

Integrative Oncology

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What is Integrative Oncology?

- Use of integrative medicine practices across the spectrum of cancer care
 - Evidence-based
 - Patient-centered
- Integrative health
 - Nutrition, physical activity, mind-body
 - Supplements/Herbs
 - Other health care systems: acupuncture, TCM, massage

Why integrative oncology?

- At least half of cancer patients are utilizing non-allopathic approaches to cancer care
- Most do not share the approach with their oncologist
- Most commonly:
 - Women, more educated, higher SES

Background

- Epidemiological data of the impact of lifestyle on cancer (66% of cancers lifestyle related)
- e.g. Role of diet: cruciferous vegetables, lycopene (tomatoes-prostate cancer)
 - Migration studies: lower rates in countries with low fat, plant based diet



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Adult Urology: Outcomes/Epidemiology/Socioeconomics

INTENSIVE LIFESTYLE CHANGES MAY AFFECT THE PROGRESSION OF PROSTATE CANCER

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Prostate Cancer

- Impact of lifestyle changes on early prostate cancer (UCSF)
- Who: men with early prostate cancer who chose observation, Gleason <7, PSA 4-10 ng/ml randomized to control or lifestyle intervention group

Assessment: Biological Endpoints

- PSA: baseline and at 1y (MSKCC)
- Testosterone levels
- Clinically relevant tissue culture: LNCaP cells
 - androgen sensitive prostate cancer cells from a human metastatic PC lesion
 - change in LNCaP cell growth is a standard test used for evaluating the effects of conventional treatments on prostate cancer in the laboratory
 - Expose LNCaP cells to patient serum exposed to therapeutic intervention/control to assess response

Study Population

- 181 eligible
- 73 declined: not willing to be randomized and either follow or not follow lifestyle changes or declined periodic testing
- 15 actually had Gleason scores ≥ 7 ng/ml
- 93 enrolled:
 - 44 intervention, 3 withdrew—too difficult to follow
 - 49 control

Participant demographic and baseline characteristics

	Intervention	Control	p Value
No. subjects	44	49	
Mean age \pm SD	65 \pm 7	67 \pm 8	0.25
% Married/cohabitating	66	76	0.31
% Employment:			0.64
Full/part time	54	49	
Retired	46	51	
Mean PSA \pm SD (ng/ml)	6.32 \pm 1.72	6.28 \pm 1.66	0.92
Mean cholesterol \pm SD (mg/dl)	204 \pm 42	203 \pm 39	0.90
Mean low density protein \pm SD (mg/dl)	129 \pm 36	127 \pm 33	0.75
Mean high density protein \pm SD (mg/dl)	48 \pm 11	50 \pm 13	0.57
Mean triglycerides \pm SD (mg/dl)	133 \pm 77	135 \pm 88	0.94
Mean Ln-CRP \pm SD	-0.0310 \pm 1.1	0.2767 \pm 0.8	0.16
Mean wt \pm SD (kg)	80 \pm 13.6	80 \pm 11.3	0.75
Mean LNCaP apoptosis \pm SD (% FBS)	48.16 \pm 22.1	44.33 \pm 33.0	0.55
Mean testosterone \pm SD (ng/dl)	414 \pm 860	387 \pm 100	0.20
Mean Gleason \pm SD (Sum)	5.7 \pm 0.5	5.7 \pm 0.7	0.80

To convert cholesterol, LDL and HDL to mmol multiply by 0.0259, to convert triglycerides to mmol multiply by 0.0113 and to convert testosterone to nmol multiply by 0.0347.

Study Intervention

- A nurse case manager contacted patients by telephone once weekly for the first 3 months and once monthly thereafter.
- A registered dietitian was available for nutrition education and counseling.
- All therapeutic decisions, including whether to undergo conventional treatment during the study course, were deferred to the personal physician of each patient.
- Control group patients were asked to follow the advice of their physicians regarding lifestyle changes.

Lifestyle Intervention

- Vegan diet: 1 daily serving of tofu, fortified soy protein powdered beverage, predominantly fruits, vegetables, whole grains (complex carbohydrates), legumes and soy products, low in simple carbohydrates and with approximately 10% of calories from fat.
 - In earlier studies most patients were able to adhere to this diet for at least 5 years
- Supplements: fish oil (3 gm daily), vitamin E (400 IU daily), selenium (200 mcg daily) and vitamin C (2 gm daily)
- Physical activity: moderate aerobic exercise (walking 30 minutes 6 days weekly)
- Stress management techniques (gentle yoga based stretching, breathing, meditation, imagery and progressive relaxation for a total of 60 minutes daily)
- 1-hour support group once weekly to enhance adherence to the intervention

Lifestyle Outcomes

Differences in lifestyle change scores between groups (p <0.001)

Group	Mean Baseline ± SE	Mean 12 Mos ± SE	Mean Baseline-12-Mo Change ± SE	F (df)
Dietary fat (% calories from fat):				
Experimental	28.9 ± 1.8	11.2 ± 0.4	-17.7 ± 1.4	130.7 (1.81)
Control	26.2 ± 1.2	25.3 ± 8.8	-0.9 ± 1.1	
Dietary cholesterol (mg/day):				
Experimental	230.4 ± 21.6	7.5 ± 1.9	-222.9 ± 21.8	98.3 (1.81)
Control	218.0 ± 19.2	182.1 ± 19.3	-35.9 ± 16.0	
Exercise (days/wk):				
Experimental	3.1 ± 0.4	4.8 ± 0.3	1.7 ± 0.4	14.7 (1.80)
Control	3.3 ± 0.4	3.3 ± 0.4	0.0 ± 0.4	
Exercise (mins/wk):				
Experimental	120.8 ± 18.8	262.9 ± 38.8	142.1 ± 32.7	11.4 (1.80)
Control	186.1 ± 27.6	160.6 ± 21.3	-25.5 ± 26.8	
Stress management (days/wk):				
Experimental	2.1 ± 0.4	5.7 ± 0.3	3.6 ± 0.4	46.2 (1.80)
Control	2.0 ± 0.4	2.3 ± 0.5	0.3 ± 0.4	
Stress management (mins/wk):				
Experimental	39.6 ± 11.0	315.7 ± 20.9	276.0 ± 20.9	102.5 (1.80)
Control	71.3 ± 22.1	75.7 ± 19.1	4.4 ± 18.0	
% Overall lifestyle index:				
Experimental	41.4 ± 3.8	94.8 ± 3.8	53.4 ± 4.2	115.2 (1.80)
Control	45.4 ± 2.9	45.1 ± 3.5	-0.3 ± 3.0	

Cancer Outcomes

Group	Mean Baseline ± SD	Mean 12 Mos ± SD	Mean Baseline-12-Mo Change ± SD	p Value
PSA (ng/ml):				
Experimental	6.23 ± 1.7	5.98 ± 1.7	-0.25 ± 1.2	0.016
Control	6.36 ± 1.7	6.74 ± 2.1	0.38 ± 1.3	
Total cholesterol (mg/dl):				
Experimental	205.0 ± 42	172.6 ± 34	-32 ± 39.4	<0.001
Control	200.6 ± 39	202.8 ± 37	2 ± 25.7	
Low density protein (mg/dl):				
Experimental	130.9 ± 35	101.2 ± 25	-30 ± 31.3	<0.001
Control	125.2 ± 33	124.1 ± 30	-1 ± 25.2	
High density protein (mg/dl):				
Experimental	47.3 ± 10	41.9 ± 12	-5 ± 8.3	<0.001
Control	48.3 ± 12	49.3 ± 12	1 ± 6.8	
Triglycerides (mg/dl):				
Experimental	133.0 ± 78	138.0 ± 96	5 ± 65.4	0.52
Control	137.1 ± 91	150.9 ± 93	14 ± 77.5	
LNCaP growth (% FBS):				
Experimental	105.50 ± 19.0	35.56 ± 9.2	-69.94 ± 19.5	<0.001
Control	91.40 ± 19.2	82.34 ± 36.8	-9.06 ± 42.8	
LNCaP apoptosis (% FBS):				
Experimental	48.16 ± 22.1	125.38 ± 127.0	77.23 ± 120.6	0.27
Control	45.16 ± 33.7	90.18 ± 128.0	45.02 ± 112.7	
Ln-CRP (mg/l):				
Experimental	-0.0310 ± 1.1	-0.2782 ± 1.0	-0.2472 ± 0.8	0.07
Control	0.2767 ± 0.8	0.2121 ± 0.9	-0.0646 ± 0.9	
Testosterone (ng/dl):				
Experimental	414.2 ± 86	443.3 ± 117	29 ± 96	0.53
Control	387.0 ± 100	435.0 ± 155	48.0 ± 123	
Wt (kg):				
Experimental	80 ± 13.8	76 ± 10.0	-4.5 ± 6.2	<0.001
Control	80 ± 11.4	80 ± 11.4	0 ± 3.9	

Results

- Lifestyle intervention:
 - No evidence of progressive disease or PSA increase
 - PSA decreased 4%
 - Growth of LNCaP prostate cancer cells (American Type Culture Collection, Manassas, Virginia)
 - Inhibited almost 8 times more by serum from the experimental than from the control group (70% vs 9%, $p < 0.001$).
 - Changes in serum PSA and also in LNCaP cell growth were significantly associated with the degree of change in diet and lifestyle.
- Control:
 - PSA increased 6%, $p = 0.016$
 - 4 experienced increase in PSA, 2 disease progression: entered standard therapy

Conclusion

- Intensive lifestyle changes may affect the progression of early, low grade prostate cancer in men. Further studies and longer term follow-up are warranted.

Question

- *Experimental serum seemed to contain something that differentially inhibited cell line growth but so what. Just because these serums were different does not mean that they were good. They might have also killed normal cells.*
- Although it is true that chemotherapy and radiation may kill normal as well cancerous cells, we are not aware of any evidence that fruits vegetables, whole grains, legumes and soy products kill normal cells. Indeed, (this) evidence suggests that substances present in these foods, such as lycopene, flavonoids, sulphoraphanes, omega-3 fatty acids, isoflavones, polyphenols, lignans and other substances, are protective of normal cells.
 - The significant correlation between degree of changes in diet and lifestyle and degree of change in PSA and LNCaP cell growth adds to the strength of evidence.

Follow-up

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Articles

Effect of comprehensive lifestyle changes on telomerase activity and telomere length in men with biopsy-proven low-risk prostate cancer: 5-year follow-up of a descriptive pilot study

Prof [Dean Ornish, MD](#)  , [Jue Lin, PhD](#), Prof [June M Chan, PhD](#), [Elissa Epel, PhD](#), [Colleen Kemp, RN](#), Prof [Gerdi Weidner, PhD](#), [Ruth Marlin, MD](#), [Steven J Frenda, MA](#), [Mark Jesus M Magbanua, PhD](#), [Jennifer Daubenmier, PhD](#), [Ivette Estay, PhD](#), [Nancy K Hills, PhD](#), [Nita Chainani-Wu, DMD](#), Prof [Peter R Carroll, MD](#), Prof [Elizabeth H Blackburn, PhD](#)

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Summary: Background

- Telomere shortness in human beings is a prognostic marker of aging, disease, and premature morbidity.

Methods

- Follow-up study in men with biopsy-proven low-risk prostate cancer and had chosen to undergo active surveillance.
- Eligible participants were enrolled from previous studies.
 - Intervention: comprehensive lifestyle changes--diet, activity, stress management, and social support
 - Control: active surveillance.
- Biological correlates: blood samples at 5 years and compared relative telomere length and telomerase enzymatic activity per viable cell with those at baseline, and assessed their relation to the degree of lifestyle changes.

Results

- Relative telomere length increased from baseline in the lifestyle intervention group, but decreased in the control group ($p=0.03$).
- Adherence to lifestyle changes was significantly associated with relative telomere length after adjustment for age and the length of follow-up ($p=0.005$).
- At 5 years, telomerase activity had decreased from baseline by 0.25 (-2.25 to 2.23) units in the lifestyle intervention group, and by 1.08 (-3.25 to 1.86) units in the control group ($p=0.64$), and was not associated with adherence to lifestyle changes (relative risk 0.93, 95% CI 0.72–1.20, $p=0.57$).

Conclusion

- Comprehensive lifestyle intervention was associated with increases in relative telomere length after 5 years of follow-up compared with controls

Take Away

- This report undoubtedly will excite the aficionados and devotees of lifestyle changes for cancer but it should also give pause to the skeptics. Appropriately it will encourage other and more vigorous scientific scrutinies of complementary medicine strategies.
- For those of us taking care of patients with prostate cancer it will reinforce the use of lifestyle changes in management.

Research Questions

- Study the impact of lifestyle modification interventions/integrative oncology therapies across the cancer treatment spectrum
 - Individual and Group settings
 - With biological correlates
- For the benefit of our patients

Where we are

- Even if scientific evidence is still meager, integrative medicine approaches have strong appeal in practicing the medical art since they *give the patient an active role in his care and promote an attitude of optimism and hope.*

Integrative Oncology

- Quality of life and more!

Thank you!

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