



LA PRESCRIZIONE DELL'ATTIVITA' FISICA NELLA PAZIENTE CON CARCINOMA MAMMARIO: PERCHE'?

Dr. Monica Turazza

UOC Oncologia Medica

«Con l'espressione **attività fisica** si designa ogni movimento del corpo prodotto dai muscoli scheletrici, che determina un **incremento del dispendio energetico**: quindi, oltre al lavoro produttivo e ai lavori domestici, tutte le attività che possono influire sul dispendio energetico quotidiano totale, in particolare quelle del tempo libero, intese come esercizio fisico, sport e attività all'aperto»

Stile di vita sportivo

Stile di vita modicamente sportivo

Stile di vita non sedentario
30m' di passeggiata/giorno
x6 volte/settimana

Stile di vita sedentario

Nel mondo:

- 1 adulto su 3 non è sufficientemente attivo

(dati OMS)

In Italia il:

✓ 21 % svolge regolare Attività Fisica

✓ 47 % non svolge alcun esercizio

(dati ISTAT)



Informativa n. 384
Febbraio 2014

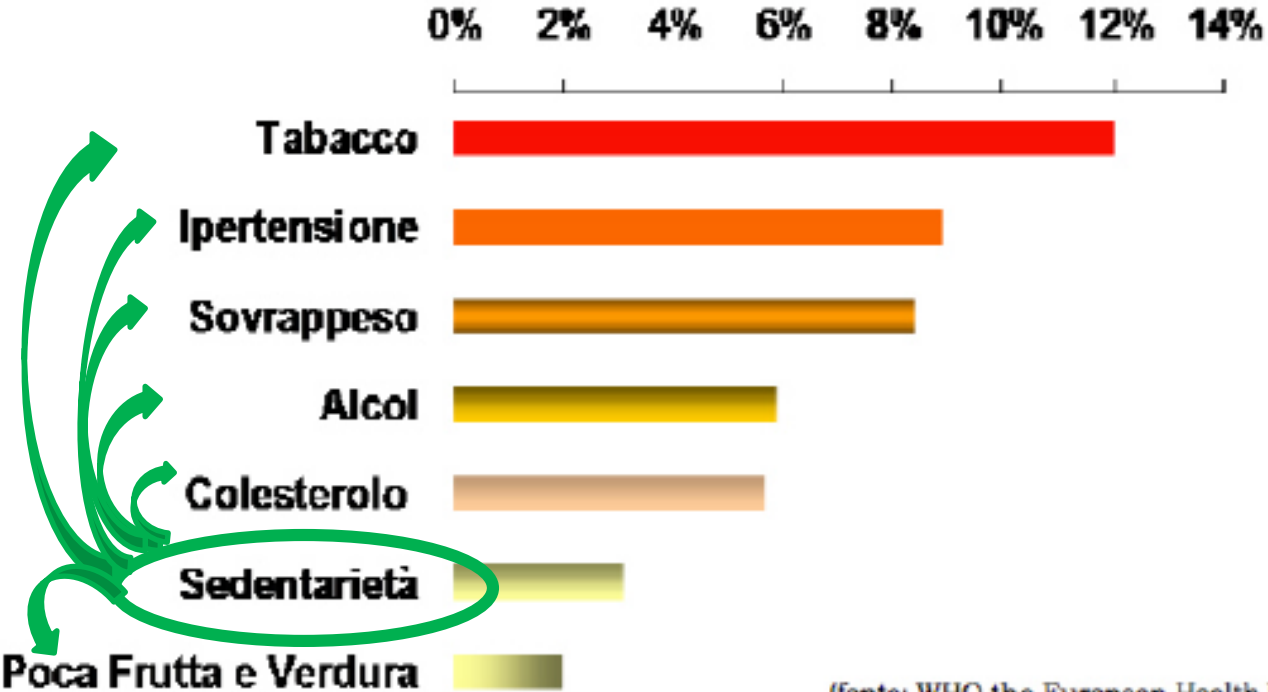
Nel 56% degli Stati membri dell'OMS sono in atto politiche per contrastare l'inattività fisica.

Gli Stati membri dell'OMS hanno concordato di ridurre del 10% l'inattività fisica entro il 2025.

Prevenzione primaria: il controllo sugli stili di vita

Le principali malattie croniche hanno alla base 7 principali fattori di rischio che sostengono quindi gran parte della spesa sanitaria:

Proporzione di disability-adjusted life year (DALY) attribuibile ai 7 principali fattori di rischio delle malattie croniche



(fonte: WHO the European Health Report)

**2-3 VOLTE
LA SETTIMANA** >>



Nordic Walking

**ESERCIZI DI FORZA,
FLESSIBILITÀ ED EQUILIBRIO**

Esercizi con i pesi, Stretching,
Esercizi propriocettivi



**3-5 VOLTE
LA SETTIMANA** >



ESERCIZI AEROBICI

Bicicletta, Nuoto, Corsa,
Cardio Fitness Training

ATTIVITÀ SPORTIVA

Calcio, Tennis, Basket, Volley



TUTTI I GIORNI >



PASSEGGIARE, FARE LE SCALE

**ANDARE AL LAVORO
A PIEDI OPPURE IN BICICLETTA**



**motilità
agilità
forza
resistenza**

**stato psico-fisico
tono dell'umore
inserimento sociale e relazionale
autostima**

**attività respiratoria
attività cardiocircolatoria
metabolismo glucidico
lipidi
peso
composizione corporea**



International Pooled Analysis of Leisure-Time Physical Activity and Premenopausal Breast Cancer in Women From 19 Cohorts

ASCO Journal of Clinical Oncology 2023

The benefits of exercise in cancer patients and the criteria for exercise prescription in cardio-oncology

Epidemiologic Reviews

© The Author 2017. Published by Oxford University Press on behalf of the Johns Hopkins Bloomberg School of Public Health. All rights reserved. For permissions, please e-mail: journals.permissions@oup.com.

Vol. 39, 2017

DOI: 10.1093/epirev/mxx007

Advance Access publication:

April 27, 2017

The Impact of Exercise on Cancer Mortality, Recurrence, and Treatment-Related Adverse Effects

REVIEW ARTICLE

Exercise in cancer

Indian J Med Paediatr Oncol | Apr-Jun 2009

REVIEWS

J Natl Cancer Inst 2012;104:815–840

Physical Activity, Biomarkers, and Disease Outcomes in Cancer Survivors: A Systematic Review

Review

Cancers 2022, 14,

Physical Activity and Cancer Care—A Review

Journal of Sport and Health Science 10 (2021):

Review

Roles and molecular mechanisms of physical exercise in cancer prevention and treatment

Physical activity after cancer: an evidence review of the international literature

British Journal Medical Practice 2014

Cancer, Physical Activity, and Exercise

Compr Physiol. 2012 October ; 2(4)

Review

Cancer
Epidemiology
Biomarkers
& Prevention

The Effect of Exercise Training on Mediators of Inflammation in Breast Cancer Survivors: A Systematic Review with Meta-analysis

Cancer Epidemiol Biomarkers Prev. 25(7). Julv 2016.

VOLUME 26 · NUMBER 24 · AUGUST 20 2008

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Influence of Pre- and Postdiagnosis Physical Activity on Mortality in Breast Cancer Survivors: The Health, Eating, Activity, and Lifestyle Study

**Being physically active reduces:
Incidence of cancer by 48%
Mortality due to cancer by 27%
(BMJ 2018;360:K134)**

- **Metanalysis on 50.000 patients with breast (and colon cancer)**
- **Exercising for 150 minutes/week**

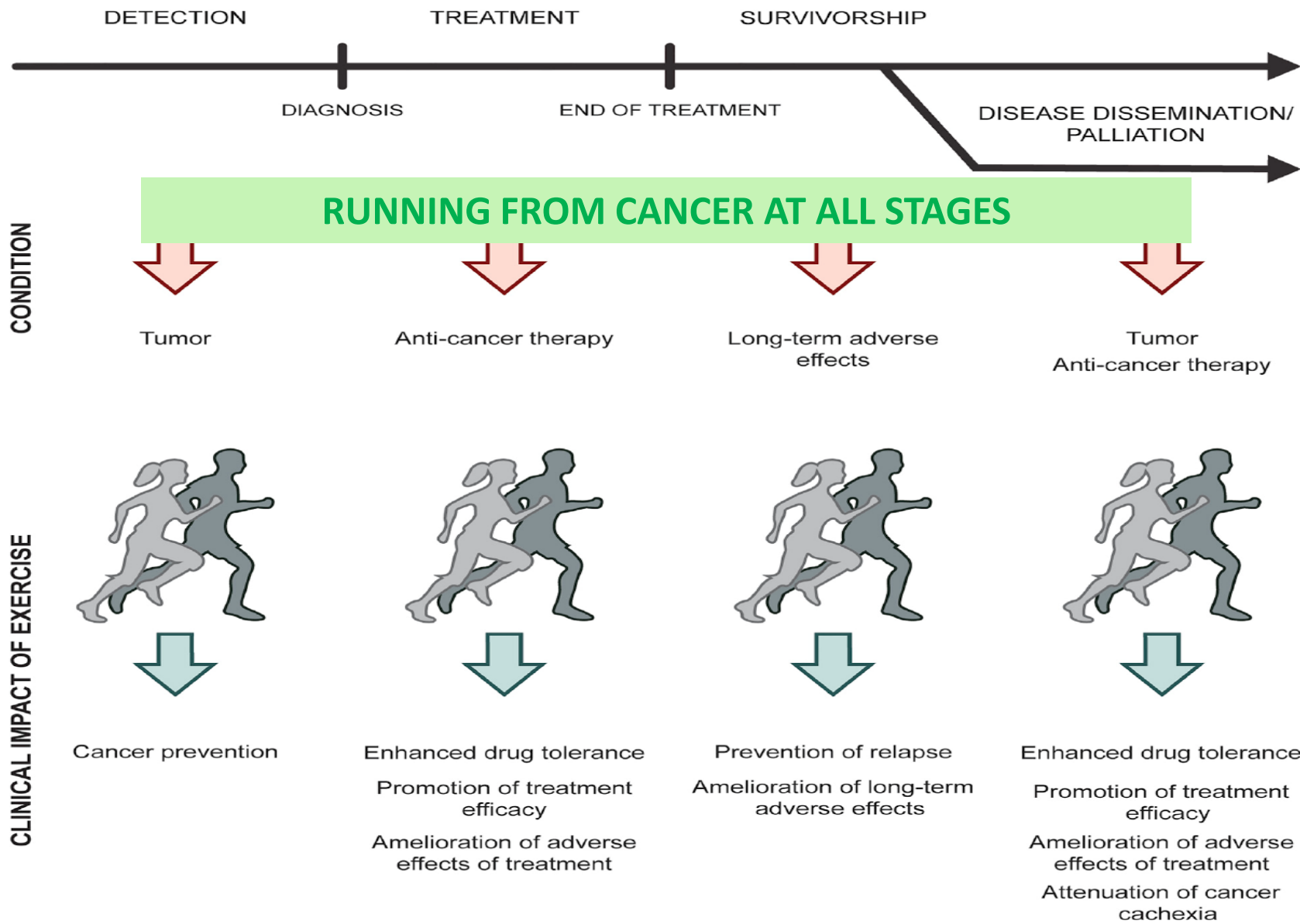
24% reduction of total mortality risk for breast cancer survivors

(28% reduction of total mortality risk for colon cancer survivors)

(Ann Oncol 2014;25:1293)



A multidisciplinary approach based on physical training and therapeutic optimization, lifestyle advice, control of risk factors and psychological support is strongly recommended in all cancer patients.



DETECTION

TREATMENT

SURVIVORSHIP

DIAGNOSIS

END OF TREATMENT

DISEASE DISSEMINATION/
PALLIATION

RUNNING FROM CANCER AT ALL STAGES

CONDITION

Tumor

Anti-cancer therapy

Long-term adverse
effects

Tumor
Anti-cancer therapy

CLINICAL IMPACT OF EXERCISE

Cancer prevention

Enhanced drug tolerance

Prevention of relapse

Enhanced drug tolerance

Promotion of treatment
efficacy

Amelioration of long-term
adverse effects

Promotion of treatment
efficacy

Amelioration of adverse
effects of treatment

Amelioration of adverse
effects of treatment
Attenuation of cancer
cachexia

ATTIVITA' FISICA e PREVENZIONE DI CARCINOMA MAMMARIO

CONTROLLO PESO CORPOREO



INSULINA E FATTORI DI CRESCITA

Un eccesso di grasso può far aumentare i livelli di insulina circolante e di altri fattori di crescita, che potrebbero stimolare la replicazione cellulare.

TESSUTO ADIPOSO

Alcune cellule del tessuto adiposo, chiamate «macrofagi», rilasciano sostanze infiammatorie (citochine) che stimolano la divisione cellulare (anche delle cellule tumorali).

ESTROGENI

gli estrogeni prodotti dal tessuto adiposo possono aumentare la velocità di proliferazione delle cellule della mammella e dell'utero, incrementando il rischio di tumore.

Curva dose-effetto



Journal of Sport and Health Science 10 (2021) 201–210

Correlazione lineare tra rischio di cancro mammario ed attività fisica sia in pre- che in postmenopausa: riduzione del rischio mediamente del 5% per ogni due ore di attività moderata-vigorosa alla settimana

Menopausal Status and exercise	BREAST CANCER RISK REDUCTION	Font
•premenopausal	27	Seminar Oncology 2010;37(3):297
•postmenopausal	31	

Features	BREAST CANCER RISK REDUCTION %	Font
<p>ER+/PR+ and HER- ER-and PR-</p> <ul style="list-style-type: none"> •Family history vs no family history •Women with child vs women without child 	<p>15 -20 27</p> <p>1 vs 21 38 vs 18</p>	<p>Crit Rev Oncol Hemat 2011;80:450</p> <p>Seminar Oncology 2010;37(3):297</p> <p>Seminar Oncology 2010;37(3):297</p>
<p>Type of activity</p> <ul style="list-style-type: none"> •recreational •occupational 	<p>21 18</p>	<p>Recent Cancer Res 2011;188:125</p>
<p>Intensity of activity</p> <ul style="list-style-type: none"> •moderate •vigorous 	<p>15 18</p>	<p>Seminar Oncology 2010;37(3):297</p>
<p>Endometrial cancer (due to obesity reduction)</p>	<p>20</p>	<p>Eur J Epidemiol 2015; 30:397</p>

ATTIVITA' FISICA E CARCINOMA MAMMARIO IN POST-DIAGNOSI

Rischio inferiore del 41% di mortalità per tutte le cause

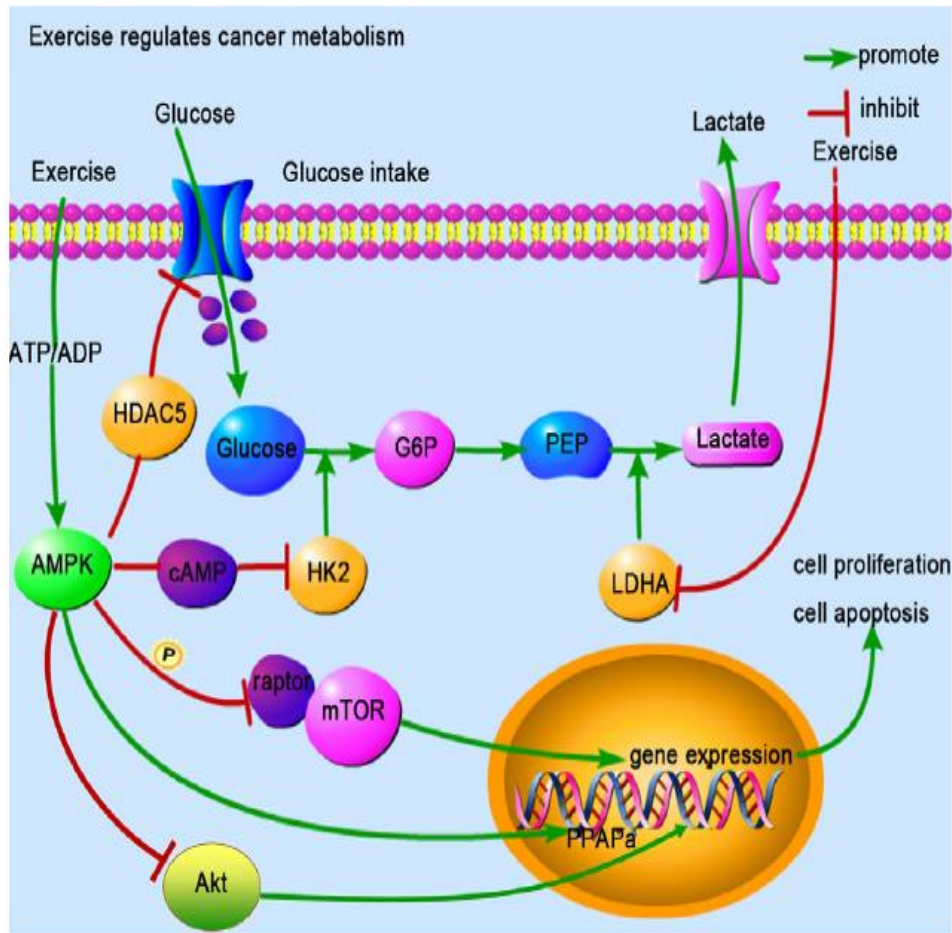


Rischio inferiore del 24% di recidiva

Rischio inferiore del 34% di decessi per cancro al seno

Review

Roles and molecular mechanisms of physical exercise in cancer prevention and treatment



Exercise can influence cancer metabolism, inhibiting aerobic glycolysis

Hypoxia can influence cancer microenvironment invasiveness

Exercise can induce apoptosis by activating the AMPK metabolic monitoring point and inhibiting the mTOR signal pathway

Physical activity prevents tumor metastasis through modulation of immune function

Physical activity=positive effect on immune system to control tumor behavior/metastasis

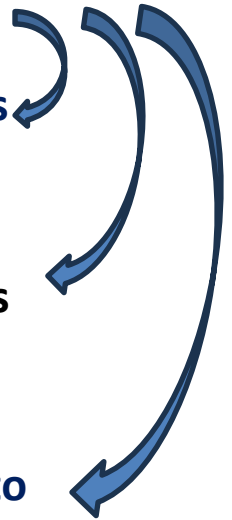
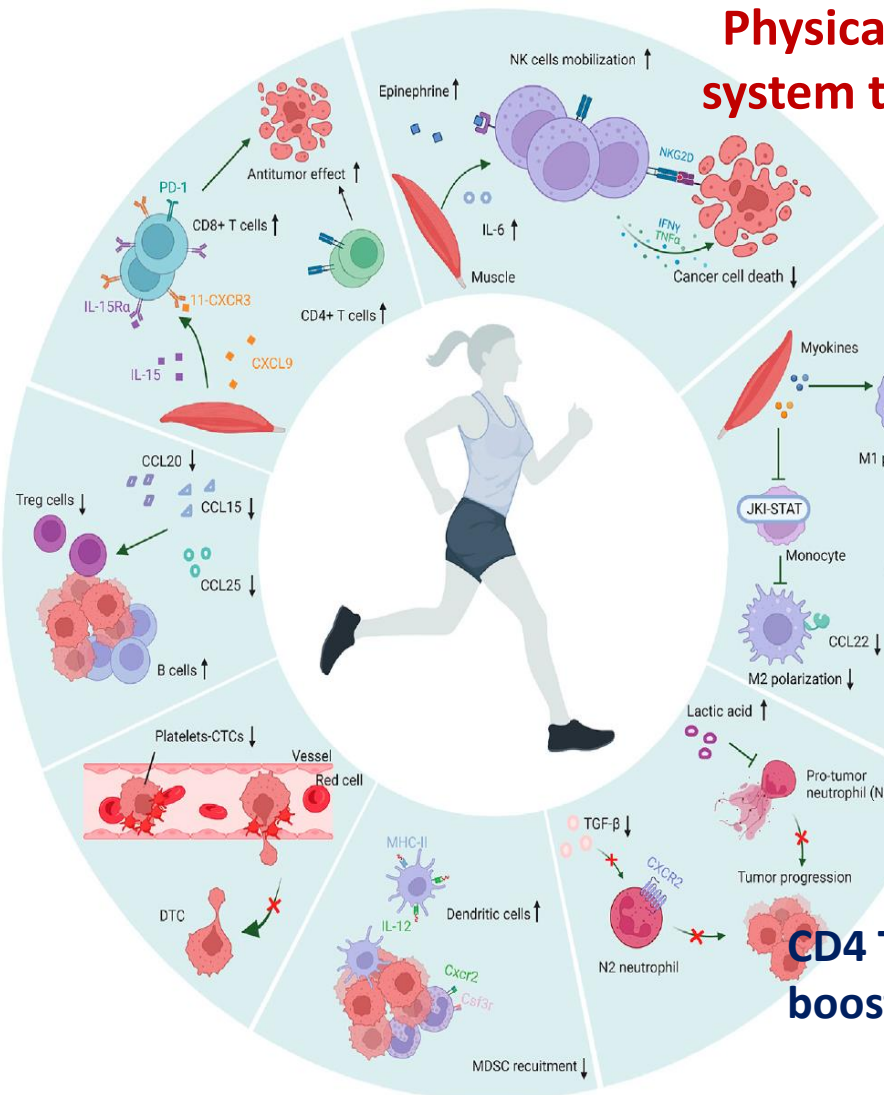
Mobilizes immune cells into circulation through stress-induced shear stress and adrenergic signaling.

Not new generation but recruiting from the innate and adaptive immune storage

NK can mediate tumor cells apoptosis

CD8 T cells can kill tumor cells by secreting TNF and IFN

CD4 T cells can produces cytokines to boost an tumor immune response



Metastatic process: invasion, intravasation, circulation, extravasation, colonization

Influence intra-tumor angiogenesis by altering vascular epithelial growth factor in serum and tumor

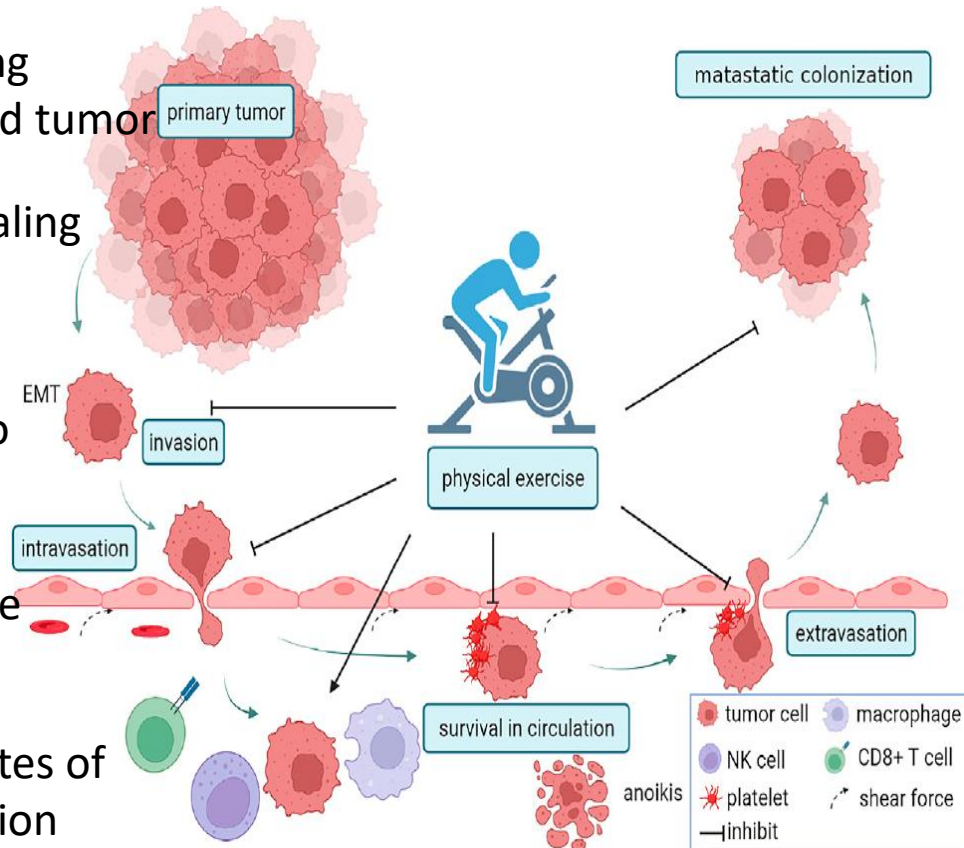
Alterate MEK/MAPK and PI3K/mTOR signaling pathway inhibiting tumor metastasis

Attenuate invasion of tumor cells via inhibiting epithelial-mesenchymal transition by leading to an intratumor increase of E-cadherine levels

Reduces CTCs by increasing vascular shear force (in sinergy with immune system surveillance

Change microinviroments of the major sites of metastasis inhibiting process of colonitaton

Induce epinephrine and norepinephrine with tumor soppresion of Hippo signaling pathway and promote phosphprilation of YAP with its cytoplasmatic sequestration deterring the tumor cell proliferaton and surviall by target genes

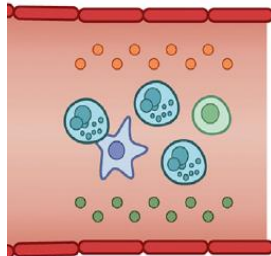


Modulation of circulating angiogenic factors and tumor biology by aerobic training in breast cancer patients receiving neoadjuvant chemotherapy



+

Chemotherapy



Improved perfusion



Exercise can delay tumor growth in association with chemotherapy:

- **three session of exercise/week**

→ increase maximum oxygen consumption

→ **increase tumor perfusion**

→ greater perfusion brings greater effect/dose of drugs that reach neoplastic cells delaying their growth

SYMPTOMS treatment-correlated	INCIDENCE
Cancer-related fatigue	60-96% (chemotherapies, surgery, radiotherapy) 40% long term therapy (endocrine)
Psychological distress (anxiety/depression)	25-30%
Weight gain	45% breast cancer
% of mineral density reduction	2.6% in menopausal females treated with aromatase inhibitors 7% in young female treated with LHRHa and aromatase inhibitors
Thromboembolism (age, pelvic involvement, type of cancer, immobility)	70% during chemotherapy and/or after surgery 62% in advanced disease 52% after radiotherapy
Constipation	immobility, analgesic therapies, antiemetics
Cardiac damage LV dysfunction	9% with Anthracyclines-containing regimens, 4-7% with HER2-target therapies
Cholesterol-LDL	Increased with aromatase inhibitors
Arthralgias	20-50% with aromatase inhibitors

Cancer-Related Adverse Effect and Cancer Site	First Author, Year (Reference No.)	Sample Size, no.	No. of RCTs	Timing	No. of Studies	No. of Patients		I^2 , %	Effect Estimate	95% CI	P Value
						Exercise	Control				
Fatigue											
Breast	Zhu, 2016 (70)	2,659	33	Mixed ^a	10	841	800	83	0.3	-1.16, 1.75	0.69
	van Vulpen, 2016 (71)	784	6	During treatment	4	N/A	N/A	N/A	-0.22	-0.38, -0.05	N/A
	Meneses-Echavez, 2015 (73)	1,156	9	Mixed	9	N/A	N/A	75	-0.51	-0.81, -0.21	0.001
	Zou, 2014 (76)	1,014	12	During treatment	6	N/A	N/A	88.6	-0.82	-1.04, -0.60	0.001
	Carayol, 2013 (77)	1,380	17	Mixed	11	N/A	N/A	72	-0.284	-0.54, -0.03	0.03
	Duijts, 2011 (78)	N/A	56	Mixed	10	N/A	N/A	N/A	-0.31	-0.53, -0.10	0.004

Quality of life											
Breast	Paramamanda, 2014 (75)	1,091	11	Mixed	6	N/A	N/A	N/A	0.34	0.09, 0.58	<0.05
	Cheema, 2014 (74)	1,652	15	Mixed	7	N/A	N/A	47	0.17	-0.03, 0.38	N/A
	Carayol, 2013 (77)	1,380	17	Mixed	9	N/A	N/A	73	0.34	0.07, 0.62	0.015
	Duijts, 2011 (78)	N/A	56	Mixed	12	N/A	N/A	N/A	0.30	0.12, 0.48	0.001

Anxiety											
Breast	Zhu, 2016 (70)	2,659	33	Mixed	5	341	361	0	-3.17	-4.76, -1.58	<0.01
	Carayol, 2013 (77)	1,380	17	Mixed	8	N/A	N/A	91	-0.52	-1.01, 0.02	0.06

Depression											
Breast	Zhu, 2016 (70)	2,659	33	Mixed	6	378	373	2	-2.08	-3.36, 0.80	0.001
	Carayol, 2013 (77)	1,380	17	Mixed	9	N/A	N/A	39	-0.27	-0.457, -0.09	0.003

Cancer-Related Adverse Effect and Cancer Site	First Author, Year (Reference No.)	Sample Size, no.	No. of RCTs	Timing	No. of Studies	No. of Patients		I^2 , %	Effect Estimate	95% CI	P Value
						Exercise	Control				
Emotional well-being, breast	Zhu, 2016 (70)	2,659	33	Mixed	8	343	316	2	0.27	0.12, 0.43	0.0006
Mental health, breast	Zhu, 2016 (70)	2,659	33	Mixed	4	125	116	18	1.4	0.09, 2.00	0.03
Body image											
Breast	Duijts, 2011 (78)		56	Mixed	6	N/A	N/A	N/A	0.28	0.08, 0.48	0.007
Sleep dysfunction											
Breast	Zhu, 2016 (70)	2,659	33	Mixed	4	64	62	0	0.32	-0.82, 1.46	0.58
Lymphedema, breast	Paramamanda, 2014 (75)	1,091	11	Mixed	8	N/A	N/A	0	-0.09	-0.23, 0.05	0.2
	Rogan, 2016 (69)	N/A	4	Posttreatment	4	N/A	N/A	0	-0.49	-0.86, -0.11	0.011
	Singh, 2016 (72)	283	11	Posttreatment	11	N/A	N/A	0	-0.1	-0.3, 0.4	0.34
Pain											
Breast	Zhu, 2016 (70)	2,659	33	Mixed	3	106	97	98	2.58	-2.65, 7.81	0.33

Jones LW, Habel LA, Weltzien E, et al. Exercise and risk of cardiovascular events in women with nonmetastatic breast cancer. *J Clin Oncol* 2016;**34**:2743–2749.

Patients with breast cancer in adjuvant therapy

Level of exercise	Risk of cardiovascular complication
2-10.9 MET-h/week	HR=0.91;95%CI, 0.76-1.09
11-24.5 MET-h/week	HR=0.79;95%CI, 0.66-0.96
>24.5 MET-h/week (*)	HR=0.65;95%CI, 0.53-0.80

(*) after a long- term follow up decreased risk for cardiovascular events (HR=0.59) was observed in group of higher levels of exercise

Nagy AC, GulAcsi BP, CserEp Z, et al. Late cardiac effect of anthracycline therapy in physically active breast cancer survivors – a prospective study. *Neoplasma* 2017;**64**:92–100.

Breast cancer patients with no cardiovascular risk factors

Prospective study (5 years after therapy with anthracycline)	Symptom /signs of cardiotoxicity %
No exercise	68.4
exercise	19.45 (p=0.0017)

Findings from this comprehensive review of observational studies, interventional trials, and meta-analyses support the view that exercise is an important adjunct therapy in the management of cancer. Specifically, this review confirms that cancer patients involved in greater levels of exercise have a lower relative risk of cancer mortality and a lower relative risk of cancer recurrence, and they experience fewer and/or less severe treatment-related adverse effects.

Exercise, Diet, and Weight Management During Cancer Treatment: ASCO Guideline

Recommendations

Question 1: *Does exercise during cancer treatment safely improve outcomes related to QoL, treatment toxicity, or cancer control?*

Recommendation 1.1. Oncology providers should recommend aerobic and resistance exercise during active treatment with curative intent to mitigate side effects of cancer treatment (Type: evidence based, benefits outweigh harms; Evidence quality: moderate to low; Strength of recommendation: strong).

Note: Exercise interventions during active treatment reduce fatigue; preserve cardiorespiratory fitness, physical functioning, and strength; and in some populations, improve QoL and reduce anxiety and depression. In addition, exercise interventions during treatment have low risk of adverse events. Evidence was not sufficient to recommend for or against exercise during treatment to improve cancer control outcomes (recurrence or survival) or treatment completion rates.

Recommendation 1.2. Oncology providers may recommend preoperative exercise for patients undergoing surgery for lung cancer to reduce length of hospital stay and postoperative complications (Type: evidence based, benefits outweigh harms; Evidence quality: low; Strength of recommendation: weak).

ATTIVITÀ FISICA E TUMORI



Attività aerobica



Attività anaerobica



Attività fisica di moderata intensità (3-6 METs*)

Richiede moderata quantità di sforzo e accelera notevolmente la frequenza cardiaca

Esempi:

- Camminata Veloce
- Danza
- Giardinaggio
- Lavori domestici
- Spostamento di carichi moderati (inferiori a 20 Kg)

Attività fisica di elevata intensità (>6METs*)

Richiede un grande sforzo e determina una respirazione rapida e un aumento sostanziale della frequenza cardiaca

Esempi:

- Corsa
- Ciclismo
- Ginnastica aerobica
- Nuoto
- Sport di squadra (calcio, pallavolo, basket)
- Spostamento di carichi pesanti (oltre 20 Kg)

Riduzione della stanchezza

Riduzione della sensazione di nausea

Rinforzo del tono muscolare e miglioramento dell'equilibrio

Miglioramento della capacità respiratoria

Riduzione di ansia e miglioramento del benessere psico-fisico

Aumento della forza e della resistenza alla fatica

Riduzione del dolore articolare

Riduzione dell'osteoporosi e mantenimento del tono muscolare

Riduzione del rischio di malattie cardiovascolari

Miglioramento della circolazione sanguigna

Controllo del peso corporeo

Miglioramento della qualità della vita complessiva

INTENSITA' DI ATTIVITA' FISICA

150 minuti di intensità moderata/settimana

75 minuti di esercizio aerobico ad intensità vigorosa/settimana

Almeno 5000 passi al giorno se si ha a disposizione un contapassi

Buon obiettivo: 180 minuti settimanali di esercizio

Auspicabile includere esercizio di resistenza 2-3 sessioni/settimana

SUGGERIMENTI

Praticare gradualmente e con regolarità

Valutare:

preferenze personali

abilità pre-diagnosi/trattamento

condizioni cliniche e tipo di terapia

Confrontarsi con:

oncologo/fisiatra/fisioterapista

Affidarsi a:

trainer





posti dedicati

È meglio rinunciare all'attività fisica in caso di:

- ◆ anemia
- ◆ forti dolori
- ◆ emorragie
- ◆ febbre
- ◆ infezioni
- ◆ recenti episodi di vomito e diarrea
- ◆ vertigini o visione offuscata
- ◆ metastasi ossee o osteoporosi con rischio di fratture
- ◆ disturbi cardiorespiratori.

Article

“OPERATION PHALCO”—Adapted Physical Activity for Breast Cancer Survivors: Is It Time for a Multidisciplinary Approach?

Arianna Murri ¹ , Daniela Vitucci ^{2,3}, Eliana Tranchita ^{1,*}, Elisa Grazioli ¹ , Stefania Gori ⁴, Alessandra Modena ⁴, Monica Turazza ⁴, Roberto Filippini ⁵, Silvia Galeazzi ⁵, Matteo Verzè ⁶, Patrizia Frittelli ⁷, Domenico Cristiano Corsi ⁸, Fabrizio Nicolis ⁶, Attilio Parisi ¹  and Claudia Cerulli ¹ 

Operation Phalco is an experimental training protocol for breast cancer survivors (**PH**ysic**AL** a**C**tivity for **O**ncology)

Institutional promoter: Aiom

Aim of the Study

The aim of this study was to evaluate the effectiveness of a multidisciplinary intervention (“PHALCO”—PHysicAL aCtivity for Oncology) that included oncologists, sport physicians, and kinesiologists on QoL and functional parameters in BC patients.

A total of 35 post-surgery BC patients (40–65 years old), risk levels 1 and 2,