

Impact of **Exercise** and **Nutrition** on the Immune System and Outcomes in NSCLC



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Contents



Exercise

1. Effect on cancer Immune
 - Molecular and biological mechanism
2. Clinical outcome
 - Perioperative impact
 - Advanced lung cancer
3. How to exercise

Nutrition

1. Lung cancer prevention
2. Sarcopenia
3. Clinical outcome
4. How to support nutrition



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Exercise and physical activity

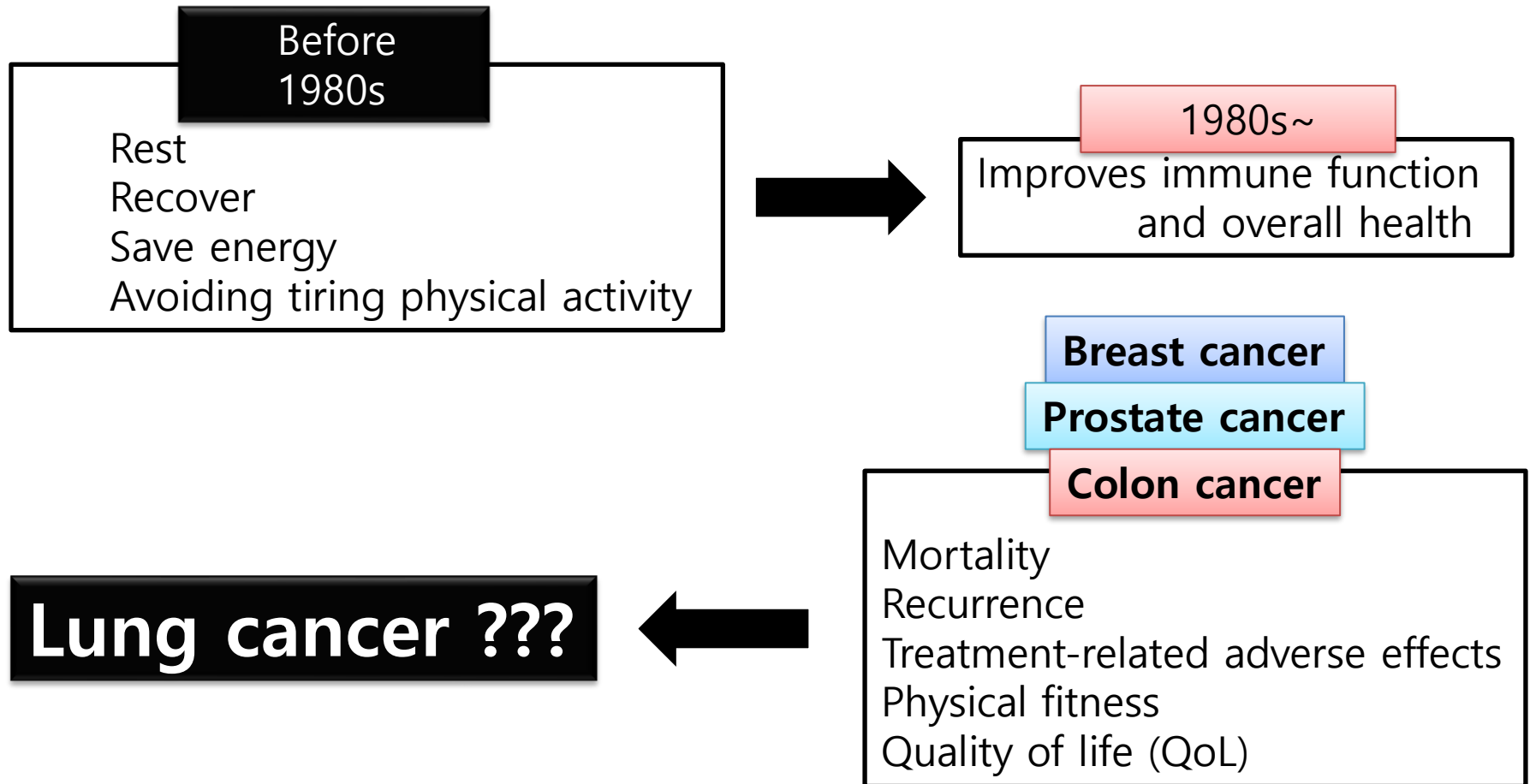
Physical activity

ANY BODILY MOVEMENT produced by **SKELETAL MUSCLES** that results in **ENERGY EXPENDITURE**

Exercise

PLANNED, STRUCTURED, AND REPETITIVE activities aimed at improving or maintaining one or more components of **PHYSICAL FITNESS**

Exercise and physical activity



Lung cancer

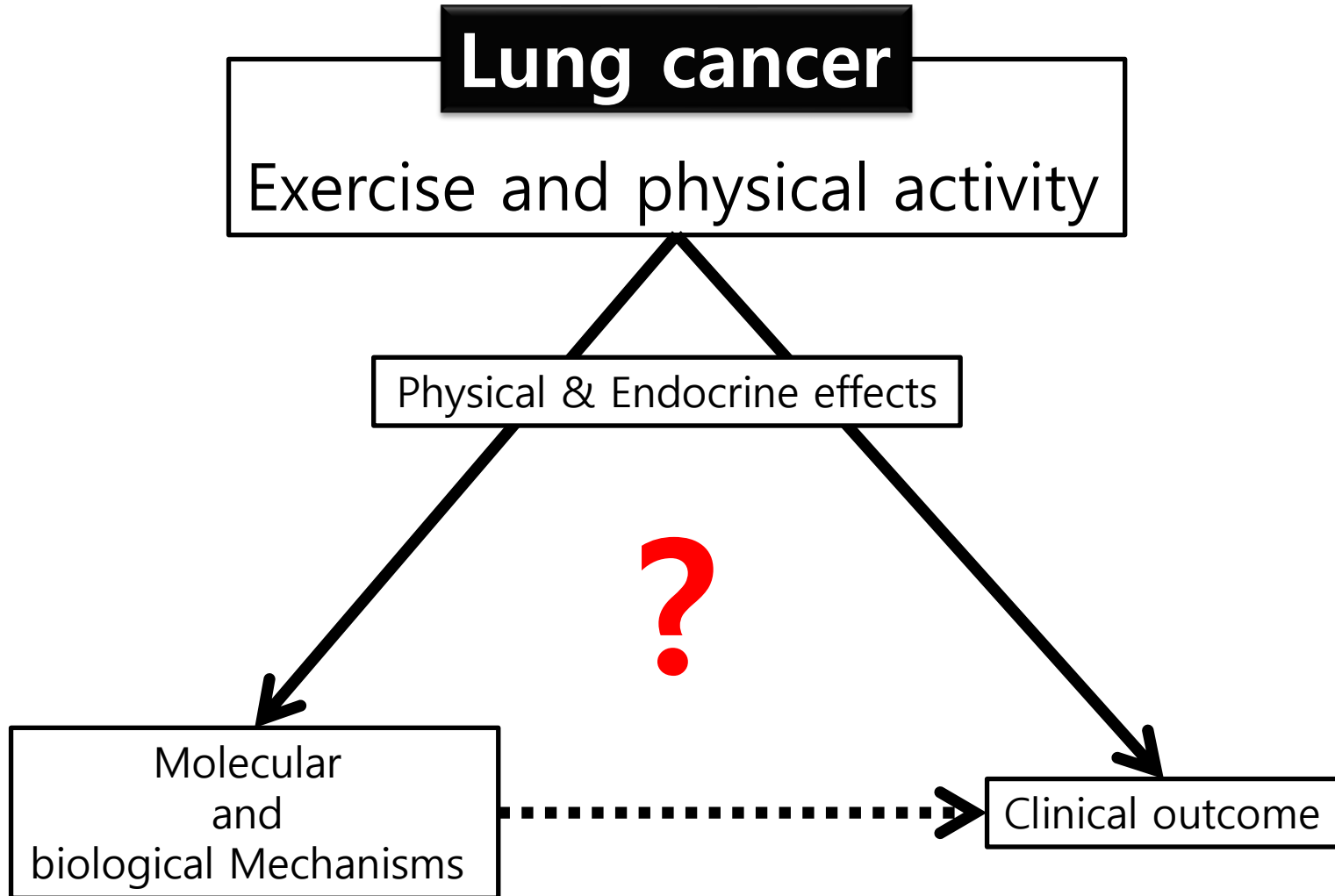
Exercise and physical activity

Physical & Endocrine effects

?

Molecular
and
biological Mechanisms

Clinical outcome





Exercise

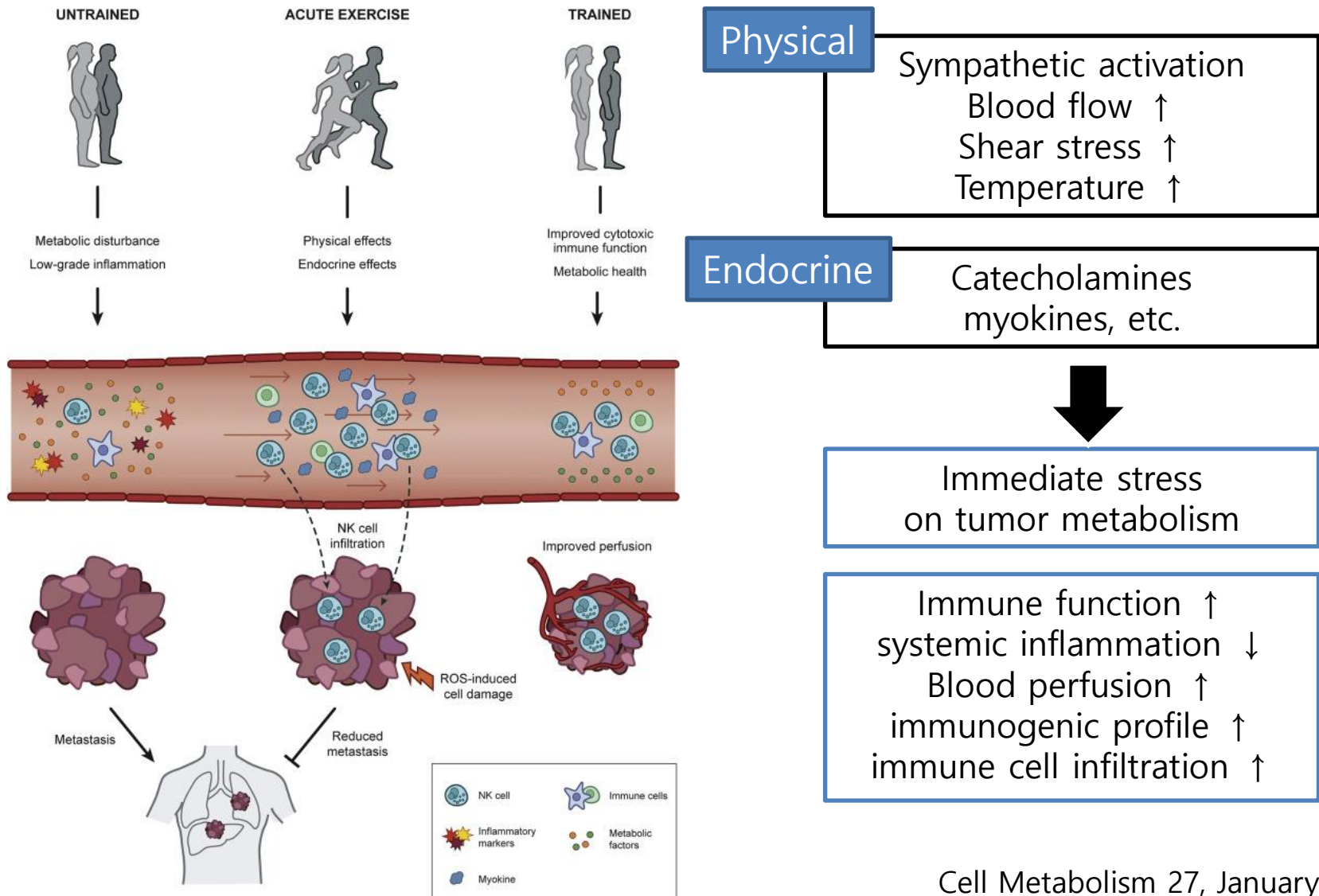
Effect on cancer Immune

MOLECULAR AND BIOLOGICAL MECHANISMS



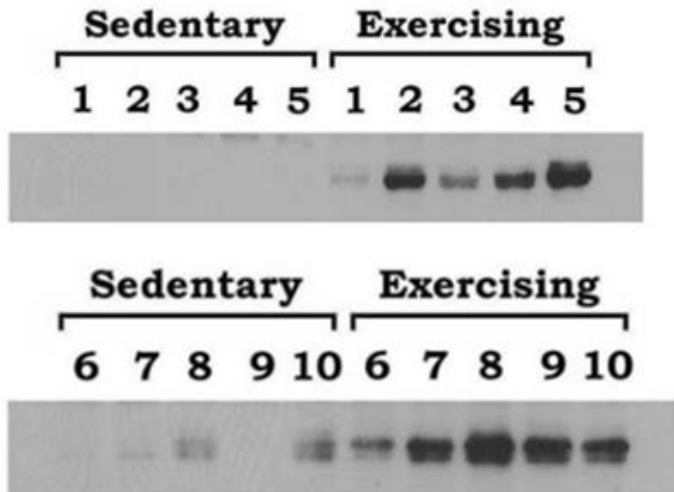
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Molecular Mechanisms Linking Exercise to Cancer Protection



p53, Apoptosis

- P53, tumor suppressor protein
- Murine model of lung ADC
- Daily **wheel running** 4 weeks



Western blots, p53

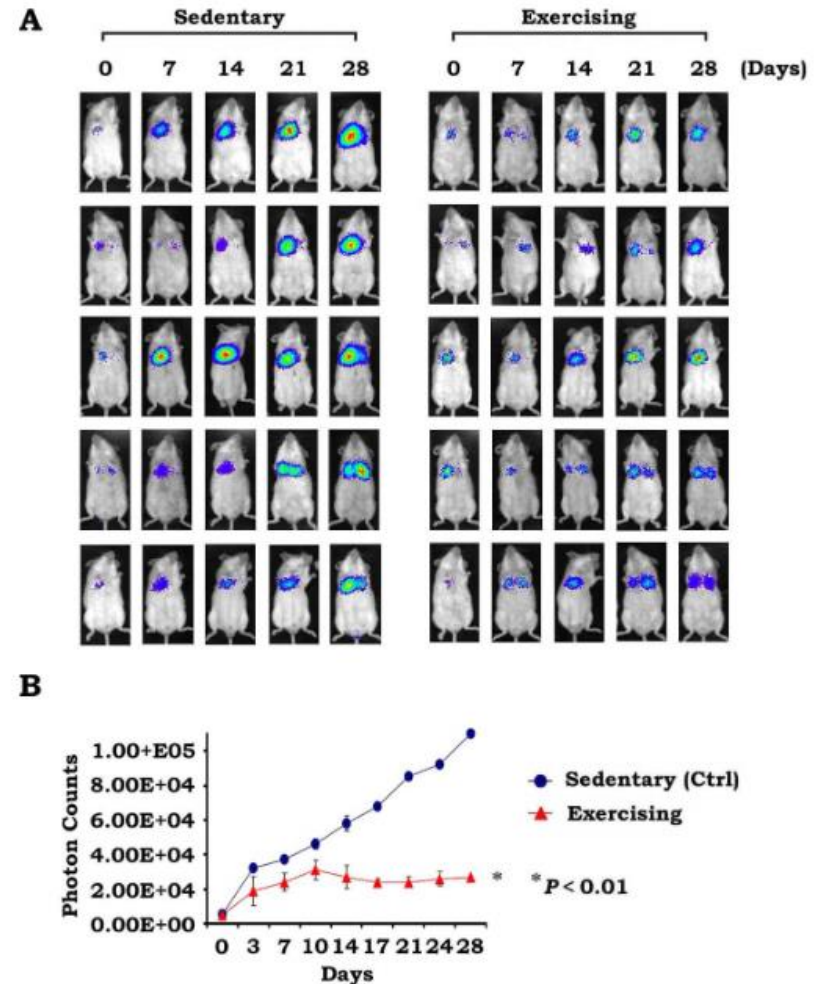


Figure 2. Exercise repressed lung tumor growth in vivo. (A) Whole-body images were taken weekly of 5 representative mice in each cohort (individual pictures of all mice are not shown because of space limitations). Each row depicts lung tumor growth of an individual mouse tumor over 4 weeks. (B) Changes in mean photon counts in lung tumors over time are compared between sedentary (control [Ctrl]) mice versus exercising mice (all mice; there were 10 mice in each group), with sedentary mice exhibiting a significantly more rapid increase in mean photon counts.

Phosphoinositide 3-kinase(PI3K)/AKT pathway, Cell proliferation

- NSCLC cells
 - A549, H460, H1299
- Normal lung fibroblasts
 - MRC5
- High intensity interval exercise
- Post exercise serum (5min, 1hr, 24hr) → cells

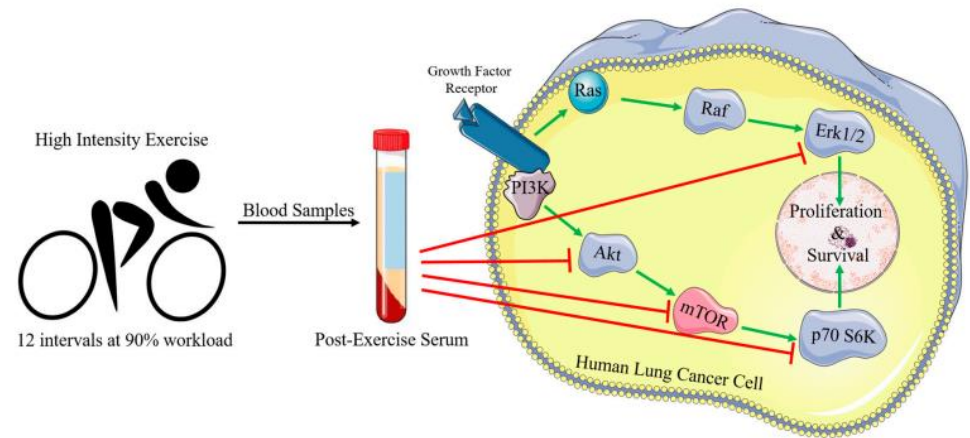
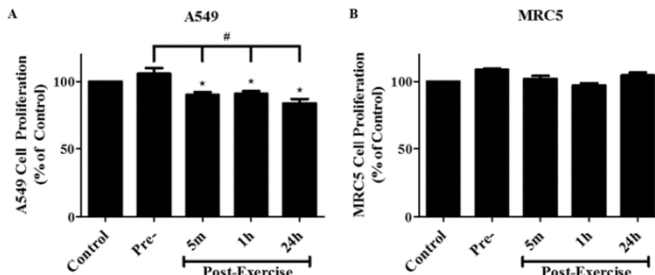
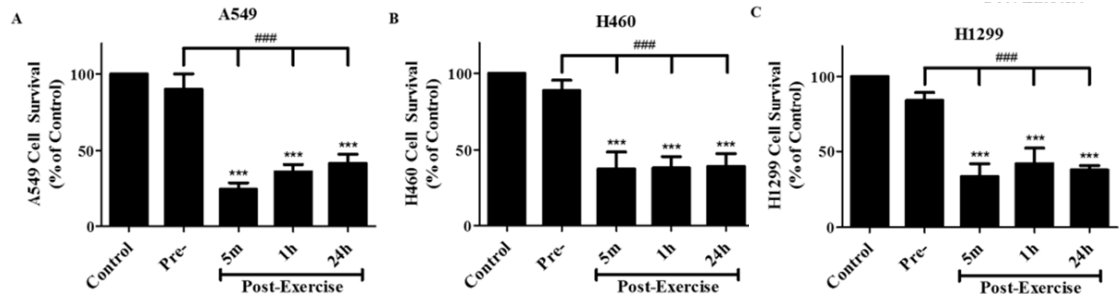


Figure 8. Potential mechanism of the inhibition of lung cancer cell proliferation and survival by post-exercise serum. Post-exercise serum inhibited Akt, mTOR, p70 S6K, and Erk1/2 phosphorylation/activation and resulted in significant inhibition of cell proliferation and survival.

Cell proliferation

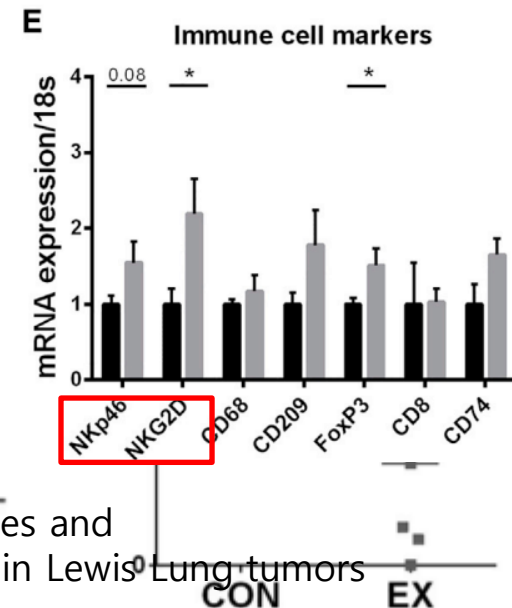
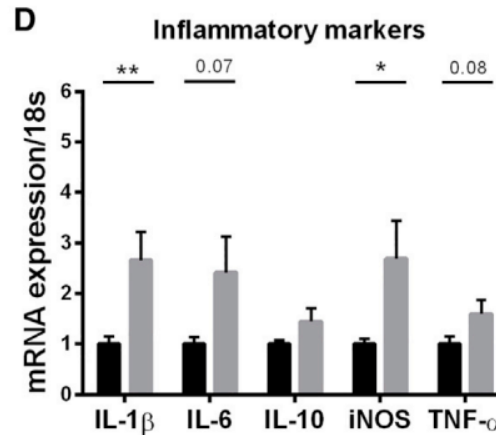
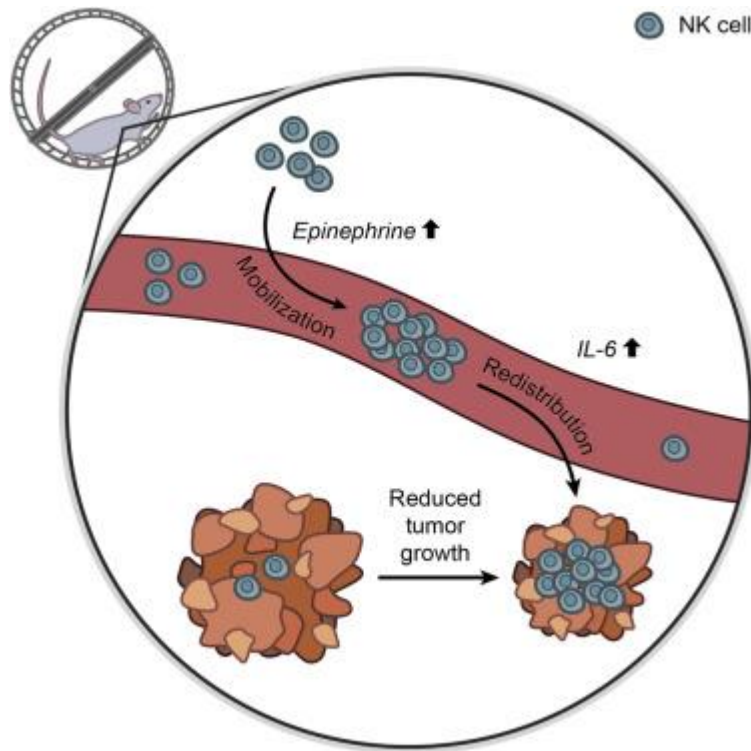


Cell survival



Immunomodulation on TME

- 6 weeks of wheel running in Lewis lung cancer (LLC) mice
- Reduced tumor volume
- Upregulation of proinflammatory cytokines



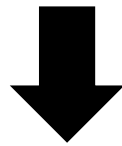
(D) inflammatory cytokines and
(E) immune cell markers in Lewis lung tumors

Frequency of immune cells

Number of tumors per lung

Molecular Mechanisms

- Emerging evidence indicates that **EXERCISE** is also directly linked to control of **TUMOR BIOLOGY**
- Not direct significance to lung cancer patients



May ultimately improve the clinical outcome



Exercise

Clinical outcome

PERIOPERATIVE IMPACT



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Pre-operative exercise

Maximize exercise capacity

Peak Oxygen Consumption

Functional capacity

Minimize the post-operative burden

Post-operative pulmonary complications

Intensive care admissions

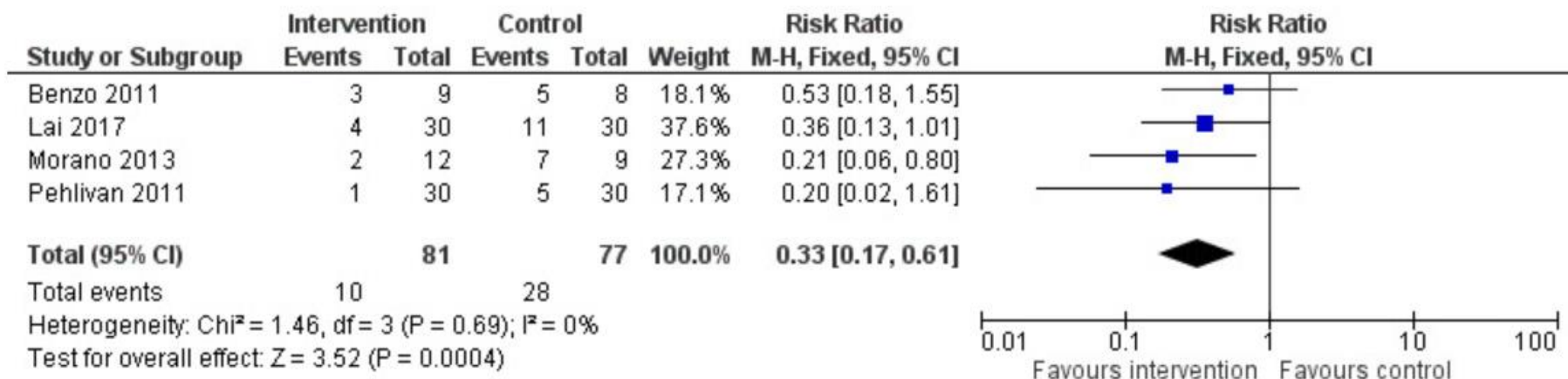
Length of hospital stay
Readmissions

Early and late mortality

Pre-operative exercise (NSCLC)

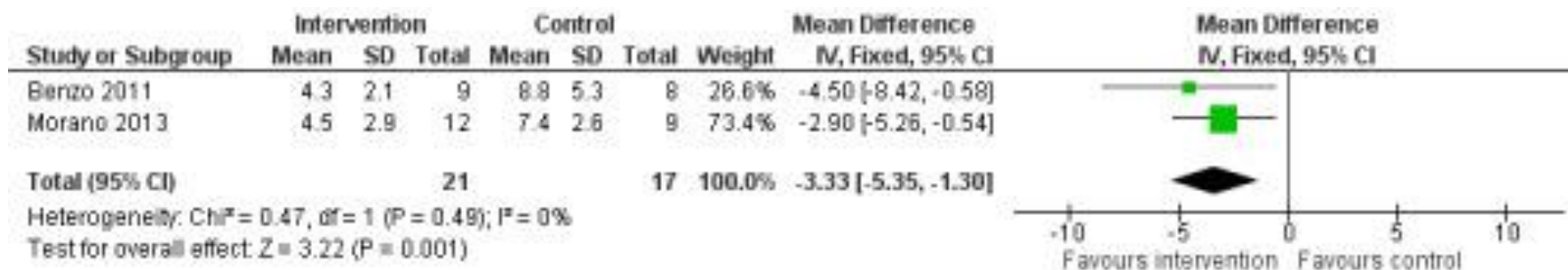
- RCT 2~4, total patients < 200
- Type, frequency, and intensity varied
 - 3 times/day for one week to 5 times/week for four weeks
 - Aerobic exercise training
 - Inspiratory muscle training and education or breathing exercises
 - Resistance training (1 study)
 - Stretches (1 study)

Postoperative pulmonary Complication

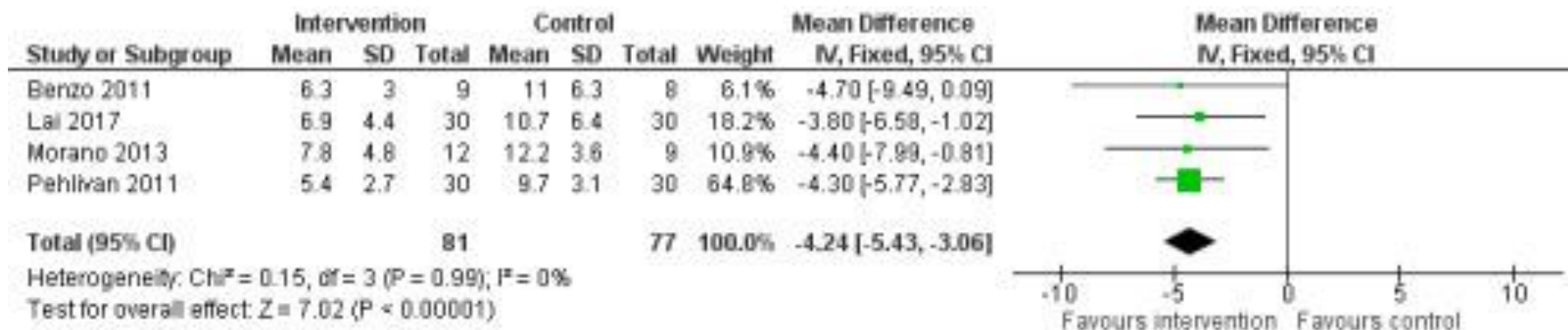


Pre-operative exercise (NSCLC)

Number of days patients needed an intercostal catheter



Postoperative length of hospital stay



Pre-operative exercise

- Type, frequency, and intensity varied
 - **Supervised training**
 - one ~ 4 weeks, 20 ~ 60 min/session
 - 2 /day ~ 3~7 sessions/week
 - Aerobic training
 - Increases the HR ≥ 5 min
 - 60–80% peak work capacity
 - Inspiratory muscle, strength, stretching training

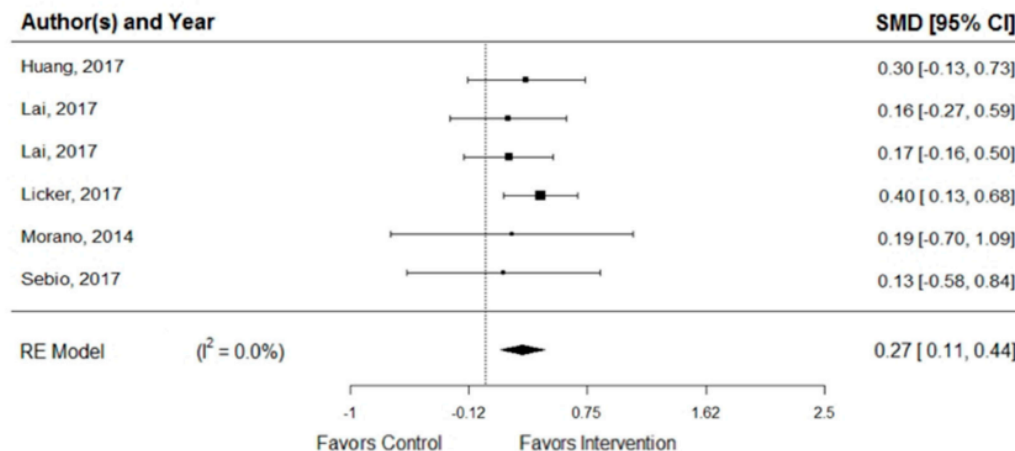


Review

Systematic Review and Meta-Analysis of Randomized, Controlled Trials on Preoperative Physical Exercise Interventions in Patients with Non-Small-Cell Lung Cancer

Ilem D. Rosero ¹, Robinson Ramírez-Vélez ¹, Alejandro Lucia ^{2,3,4}, Nicolas Martínez-Velilla ^{1,4}, Alejandro Santos-Lozano ^{2,5}, Pedro L. Valenzuela ⁶, Idoia Morilla ¹ and Mikel Izquierdo ^{1,4,*}

Functional capacity, 6MWD



Pre-operative exercise

Maximize exercise capacity

Peak Oxygen Consumption

Functional capacity

Minimize the post-operative burden

Post-operative pulmonary complications

Intensive care admissions

Length of hospital stay
Readmissions

Early and late mortality

Lack of
Large RCTs
Mortality data
Long term benefits data
Cost-effectiveness data

Acute post-operative exercise (in-hospital)

Bed rest

Physical deconditioning
Diminished muscle mass
Increased pulmonary complications
 (atelectasis and pneumonia)
Increased risk of VTE

'early mobilization'

Recommendations	Evidence level	Recommendation grade
Intercostal muscle- and nerve-sparing techniques are recommended	Moderate	Strong
Reapproximation of the ribs during thoracotomy closure should spare the inferior intercostal nerve	Moderate	Strong
Surgical technique A VATS approach	Enhanced recovery after surgery (ERAS) protocols	
Postoperative phase		
Chest drain management		
The routine application of external suction should be avoided	Low	Strong
Digital drainage systems reduce variability in decision-making and should be used	Low	Strong
Chest tubes should be removed even if the daily serous effusion is of high volume (up to 450 ml/24 h)	Moderate	Strong
A single tube should be used instead of 2 after anatomical lung resection	Moderate	Strong
Urinary drainage		
In patients with normal preoperative renal function, a transurethral catheter should not be routinely placed for the sole purpose of monitoring urine output	Moderate	Strong
It is reasonable to place a transurethral catheter in patients with thoracic epidural anaesthesia	Low	Strong
Early mobilization and adjuncts to physiotherapy		
Patients should be mobilized within 24 h of surgery	Low	Strong
Prophylactic minitracheostomy use may be considered in certain high-risk patients	Low	Weak

Post-operative exercise

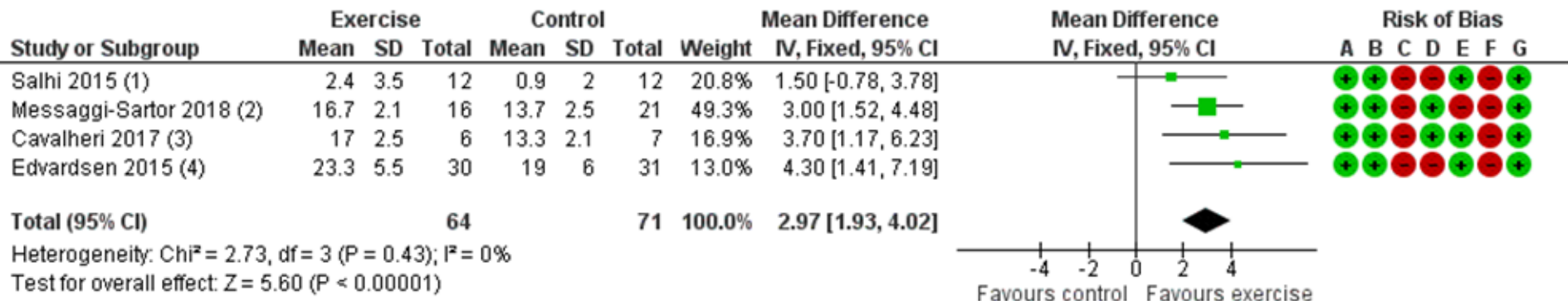
Recovery

Rehabilitation

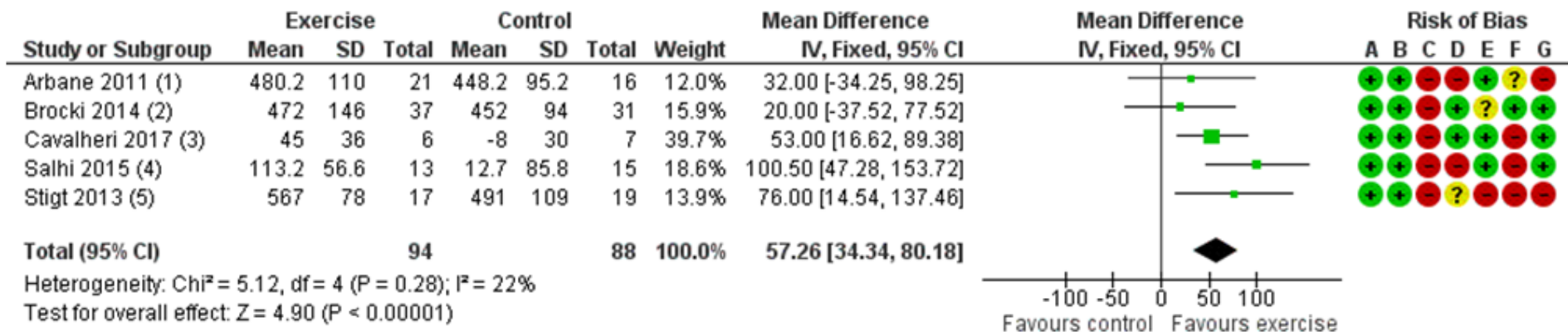
- Published RCTs commenced Frequency
 - 5–10 weeks following surgery
 - 6–12 weeks in duration (up to 20 weeks)
 - 2 to 3 times/week with **supervisor**
 - Supplemented with **home-based** exercise to achieve 5 times/week
- Exercise prescription
 - Aerobic exercise (moderate intensity)
 - High-intensity interval training on a stationary bike or a treadmill
 - Whole-body resistance training
 - Inspiratory muscle training
- Similar to **pulmonary rehabilitation with COPD**

Post-operative exercise

Exercise capacity (VO_2 peak in mL/kg/min)

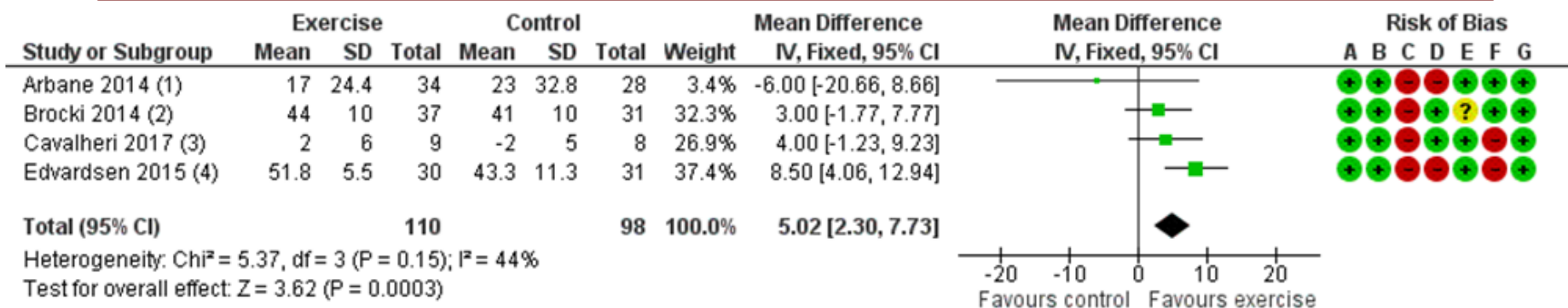


Exercise capacity (6MWD in metres)

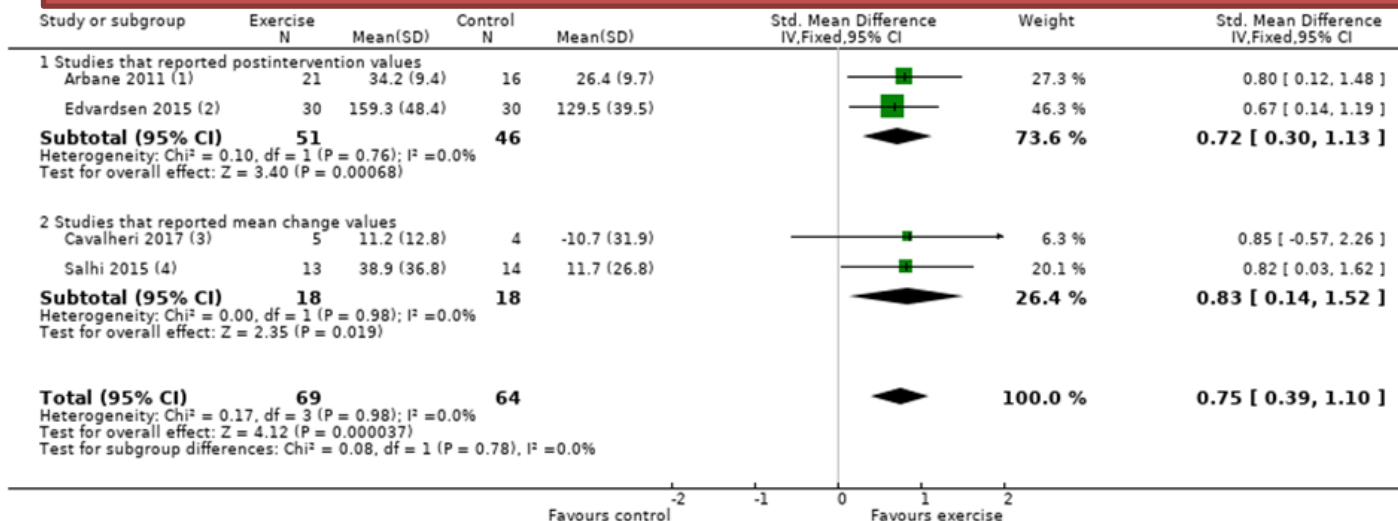


Post-operative exercise

General health-related quality of life (SF-36 - physical component score)



Force-generating capacity of peripheral muscle (quadriceps)





Exercise

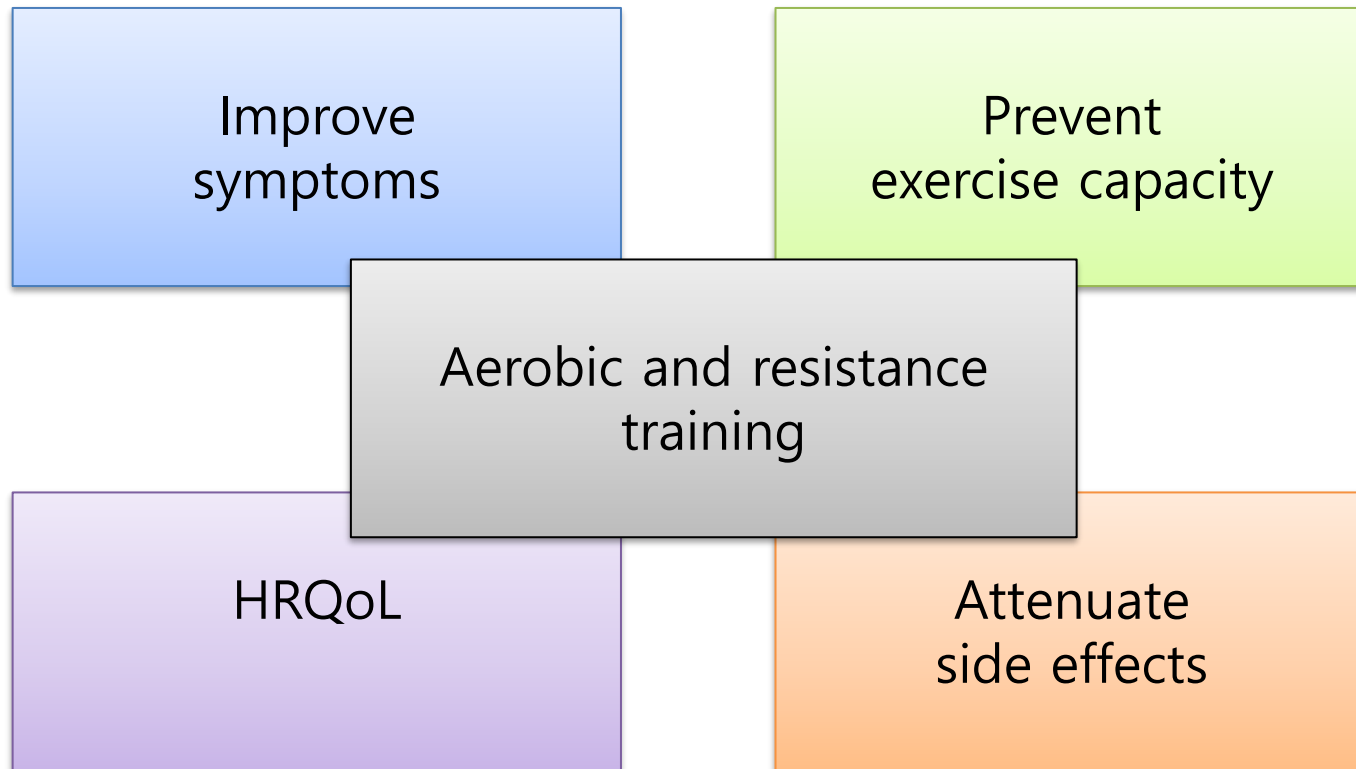
Clinical outcome

ADVANCED LUNG CANCER



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Exercise training in advanced stage lung cancer

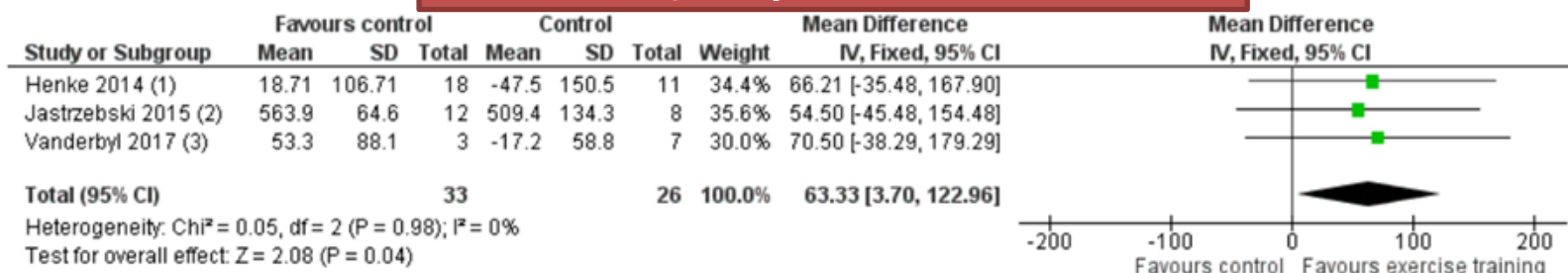


Exercise training in advanced stage lung cancer

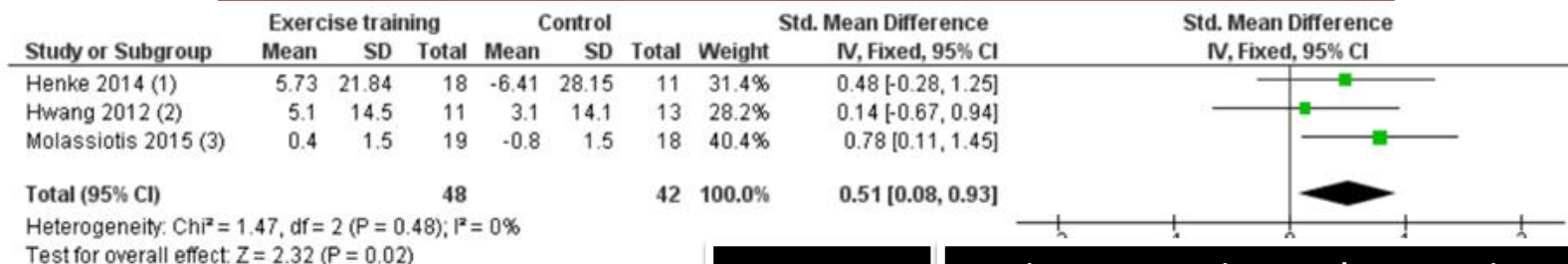
- **Very low to low certainty** for the effectiveness
 - Fewer RCT
 - Small sample sizes
 - Overall high risk of bias
(dyspnea, severe cancer related symptom, various regimen, etc.)
- A Cochrane review 6 RCT (total patients < 150)
 - During medical treatment
 - Length 6 to 12 weeks
 - **Supervised exercise** from 1 to 5 days a week

Exercise training in advanced stage lung cancer

Exercise capacity (6MWD in metres)

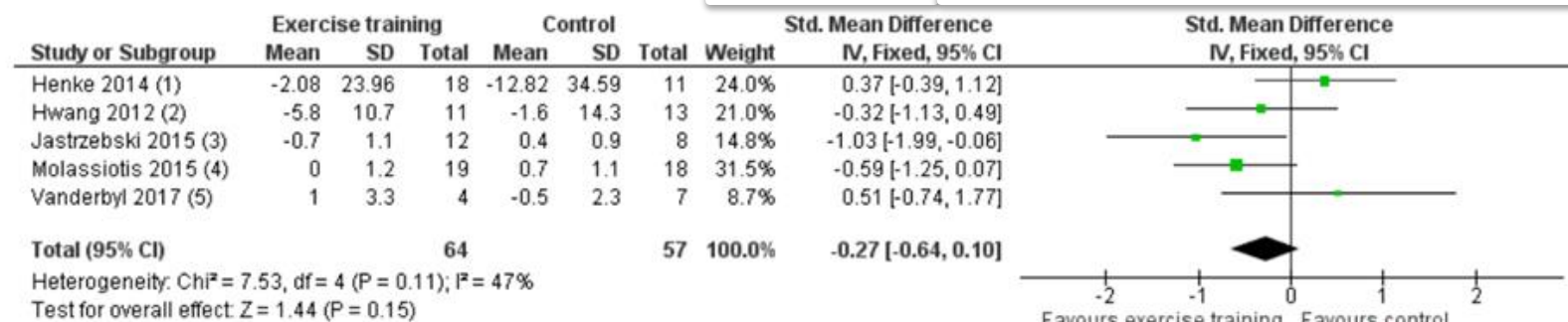


Disease-specific global health-related quality of life

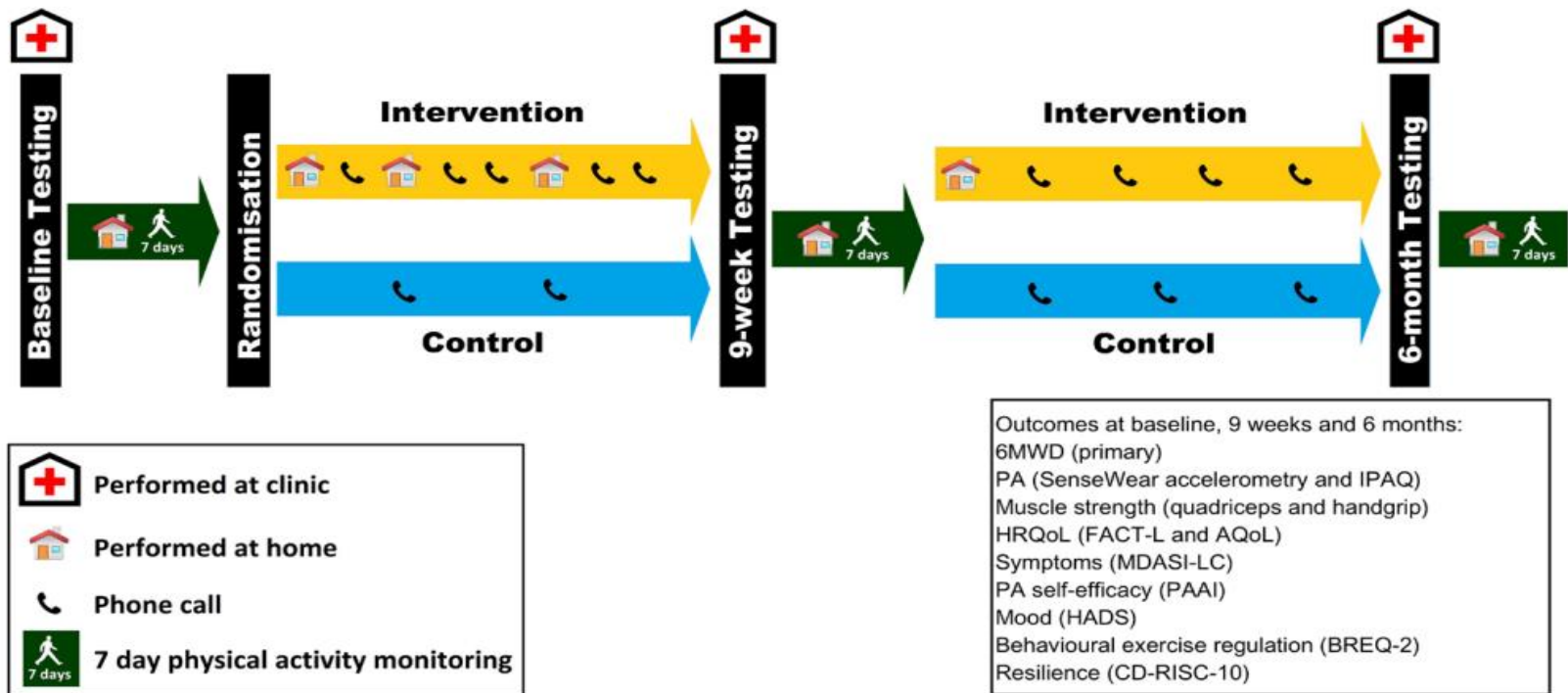


Dyspnea

Fatigue, anxiety, depression, FEV1



Efficacy of home-based rehabilitation



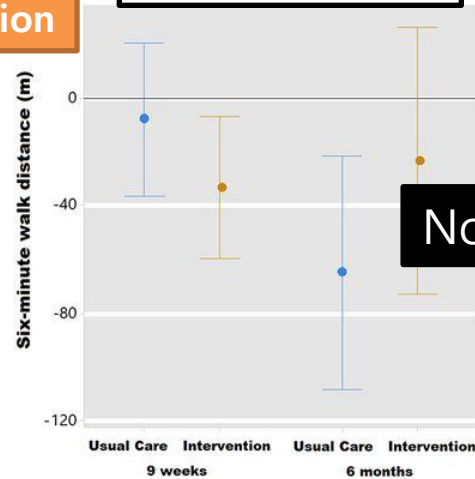
- Inoperable NSCLC (n=90)
- American College of Sports Medicine guidelines
 - Walking (preferred form of aerobic exercise in lung cancer patients)
 - Minimum of 10 min walking twice weekly at a moderate intensity
 - Resistance training

Efficacy of home-based rehabilitation

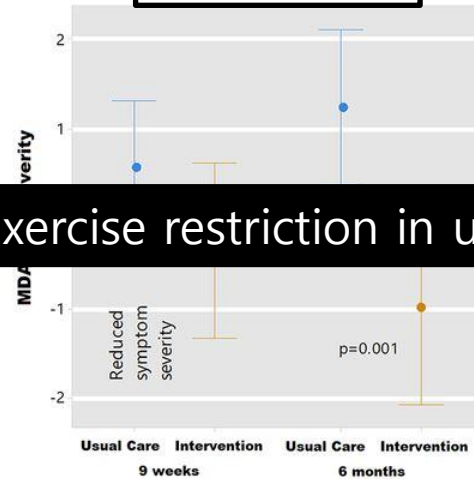
Usual care

intervention

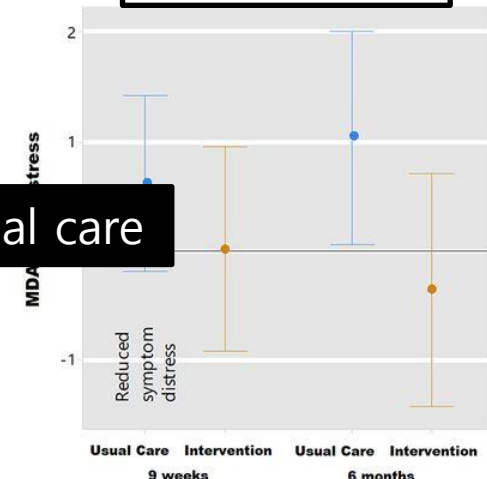
6 min walk distance



Symptom levels

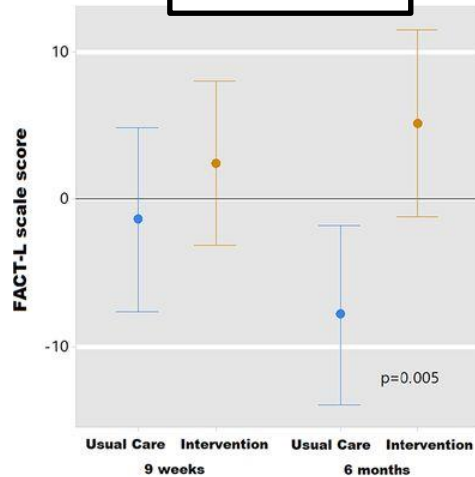


Symptom distress

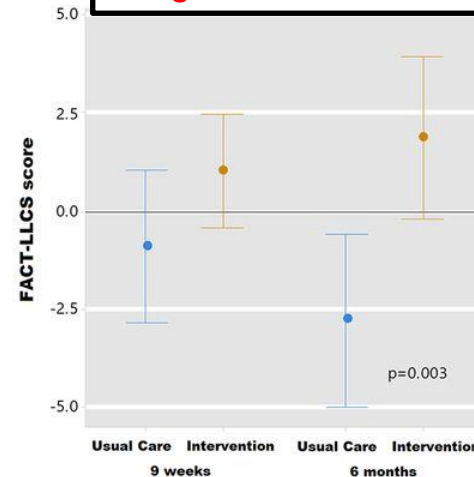


No exercise restriction in usual care

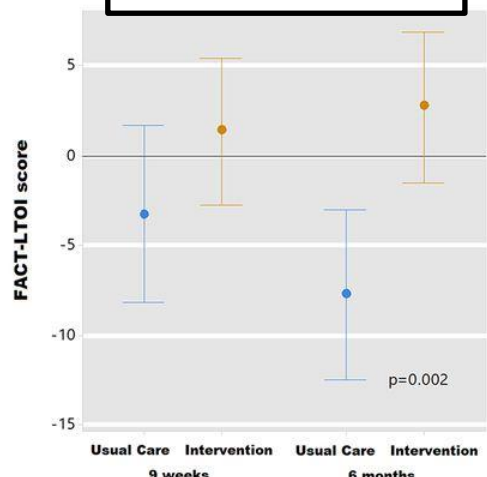
FACT-L scale



Lung Cancer Subscale



Trial Outcome Index



Efficacy of home-based rehabilitation

Baseline AGE

Intervention group (n=45)

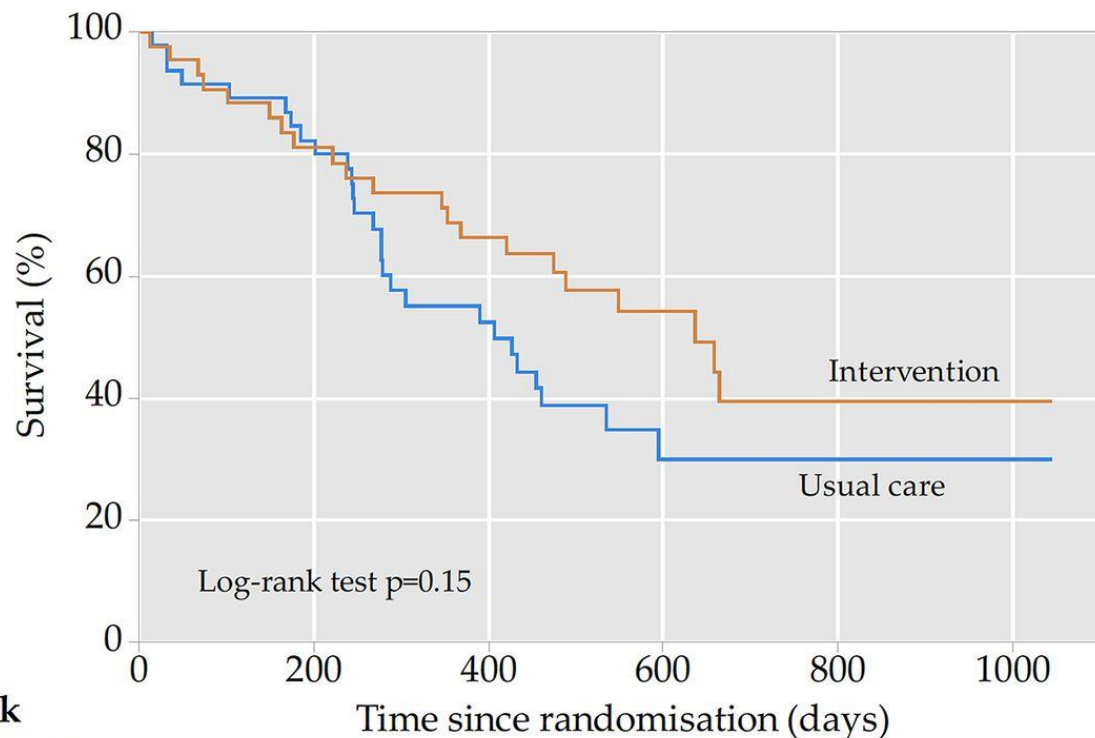
Usual care (n=47)

64.6 (13.4)

62.5 (10.9)

Significantly different
(mean (95% CI)

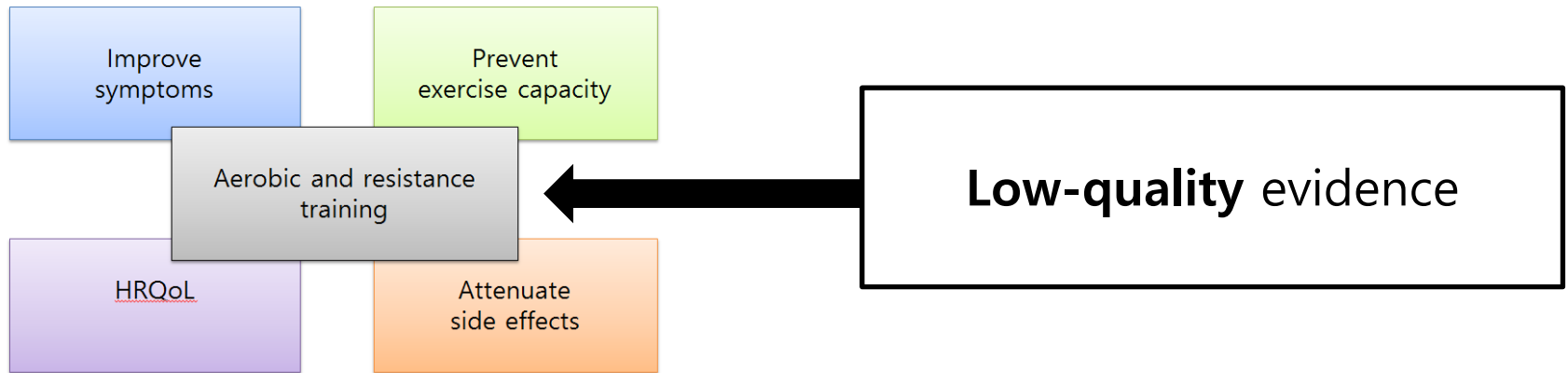
6.4 (2.9 to 9.9) years,
 $p=0.0004$)



Number at risk (number censored)

Intervention	45 (0)	33 (4)	26 (5)	12 (15)	2 (22)	0 (24)
Usual care	47 (0)	35 (4)	20 (7)	6 (14)	3 (17)	1 (19)

Exercise training in advanced stage lung cancer



**Low
risk of harm**

**Need for high-quality
RCT**



Exercise

How to exercise

HOW TO EXERCISE



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Peri-operative exercise

-호흡재활 지침서 2015-

- 수술 전후 호흡재활은 폐와 관련된 상태를 최적화할 수 있으며, 수술 후 합병증 예방 및 빠른 회복에 도움을 준다.
- 특히 폐절제술, 폐용적축소수술의 경우 적극적인 수술 전후 호흡재활이 필요하다.
- 폐이식 수술 전후의 호흡재활은 모든 폐이식 환자들에게 필수적인 프로그램이다.

표 6-6. 폐암을 포함하여 흉부 또는 상복부 수술 예정인 환자의 호흡재활 프로그램 내용

- Exercise training to increase muscle strength and endurance
- Pulmonary rehabilitation once chemotherapy or radiation therapy is completed
- Self-management strategies
- Assessment of need for assistive equipment and services
- Psychosocial intervention: coping, stress, and anxiety management techniques
- Education
 - Breathing retraining
 - Pacing
 - Energy conservation
 - Nutrition
 - When to seek health care services

Barriers limiting to exercise

- Most patients are **insufficiently active or sedentary**
- **low adherence and high drop-out rate**
 - Cancer-related side effects
 - Lack of interest and motivation
- Specifically related to health status (Age, sarcopenia, comorbidity)
- Lack of access to services
- Lack of interest
- Disease course and therapeutic approach
- Environmental and personal exercise preferences
- Social implications

Role in supporting patients with lung cancer to be physically active

- Doctors discussing physical activity with their patients
'Exercise as part of their cancer management'
 - Encourage increased physical activity, avoid sedentary time
 - Support setting individualized activity goal
 - Involve family and caregivers
 - Assess symptoms and assist
 - Understanding safety criteria
 - Refer to an exercise professional
 - Empower patients to take control their own goal
- Exercise testing and prescription for patients with lung cancer adheres to

GENERAL PRINCIPLES

ACSM(American College of Sports Medicine) Guidelines for Exercise and Cancer

What can exercise do?

What can exercise do?

- **Prevention of 7 common cancers***

Dose: 2018 Physical Activity Guidelines for Americans: 150-300 min/week moderate or 75-150 min/week vigorous aerobic exercise

- **Survival of 3 common cancers****

Dose: Exact dose of physical activity needed to reduce cancer-specific or all-cause mortality is not yet known; Overall more activity appears to lead to better risk reduction

**bladder, breast, colon, endometrial, esophageal, kidney and stomach cancers*

***breast, colon and prostate cancers*

	Physical Function	3x/week for 30-60 min per session of moderate to vigorous	2-3x/week of 2 sets of 8-12 reps for major muscle groups at moderate to vigorous intensity	3x/week for 20-40 min per session of moderate to vigorous aerobic exercise, plus 2-3x/week of resistance training 2 sets of 8-12 reps for major muscle group at moderate to vigorous intensity
	Anxiety	3x/week for 30-60 min per session of moderate to vigorous	Insufficient evidence	2-3x/week for 20-40 min of moderate to vigorous aerobic exercise plus 2x/week of resistance training of 2 sets, 8-12 reps for major muscle groups at moderate to vigorous intensity
	Depression	3x/week for 30-60 min per session of moderate to vigorous	Insufficient evidence	2-3x/week for 20-40 min of moderate to vigorous aerobic exercise plus 2x/week of resistance training of 2 sets, 8-12 reps for major muscle groups at moderate to vigorous intensity
	Lymphedema	Insufficient evidence	2-3x/week of progressive, supervised, program for major muscle groups does not exacerbate lymphedema	Insufficient evidence
Moderate Evidence				
	Bone health	Insufficient evidence	2-3x/week of moderate to vigorous resistance training plus high impact training (sufficient to generate ground reaction force of 3-4 time body weight) for at least 12 months	Insufficient evidence
	Sleep	3-4x/week for 30-40 min per session of moderate intensity	Insufficient evidence	Insufficient evidence

Citation: bit.ly/cancer_exercise_guidelines

Moderate intensity (40%-59% heart rate reserve or VO₂R) to vigorous intensity (60%-89% heart rate reserve or VO₂R) is recommended.

Exercise
is Medicine®

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LEADING THE WAY

NCCN Guidelines Version 3.2021

Survivorship: Physical Activity

GENERAL PRINCIPLES OF PHYSICAL ACTIVITY

- Physical activity and exercise recommendations should be tailored to individual's **Survivor's abilities and preference**
- Physical activity for cancer survivors:
 - Survivors should **At least 150 min of weekly activity** **Ultimate goal of 300 min** **Moderate intensity** activity or 75 minutes of vigorous intensity activity or equivalent combination spread out over the course of the week.
 - Two to three sessions per week of strength/resistance training that include major muscle groups ([See SPA-A](#))
 - Stretch major muscle at least 2 days/wk** week on days that other exercises are performed
- Engage in general physical activity daily (eg, take the stairs, park in the back of parking lot)
 - Physical activity includes exercise, daily routine activities, and recreational activities
- Avoid prolonged sedentary behavior (eg, sitting for long periods)
 - Schedule movement/activity breaks regularly
 - Stand or move while** on the phone, using the computer, or watching television

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NCCN Guidelines Version 3.2021

Survivorship: Physical Activity

GUIDANCE FOR RESISTANCE TRAINING RECOMMENDATIONS

- Health benefits of resistance training include improvement in **Muscle strength, endurance, functional status, bone density** maintenance/improvement in bone density
- Core and strength training is important to **Maintain balance, minimize fall risk**
- All **Major muscle groups** (ie, neck, shoulders, arms, back, core, and legs) should be incorporated into a resistance training program.
- Resistance training
 - Frequency: **2~3 times/wk** adequate rest between sessions
 - Intensity: **2~3 sets of 10~15 repetitions** 10~15 repetitions per set; consider increasing weight amount as tolerated w/ **Exercise specialist if available**
 - Rest: 2- to 3-minute rest period between sets and exercises
 - For survivors who wish to start resistance training, refer to trained personnel or **Exercise specialist if available**
- Utilize weight amount that would allow for performance of 10–15 repetitions.
- For survivors at risk for or with lymphedema, [See SLYMPH-B](#).

EXAMPLES OF PHYSICAL ACTIVITY		
Light Exercise^a (No noticeable change in breathing pattern) • Leisurely biking at 5 miles/hour or less • Activity-promoting video game • Light housework (light sweeping, dusting) • Bowling • Playing catch • Slow walking • Child care • Restorative yoga • Tai chi	Moderate Exercise^b (Can talk, but not sing) • Ballroom/line dancing • Biking on level ground or with few hills • General gardening • Baseball, softball, volleyball • Doubles tennis • Using a manual wheelchair • Brisk walking • Water aerobics • Moderate-intensity yoga (ie, Vinyasa) • Pilates	Vigorous Exercise^b (Can say a few words without stopping to catch a breath) • Aerobic/Fast dancing • Biking faster than 10 miles/hour • Heavy gardening • Hiking uphill • Jumping rope • Martial arts • Race walking, jogging, running • Running sports (basketball, hockey, soccer) • Swimming (fast pace or laps) • Singles tennis • Stair climbing • High-intensity yoga

Brisk walking

STRATEGIES TO INCREASE PHYSICAL ACTIVITY
• Physician recommendation • Referral to trained personnel or exercise specialist if available • Supervised exercise program or classes • Telephone counseling • Motivational interviewing^c • Evaluate readiness to change, importance of change, self-efficacy • Cancer survivor-specific print materials (See SURV-B 2 of 2) • Set short- and long-term goals • Consider use of pedometer or wearable fitness tracker to monitor activity goals (eg, obtain 10,000 steps per day) • Encourage social support (exercise buddy, group)

^aFrom the National Heart, Lung, and Blood Institute (http://www.nhlbi.nih.gov/health/public/heart/obesity/lose_wt/phy_act.htm) and the Compendium of Physical Activities (<https://sites.google.com/site/compendiumofphysicalactivities>).

^bReproduced and adapted from U.S. Department of Health and Human Services. Move Your Way. Washington, DC: U.S. Department of Health and Human Services. <https://health.gov/moveyourway>. Accessed March 16, 2020.

^cConsider referral to trained personnel.

ACS, ACSM and NCCN guideline

**Avoiding inactivity
Engage in regular physical activity**

>150 min/wk of moderate aerobic activity
or
>75 min/wk of vigorous aerobic activity

Flexibility and strength exercise
2~3 times/wk

Stretch major muscle group
2 times/wk

Physically deconditioned patients

Individual survivor's abilities and preference

Flexible
Start easily
Progress slowly

Cancer specific consideration

- ACSM guidelines-

Issue	Advice
Comorbid disease	Complete screening in line with general guidelines and choose exercises that avoid exacerbation of symptoms , for example hydrotherapy .
Bony metastases	Avoid strength assessment of muscles that attach to or act on a bony lesion site . Sites without metastases can be tested. Advise patients to avoid weights involving the affected bones and try swimming . Do not avoid resistance training .
Peripheral neuropathy	Assess balance, mobility and falls risk and modify exercise prescription as required (eg use a Stationary cycle or water rather than a treadmill for aerobic exercise).
Infection and Immunity	Advise patients that exercising with a fever is contraindicated . Precautions exist for patients with impaired hematological parameters; for example, patients with low neutrophil counts ($\leq 0.5 \times 10^9$ cells/ μ L) should avoid public gyms.
Cancer cachexia	Commence with prescription for resistance training only to increase muscle mass

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Nutrition

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Nutrition

LUNG CANCER PREVENTION

Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study

- 29,133 men
- Smoker 50-69 years
 - α -tocopherol (50 mg)
 - β -carotene (20 mg)
 - α -tocopherol + β -carotene
 - placebo
- Daily, median, 6.1 yrs

Table 3. Number of cases, age- and cigarette-adjusted incidence rates (per 10⁵ person-years), and relative risk from proportional hazards models for lung cancer by β -carotene intervention and level of base-line lung cancer risk factors*

	β -Carotene		No β -carotene		RR (95% CI)†
	No. of cases	Rate	No. of cases	Rate	
Total	482	580	412	497	1.16 (1.02-1.33)
Factor and category					
Age, y‡					
50-54	75	249	57	182	1.34 (0.95-1.90)
55-59	142	515	126	462	1.11 (0.87-1.41)
60-64	163	890	156	868	1.03 (0.82-1.28)
65-69	102	1241	73	907	1.39 (1.03-1.88)
					P for trend = .72
Cigarettes/day‡					
5-19	127	410	130	431	0.97 (0.76-1.23)
20-29	244	635	196	500	1.25 (1.04-1.51)
≥30	111	746	86	563	1.28 (0.97-1.70)
					P for trend = .15
Years of cigarette smoking					
≤30	40	349	31	222	1.28 (0.80-2.05)
31-35	61	560	44	294	1.44 (0.98-2.12)
36-41	142	579	133	554	1.06 (0.84-1.34)
>41	237	1017	204	884	1.15 (0.96-1.39)
					P for trend = .78
Cigarette smoke inhalation					
Never/seldom	30	415	27	368	1.10 (0.66-1.86)
		565		518	1.08 (0.87-1.34)
		629		510	1.23 (1.04-1.47)
					P for trend = .42
		655	11	677	0.79 (0.33-1.88)
		580	401	493	1.17 (1.03-1.34)
					P for interaction = .38

β -Carotene supplementation
 → lung cancer risk ↑
 (RR = 1.16; 95% CI = 1.02-1.33; P = 0.02)

†Relative risk (95% confidence interval). Two-sided P values.

‡Crude rates are presented for strata of age and cigarettes per day.

subgroup and included age, number of cigarettes smoked daily, years of cigarette smoking, body mass index (0, 1) for α -tocopherol and β -carotene intervention group. Interaction between intervention (yes, no) and cigarette smoking (yes, no) was tested using a cross-products term. Number of cases within intervention arm and factor reflect those with available data.

Impact of nutrition on the lung cancer Prevention

World Cancer Research Fund



American Institute for Cancer Research



Continuous Update Project

Analysing research on cancer prevention and survival



Diet, nutrition, physical activity and **lung cancer**

Revised 2018

- The International Agency for Research on Cancer (IARC) has graded arsenic and arsenic compounds as Class 1 carcinogens. The grading for this entry applies specifically to inorganic arsenic in drinking water.
- The evidence is derived from studies using high-dose supplements (20 mg/day for beta-carotene; 25,000 IU/day for retinol) in current and former smokers.
- The evidence applies to current and former smokers only.
- The evidence applies to current smokers only.
- The evidence applies only to individuals who have never smoked.

2017	DIET, NUTRITION, PHYSICAL ACTIVITY AND LUNG CANCER		
		DECREASES RISK	INCREASES RISK
STRONG EVIDENCE	Convincing		Arsenic in drinking water ¹ High-dose beta-carotene supplements ²
	Probable		
	Limited – suggestive	Vegetables ³ Fruit ³ Foods containing carotenoids Foods containing beta carotene Foods containing retinol	Red meat Processed meat Alcoholic drinks

ARSENIC in drinking water

Beta-CAROTENE supplements in current and former smokers

Impact of nutrition on the lung cancer Prevention –limited evidence

Decreases risk

- Vegetables, and Fruits
in current and former smokers
- **Foods** containing carotenoids
- **Foods** containing beta-carotene
- **Foods** containing retinol
- **Foods** containing Vitamin C
in current smoker
- **Foods** containing isoflavones
in never smoker
- Physical activity

Increases risk

- Red meat
- Processed meat
- Alcoholic drinks



Nutrition

SARCOPENIA

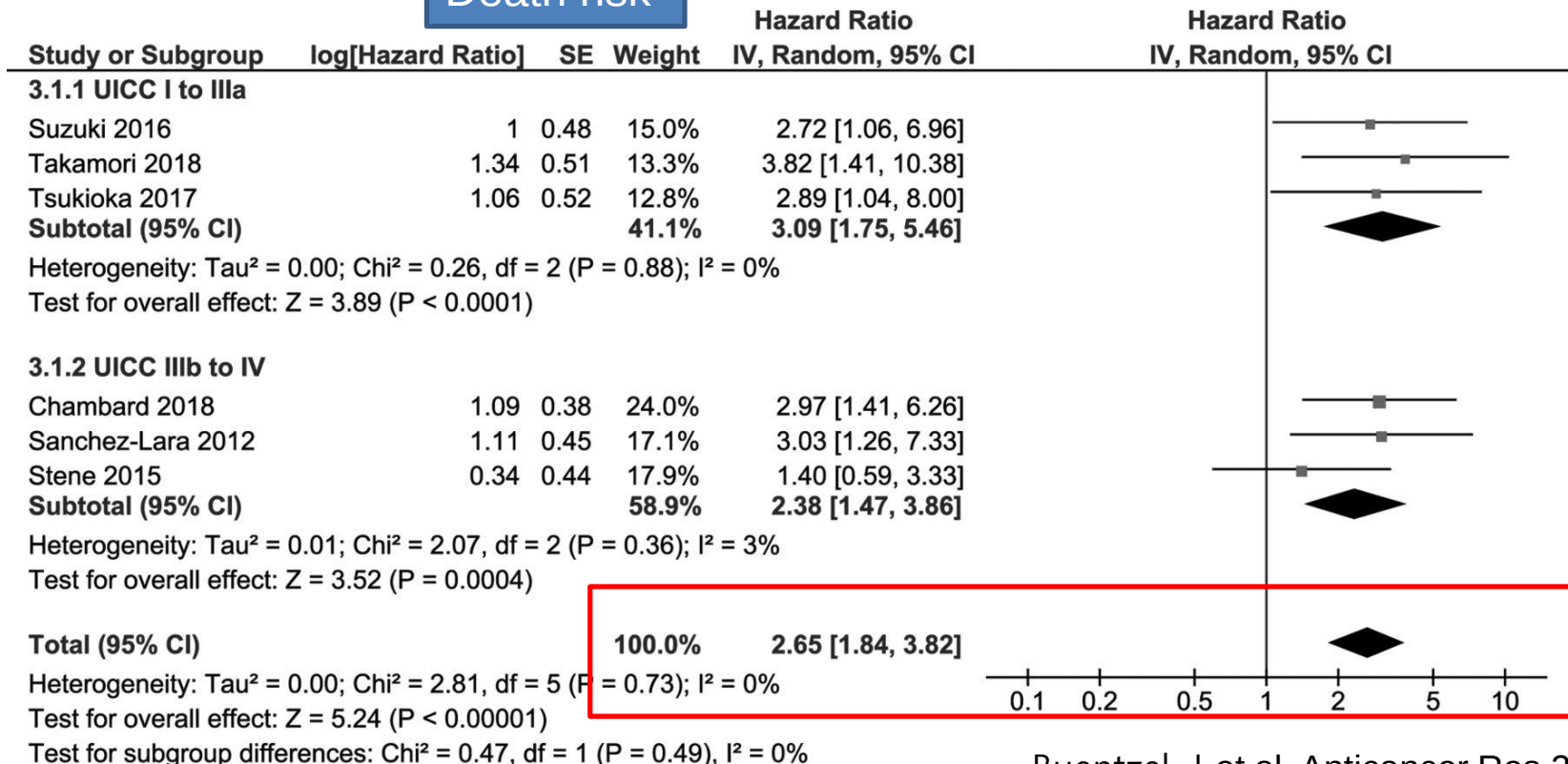


Risk factor for death

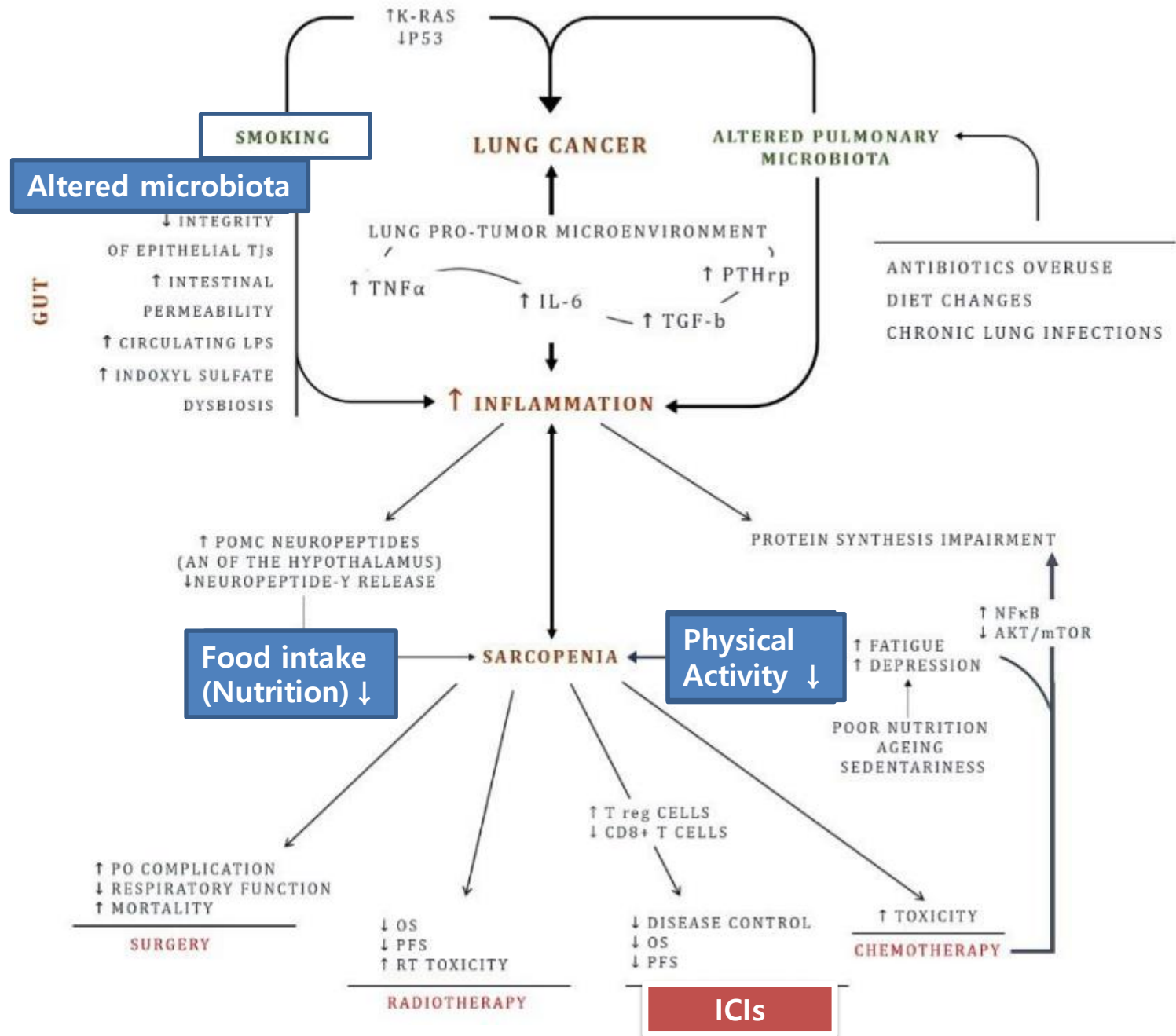
Sarcopenia is independent risk factor

→ Worse prognosis and increased death risk

Death risk

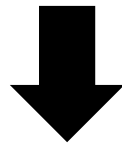


Lung cancer risk focus on chronic inflammation and sarcopenia



Nutritional approaches

- Nutritional approaches to prevent and treat cancer **Sarcopenia**
 - Adequate energy intake
 - Adequate supply of protein for maintenance or gain of muscle
 - Use of supplements



Nutritional counselling, planning



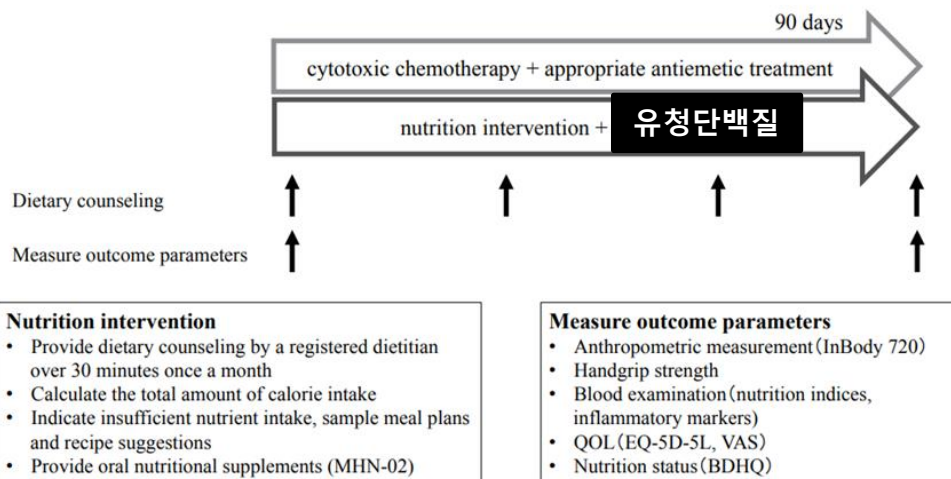
Nutrition

CLINICAL OUTCOME



인제대학교 해운대백병원

Early **nutritional** intervention with a dietary **counselling**



- Dietary counseling 30min/month
- Calculated the total calorie intake
- Indicate insufficient intake, sample meal plans and recipe suggestions
- Oral nutritional supplements (유청단백)

Table 4. Body weight change in the study patients and retrospective controls

		Patients	Retrospective controls	Unadjusted analysis*			IPTW analysis†		
				OR	95% CI	P value	OR	95% CI	P value
<i>n</i>		10	38						
Body weight change	Gain	6 (60%)	8 (21%)	5.6	1.2–25	0.044	8.4	1.6–42	0.01
	Loss	4 (40%)	30 (79%)						

IPTW analysis for the study patients versus retrospective controls was estimated using a logistic regression model based on age, sex, chemotherapy (platinum-based doublet chemotherapy or non-platinum chemotherapy), body height, and body weight.

*chi-square test; †generalized estimating equations.

CI, confidence interval; IPTW, inverse probability of treatment weight; OR, odds ratio.

Eicosapentaenoic Acid (EPA)

Table 4

Global, functional and symptom scales of Health-Related Quality of Life, differences within (Friedman test) and between ONS-EPA and C groups (*t*-student).

		Control	Δ	ONS-epa	Δ	<i>p</i> **
Global health status	T0	62.3 $\pm$ 23	-6.0 $\pm$ 2	54.3 $\pm$ 28	11.1 $\pm$ 4	0.136
	T1	56.1 $\pm$ 23		61.8 $\pm$ 18		
	T2	56.5 $\pm$ 26		65.4 $\pm$ 23		
	<i>p</i> *	0.209		0.021		
Functional Scales						
Physical functioning	T0	74.0 $\pm$ 23	-1.8 $\pm$ 0.3	64.5 $\pm$ 31	8 $\pm$ 3	0.419
	T1	67.6 $\pm$ 29		66.9 $\pm$ 25		
	T2	72.3 $\pm$ 27		72.5 $\pm$ 22		
	<i>p</i> *	0.802		0.507		
Symptom scales						
Fatigue	T0	35.9 $\pm$ 21	-1.2 $\pm$ 0.7	42.7 $\pm$ 24	-10.4 $\pm$ 6	0.04
	T1	38.5 $\pm$ 27		39.9 $\pm$ 20		
	T2	34.7 $\pm$ 20		32.3 $\pm$ 24		
	<i>p</i> *	0.772		0.05		
Appetite	T0	36.8 $\pm$ 34	-8.6 $\pm$ 4	41.5 $\pm$ 34	-6.6 $\pm$ 2	0.05
	T1	39.3 $\pm$ 34		27.3 $\pm$ 25		
	T2	28.2 $\pm$ 30		34.9 $\pm$ 31		
	<i>p</i> *	0.454		0.05		
N/V	T0	8.2 $\pm$ 14	11.4 $\pm$ 7	19.5 $\pm$ 23	8.4 $\pm$ 3	0.830
	T1	28.0 $\pm$ 69		33.0 $\pm$ 24		
	T2	19.6 $\pm$ 21		27.9 $\pm$ 30		
	<i>p</i> *	0.02		0.10		
Neuropathy	T0	11.7 $\pm$ 22	20.1 $\pm$ 13	19.9 $\pm$ 29	1 $\pm$ 0.4	0.05
	T1	20.5 $\pm$ 16		22.0 $\pm$ 27		
	T2	31.8 $\pm$ 30		20.9 $\pm$ 25		
	<i>p</i> *	0.004		0.951		
Diarrhoea	T0	6.1 $\pm$ 13	2.4 $\pm$ 1	20.0 $\pm$ 27	-8 $\pm$ 6	0.19
	T1	14.7 $\pm$ 24		19.2 $\pm$ 26		
	T2	8.6 $\pm$ 14		12.0 $\pm$ 12		
	<i>p</i> *	0.320		0.438		

ONS-EPA = Oral nutritional supplement containing eicosapentaenoic acid.

Δ = differences between T0 and T2 within groups.

**p* within groups. Friedman Test.

***p* between groups. *T*-Student.

- NSCLC 92 pts
- Paclitaxel + platinum 2cycle
- No difference in OS

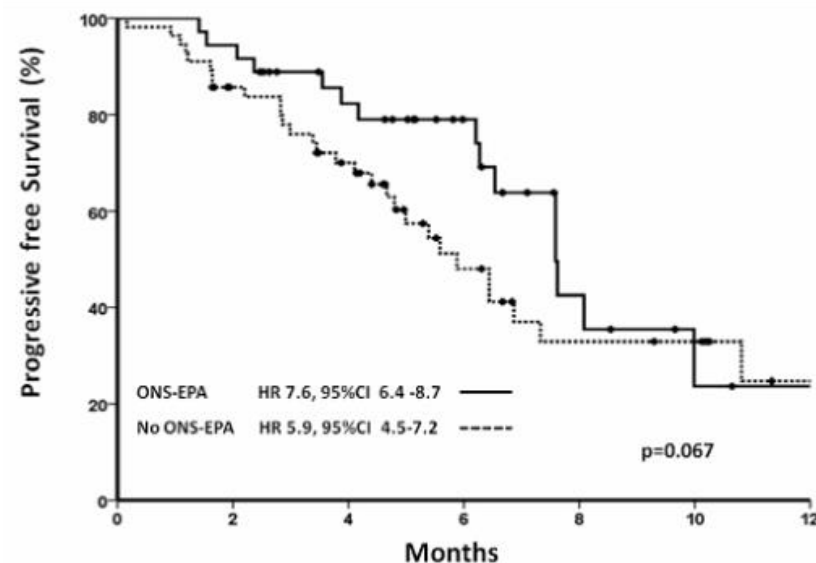


Fig. 2. Progression free survival Kaplan Meyer curves of ONS-EPA and C groups.

ProSure

- Nutritional supplement with eicosapentaenoic acid (ProSure) as a **Donation**, with no interference in the trial design and results analysis.



Fish oil supplementation

-Fish oil EPA-

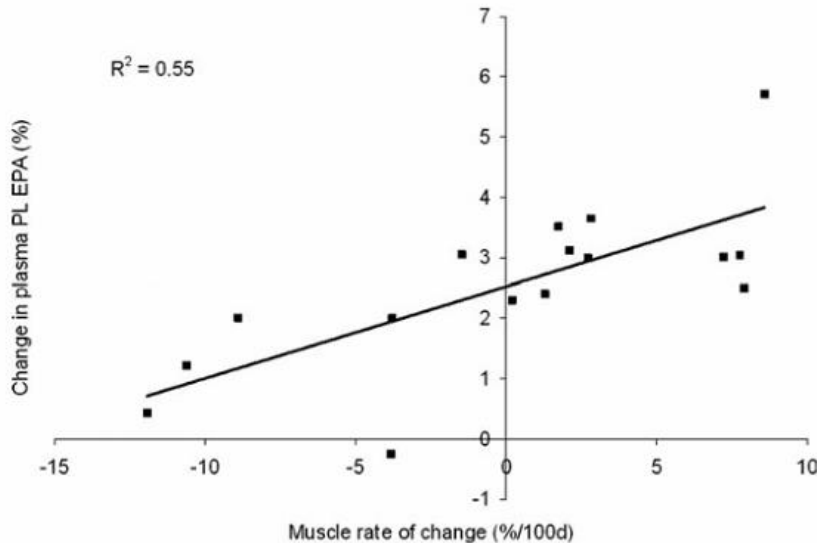


Figure 1. Relation between change in plasma phospholipid (PL) eicosapentaenoic acid (EPA) and change in muscle from baseline to end of fish oil supplementation is shown (n = 16).

- N=16(fish oil, 2.2gEPA/day)/40
- NSCLC Receiving 1st line CTx.
- Gain or maintain muscle mass

Changes	Standard of Care Group	Fish Oil Group	Reference Group
Weight change, kg	-2.3 ± 0.9	0.5 ± 1.0 ^b	1.9 ± 0.3
Muscle rate of change, %/100 d	-6.8 ± 2.6	0.1 ± 1.6 ^b	-6.0 ± 0.9
IMAT rate of change, %/100 d	9.5 ± 5.2	-16.4 ± 13.9 ^b	11.1 ± 3.5
TAT rate of change, %/100 d	-3.9 ± 5.0	-5.0 ± 6.5	-6.0 ± 4.6

CT indicates computed tomography; IMAT, intermuscular adipose tissue; TAT, total adipose tissue.

^aThe number of patients varies because of images outside the viewing field. Results are shown as the mean ± standard error.

^bSignificantly different from standard of care ($P < .05$, using the two-sample Student *t* test).

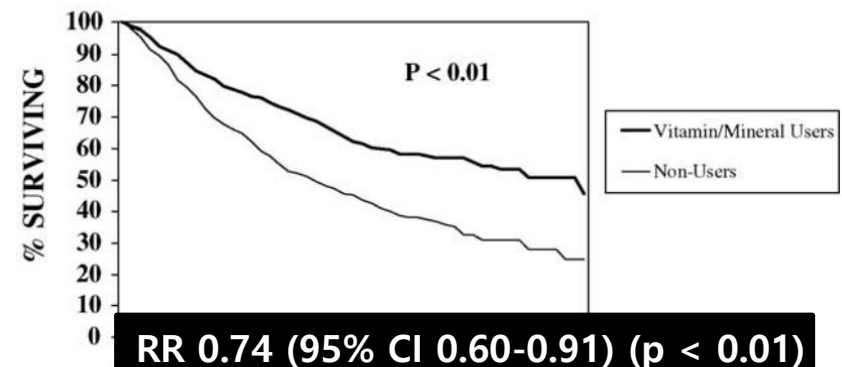
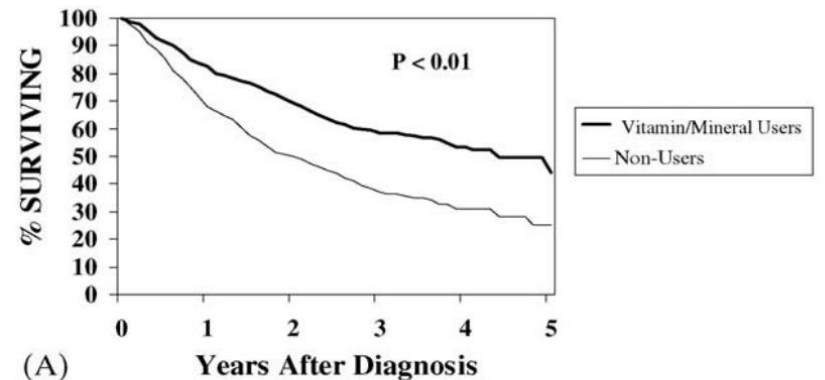
Pathologic type 구분 X
Chemo regimen 구분 X

Vitamin/mineral supplements

- ACS states that taking a **daily multi-vitamin/mineral** during treatment in **amounts not exceeding** the Recommended Daily Value could benefit those having **difficulty consuming a healthy diet**

Table 1 Baseline characteristics

	Vitamin/mineral users (n = 714)	Non-users (n = 415)	p-Value
Median age (25th, 75th percentile)	67 (59, 73)	67 (59, 74)	0.50
Male (%)	55	65	< 0.01
Pack-years of smoking (%)			
0	17	12	< 0.01
1–20	16	10	
21–40	22	24	
41–60	21	25	
Over 60	24	29	
Co-morbid conditions (at diagnosis) (%)			
Chronic obstructive pulmonary disease	36	40	0.17
Asthma	12	9	0.2
Other lung disease	19	17	0.59
Other cancer (not gender-related)	22	20	0.5
Diabetes	3	4	0.45
Heart disease	7	7	0.94
Cerebral vascular accident	0.4	2	0.06
Hypertension	6	5	0.66
Tumor histology (%)			
Adenocarcinoma	62	53	< 0.01
Squamous	26	30	
Other	12	17	
Stage (%)			
IA	26	19	0.02
IB	16	18	
IIA	4	3	
IIB	9	8	
IIIA	15	17	
IIIB	10	11	
IV	20	23	
Treatment 6 months after diagnosis (%)			
Chemotherapy	33	37	0.17
Radiation	25	36	< 0.01
Surgery	72	65	0.02



Adjustment for multiple prognostic factors



Nutrition

HOW TO SUPPORT NUTRITION



인제대학교 해운대백병원

Management of Cancer Cachexia: ASCO Guideline

Eric J. Roeland, MD¹; Kari Bohlke, ScD²; Vickie E. Baracos, PhD³; Eduardo Bruera, MD⁴; Egidio del Fabbro, MD⁵; Suzanne Dixon, MPH, MS, RD⁶; Marie Fallon, MD⁷; Jørn Herrstedt, MD, DMSci⁸; Harold Lau, MD⁹; Mary Platak, PhD, MS, RD¹⁰; Hope S. Rugo, MD¹¹; Hester H. Schnipper, LICSW, BCD, OSW-C¹²; Thomas J. Smith, MD¹³; Winston Tan, MD¹⁴; and Charles L. Loprinzi, MD¹⁵

Recommendations

Nutritional Interventions

Recommendation 1.1. Clinicians may refer patients with advanced cancer and loss of appetite and/or body weight to a registered dietitian for assessment and counseling, with the goals of providing patients and caregivers with practical and safe advice for feeding; education regarding high-protein, high-calorie, nutrient-dense food; and advice against fad diets and other unproven or extreme diets (Type of recommendation: informal consensus; Evidence quality: low; Strength of recommendation: moderate).

Recommendation 1.2. Outside the context of a clinical trial, clinicians should not routinely offer enteral tube feeding or parenteral nutrition to manage cachexia in patients with advanced cancer. A short-term trial of parenteral nutrition may be offered to a very select group of patients, such as patients who have a reversible bowel obstruction, short bowel syndrome, or other issues contributing to malabsorption, but otherwise are reasonably fit. Discontinuation of previously initiated enteral or parenteral nutrition near the end of life is appropriate (Type of recommendation: informal consensus; Evidence quality: low; Strength of recommendation: moderate).

Information about additional nutritional interventions considered by the Expert Panel is provided in [Table 1](#).

Pharmacologic Interventions

Recommendation 2.1. Evidence remains insufficient to strongly endorse any pharmacologic agent to improve cancer cachexia outcomes; clinicians may choose not to offer medications for the treatment of cancer cachexia. There are currently no FDA-approved medications for the indication of cancer cachexia (Type of recommendation: evidence based; Evidence quality: low; Strength of recommendation: moderate).

Recommendation 2.2. Clinicians may offer a short-term trial of a progesterone analog or a corticosteroid to patients experiencing loss of appetite and/or body weight. The choice of agent and duration of treatment depends on treatment goals and assessment of risk versus benefit (Type of recommendation: evidence based; Evidence quality: intermediate; Strength of recommendation: moderate).

Information about additional pharmacologic interventions considered by the Expert Panel is provided in [Table 1](#).

Other Interventions

Recommendation 3. Outside the context of a clinical trial, no recommendation can be made for other interventions, such as exercise, for the management of cancer cachexia.

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TABLE 1. Summary of Recommendations for the Treatment of Cancer Cachexia in Patients with Advanced Cancer

Intervention	Strength of Recommendation	Strength of the Evidence	Benefits ^a	Harms ^a
Nutritional interventions				
Dietary counseling ^{25,26,37}	Moderate in favor	Low	Moderate	Low
Parenteral or enteral nutrition (routine use) ^{31,42}	Moderate against	Low	Low	Moderate to high
Omega-3 fatty acids ^{25,29,40}	No recommendation	Low	Low	Low
Vitamins, minerals, and other dietary supplements ³⁸	No recommendation	Low	Low	Low
Pharmacologic interventions				
Progesterone analogs ^{30,33,35,36,43}	Moderate in favor	Intermediate	Moderate	Moderate
Corticosteroids ⁴³	Moderate in favor	Intermediate	Moderate	Moderate
Anamorelin ^{24,32,68}	No recommendation (not commercially available)	Intermediate	Moderate	Low
Olanzapine ⁵⁶	No recommendation	Low	Moderate	Low
Androgens ^{36,43,59}	No recommendation	Low	Moderate	Low
Thalidomide ^{34,36}	No recommendation	Low	Low	Low
NSAIDs ^{39,41}	No recommendation	Low	Low	Low
Cyproheptadine ⁴³	No recommendation	Low	None	Low
Cannabinoids ^{36,43}	Weak against	Low	None	Low
Melatonin ^{36,43}	Weak against	Low	None	Low
TNF inhibitors ^{36,43}	Moderate against	Intermediate	None	Moderate
Hydrazine sulfate ⁴³	Strong against	Intermediate	None	Moderate
Other interventions				
Exercise ²⁷	No recommendation	Low	Unknown	Unknown

Abbreviations: NSAIDs, nonsteroidal anti-inflammatory drugs; TNF, tumor necrosis factor.

^aCategorization of benefits and harms was based on use of the intervention for cancer cachexia in the populations that were enrolled in randomized controlled trials.

NCCN Guidelines Version 3.2021

Survivorship: Nutrition and Weight Management

GENERAL PRINCIPLES OF NUTRITION

- Assess dietary pattern for daily intake of fruits, vegetables, and unrefined grains; added fats and/or sugar; and red meats, processed meats and food, alcohol.
- Assess timing of meals and snacks, portion size, frequency of eating out, and use of added fats and/or sugars to foods or beverages.
- All survivors should be encouraged to:
 - ▶ Make informed choices about food to ensure variety and adequate nutrient intake.
 - ▶ Limit red meat < 0.5kg/week and avoid processed meat.
 - ▶ Limit refined sugars and saturated fats.
 - ▶ Eat a diet that is at least 50% plant-based, with a majority of food being vegetables, fruit, and whole grains.^{a,b}
 - ▶ Track calorie intake.
 - ◊ Self-monitoring of caloric density and intake has been shown to be an effective strategy for weight management.
 - ◊ Prolonged fasting X fasting may maximize caloric and nutrient intake.
 - ▶ Consume alcohol sparingly if at all.
- For patients desiring further recommendations for dietary guidelines
 - ▶ Consider referral to a dietitian or nutritionist.
 - ▶ The USDA approximate food plate volumes (www.choosemyplate.gov) are:
 - ◊ Vegetables and fruits should comprise half the volume of food on the plate
 - ◊ Vegetables: 30% of plate; fruits 20% of plate
 - ◊ Whole grains: 30% of plate
 - ◊ Protein: 20% of plate
- Recommended sources of dietary components:
 - ▶ Fat: plant sources such as olive or canola oil, avocados, seeds and nuts, and fish
 - ▶ Carbohydrates: fruits, vegetables, whole grains, and legumes
 - ▶ Protein: poultry, fish, legumes, low-fat dairy foods, and nuts
- Currently there is no consensus either refuting or supporting the role of soy food (3 or fewer servings per day) of soy foods is considered prudent.



ption

Summary -Exercise-



- Exercise is directly linked to control of tumor biology
- Perioperative exercise is recommended
- Exercise in advanced lung cancer has low certainty, but a low risk of harm
- Exercise is part of lung cancer management
- Encourage increased physical activity and avoid sedentary time

Summary

-Nutrition-



- Arsenic in drinking water and high dose β - carotene are risk factors of lung cancer
- Sarcopenia is an independent risk factor of lung cancer mortality
- Nutritional approach is needed for the prevent and treat of cancer sarcopenia (nutritional counselling and planning)



감사합니다.



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