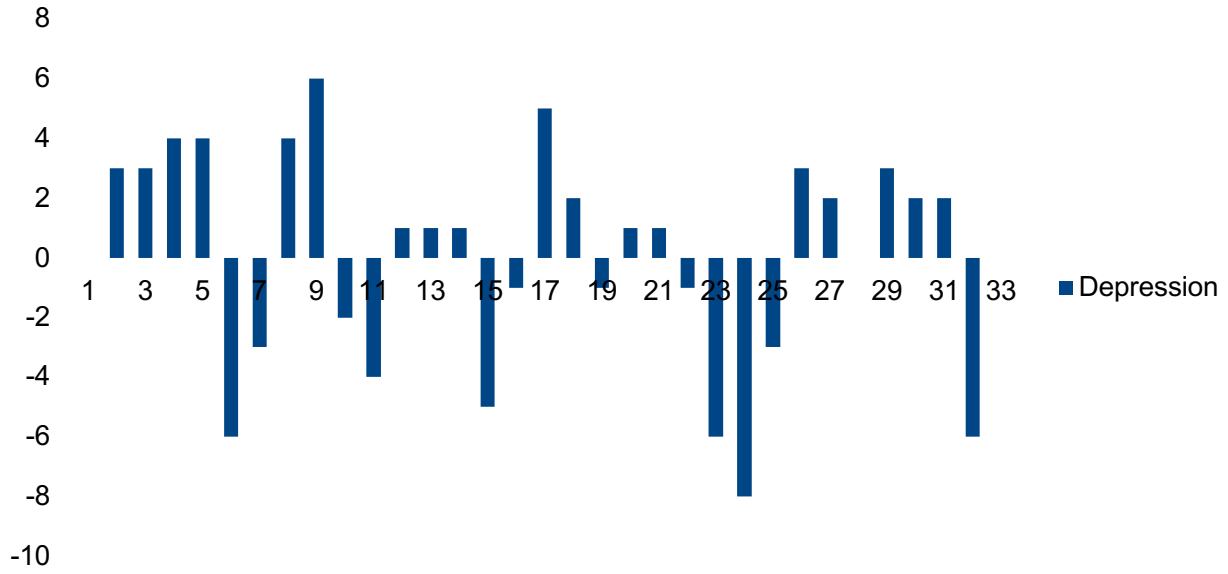
Graph 5. Overall pain reduction of 53% after treatments. Difference of pain rating before and after the treatments



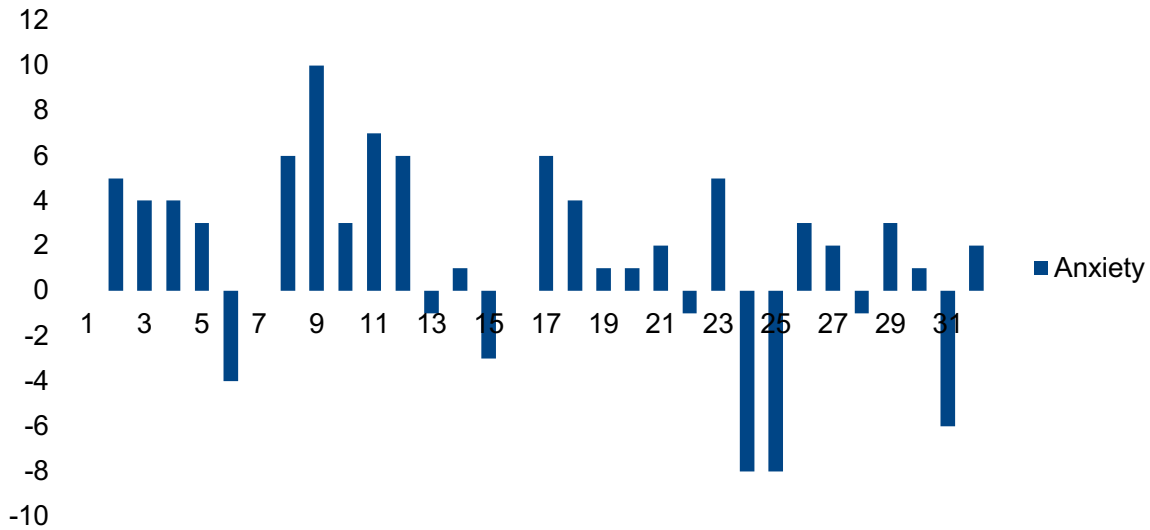
Graph 6. Overall reduction in fatigue by 53% after treatments. The results were evaluated only on 50 patients who presented fatigue and one month after the end of the tests.¹⁵
Differences in the assessment of fatigue before and after treatments



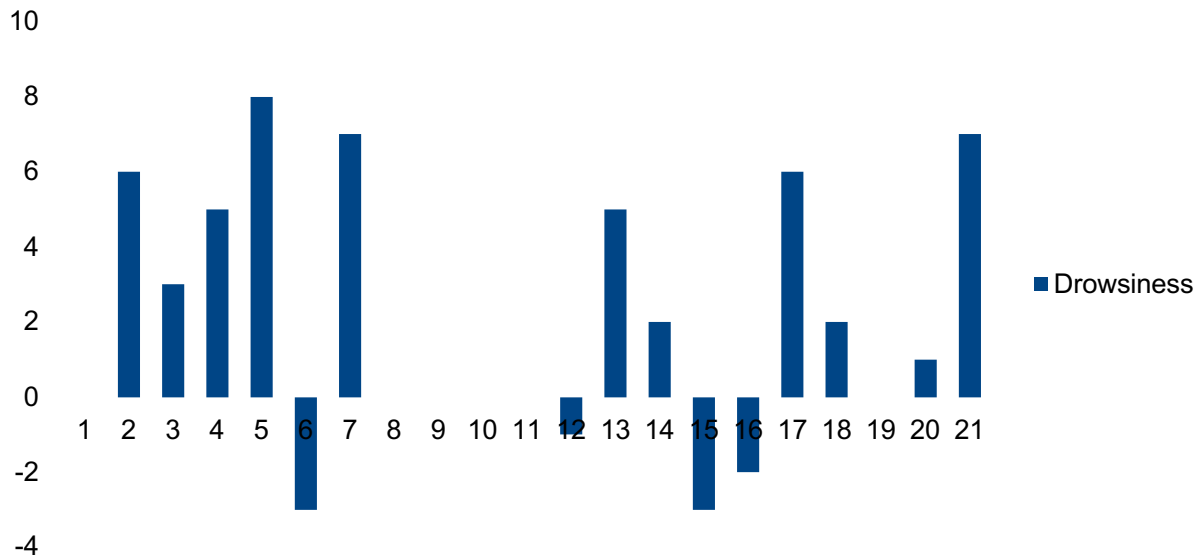
Graph 7. The results were evaluated only on 21 patients who presented nausea, 5 of whom were undergoing chemotherapy with anthracyclines and one month after the end of the same.
Difference in the assessment of nausea before and after treatments



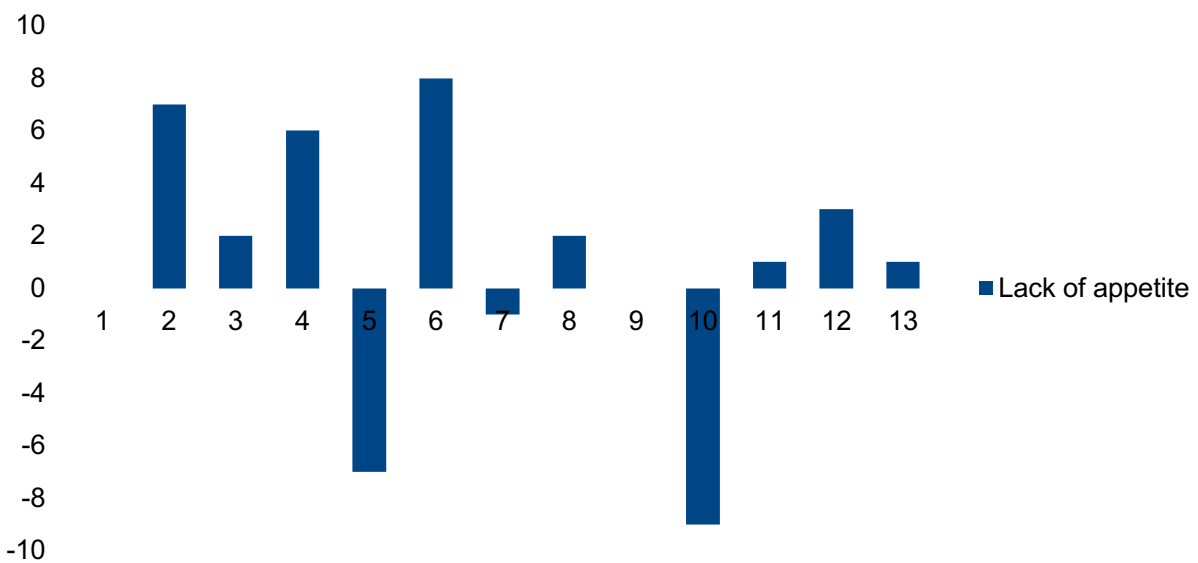
Graph 8. The results were evaluated only on 33 patients who had depression and one month after their completion. Difference in the assessment of depression before and after treatments



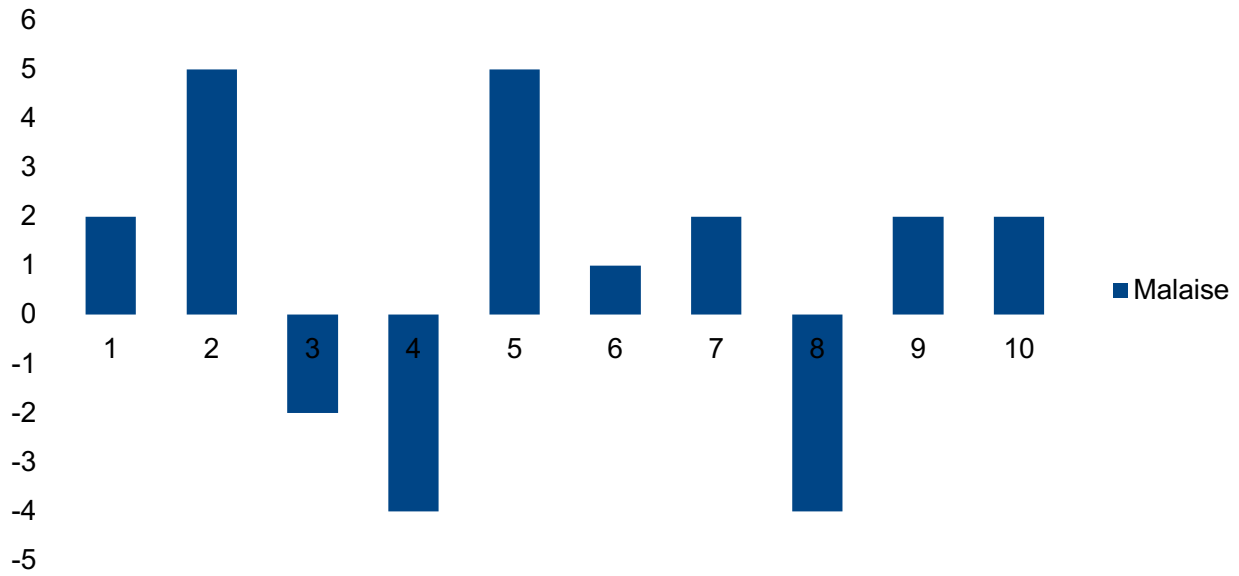
Graph 9 The results were evaluated only on 32 patients who presented anxiety and one month later end of the same. Difference in the assessment of anxiety before and after treatments



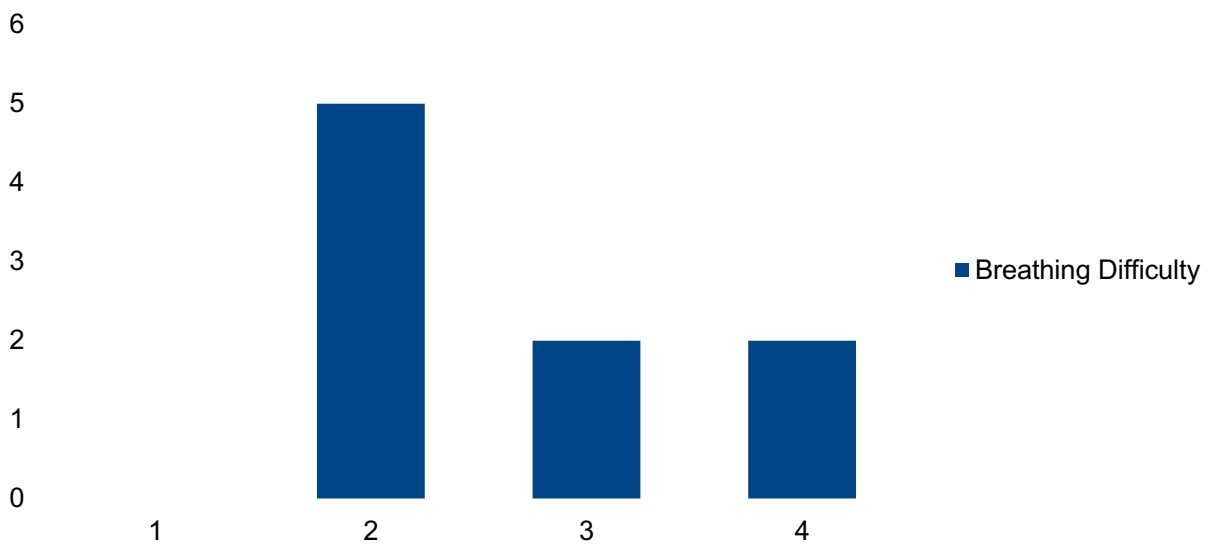
Graph 10. The results were evaluated only on 11 patients who showed drowsiness and one month after the end of the tests. Difference in the assessment of drowsiness before and after treatments



Graph 11. The results were evaluated only on 13 patients who had loss of appetite and one month after the end of the tests. Difference in the assessment of lack of appetite before and after treatments



Graph 12. The results were evaluated only on 11 patients who presented general malaise before the treatments and one month after the end of the same.
Difference in the assessment of malaise before and after treatments



Graph 13. The results were evaluated only on 4 patients who presented respiratory difficulty.
Difference in the assessment of breathing difficulty before and after treatments

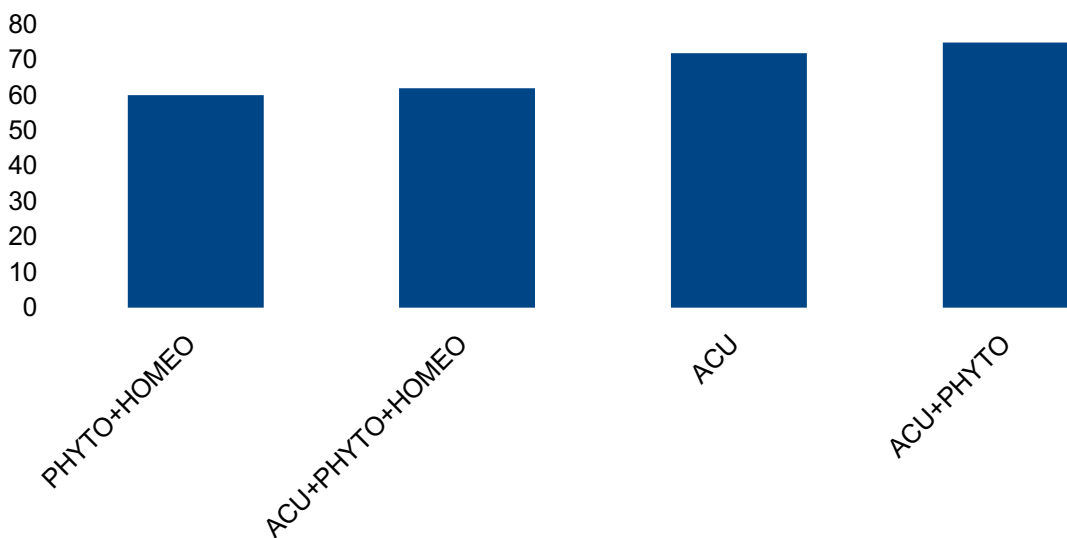
CONCLUSION

Integrative Medicine can help reduce the side effects of conventional cancer treatments and can help patients improve their subjective quality of life (Table 2 and Graph 14). It therefore seems reasonable to offer an integrative approach as part of standard patient care. Integrated Oncology combines lifestyle counseling, body-mind activities and complementary therapies with standard cancer care to improve symptom management, adherence to oncology protocols and overall quality of life before, during and after treatments.⁵¹ In the clinical management of a patient diagnosed with breast cancer, adequate preoperative evalua-

tion should include nutritional and physical activity screening and body composition analysis in order to uncover critical issues and take advantage of lifestyle interventions to improve results. Alongside and beyond traditional cancer care, this integrative approach should be ensured to address the multiple unmet needs of each cancer patient, in order to achieve truly person-centered, rather than disease-focused, medicine. The coordination of integrative medicine with conventional cancer treatment and the implementation of standardized procedures would ensure that patient care can be provided at the highest quality standards, with the highest standards of information and with maximum treatment safety.⁴⁸

COMPLEMENTARY MEDICINE	PATIENTS
ACUPUNCTURE	18
PHYTOTHERAPY + ACUPUNCTURE	31
HOMEOPATHY + ACUPUNCTURE	6
HOMEOPATHY + PHYTOTHERAPY + ACUPUNCTURE	6

Table 2. In the population under examination, the evaluation of ESAS2 results after integrated therapy treatments showed that in patients undergoing acupuncture and phytotherapy treatments, an improvement in pain emerged in 75% of cases, with a percentage of 72% in patients undergoing acupuncture only, 62% in patients undergoing acupuncture, phytotherapy and homeopathy treatments and 60% in patients undergoing phytotherapy and homeopathy.



Graph 14. Percentage of responses with the combination of treatments. Treatment's type: Response percentage

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Author contribution

FC and AG conceived and designed the study. FC, AG and SB drafted the manuscript. FC, AG, CF, SB and GF performed the acquisition, analysis or interpretation of data. Critical revision performed by FC, AG, MB and GM. Statistical analysis performed by AG. Administrative, technical, or material support performed by SB, RF, MF, CC, AM, AF, PP and CB. Supervision of manuscript was carried out by FC, MB and AG.

All authors read and approved the final manuscript.

Conflict of interest

No conflict of interest to declare.

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