

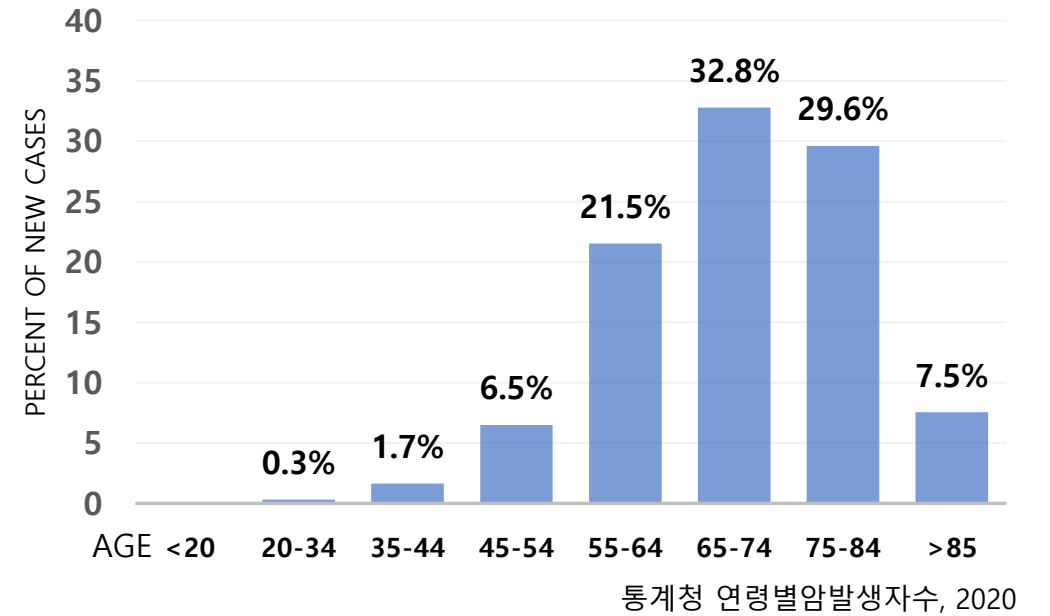
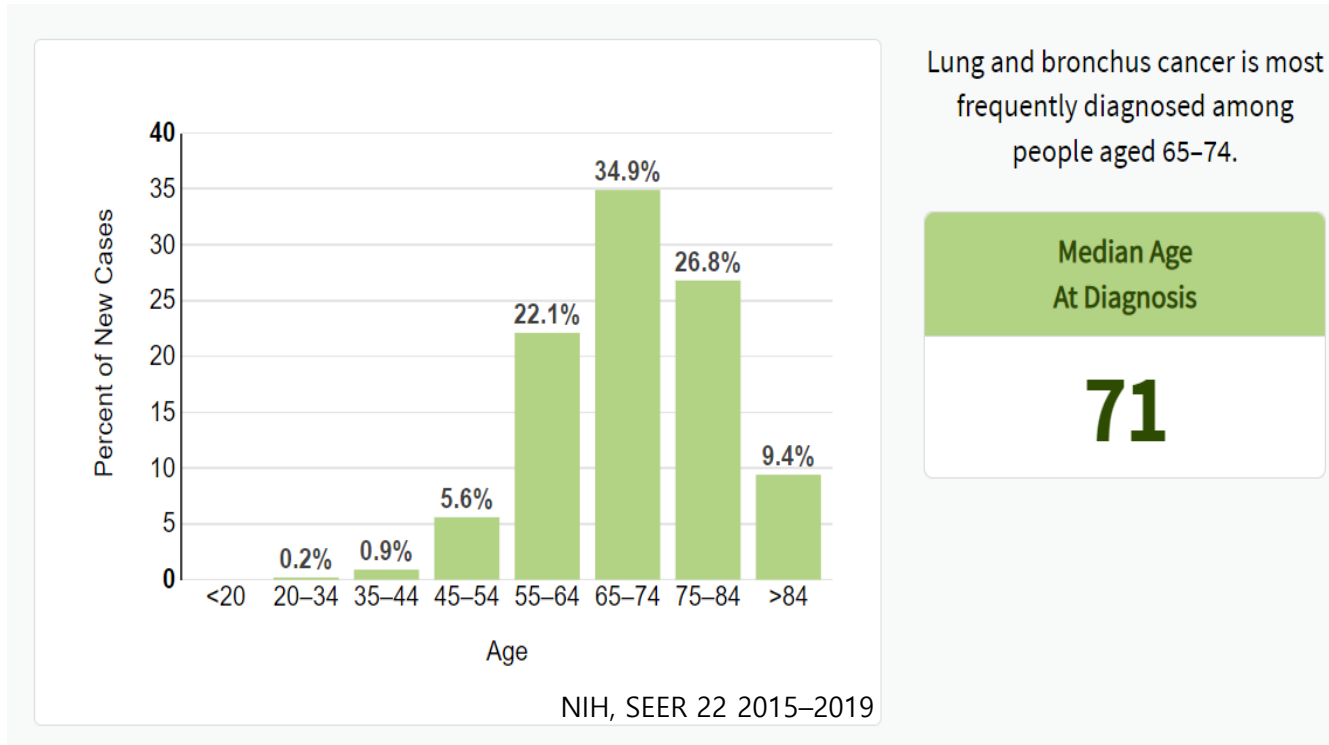
Treatment of Lung Cancer in Elderly Patients

Hyung-Joo Oh

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Old age in lung cancer

➤ Lung cancer by age group

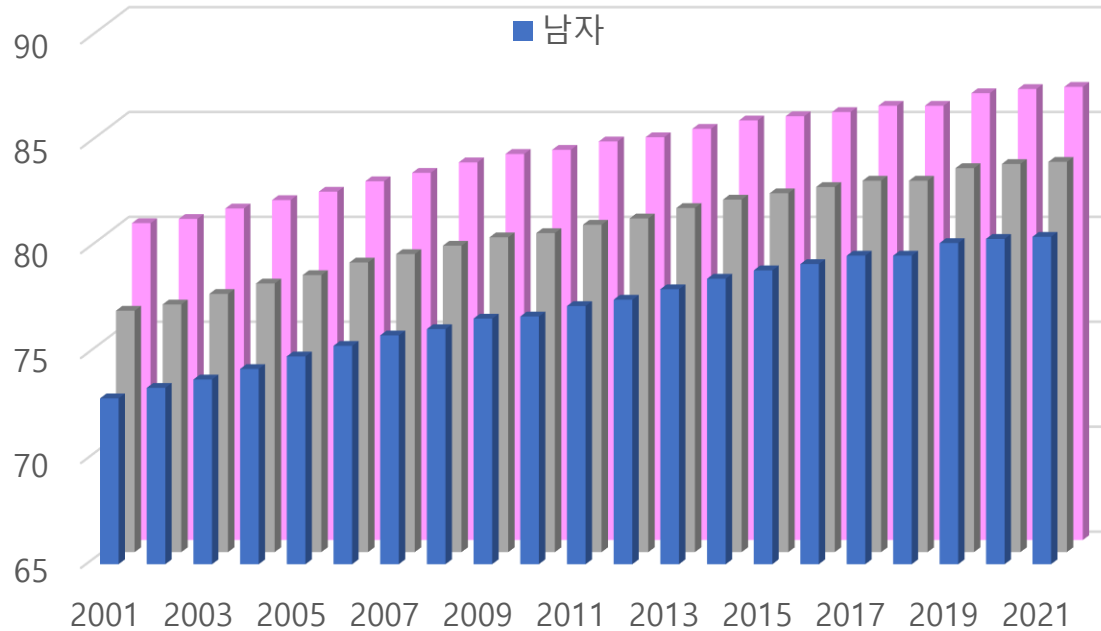


2020 국내 폐암 발생자수 28494 중 **80세 이상 5822 명(20.1%)**

Old age in lung cancer

- **Life expectancy*** in Korea at 2021: **83.6 year-old**, 86.6 in female, 80.6 in male

평균기대수명



*Number of years a **newborn infant would live** if prevailing patterns of **mortality at the time of its birth** were to stay the same throughout its life

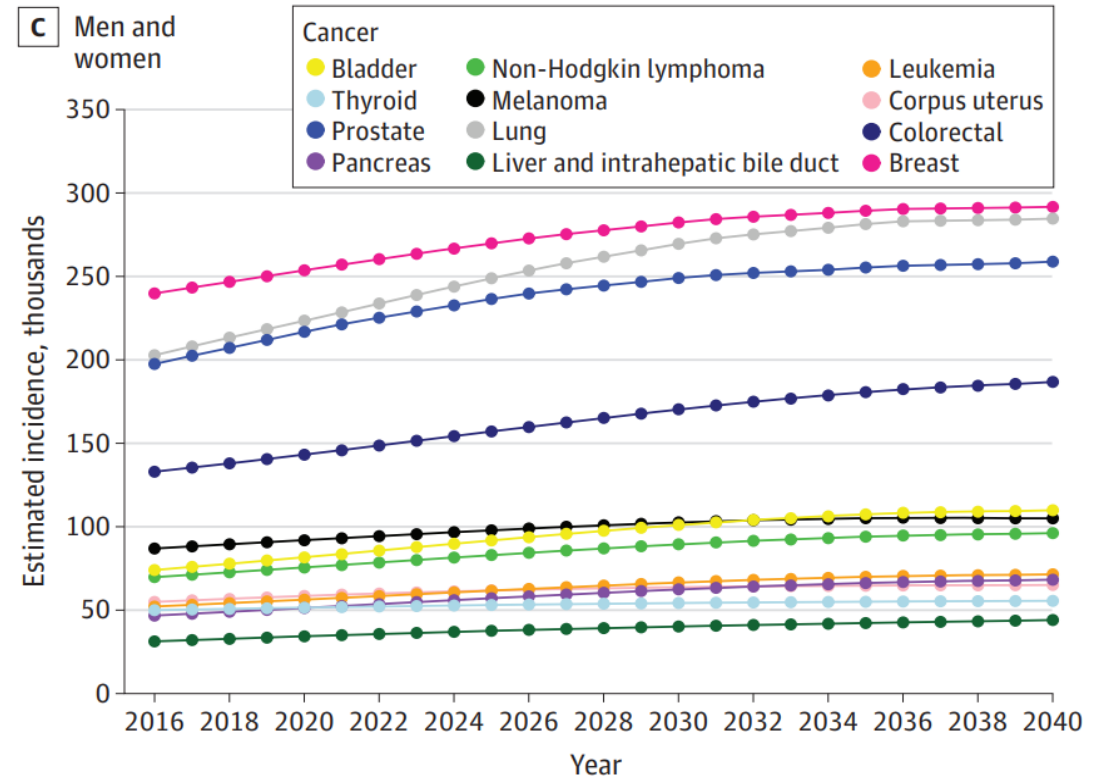


Figure 1. Estimated **Cancer Incidence Based on Demographic Changes** and Average Annual Percentage Change (AAPC) for the Top 10 Common Cancers in **US**

The limitation of interpretation of the clinical trials in elderly patients

- Old age and low performance status

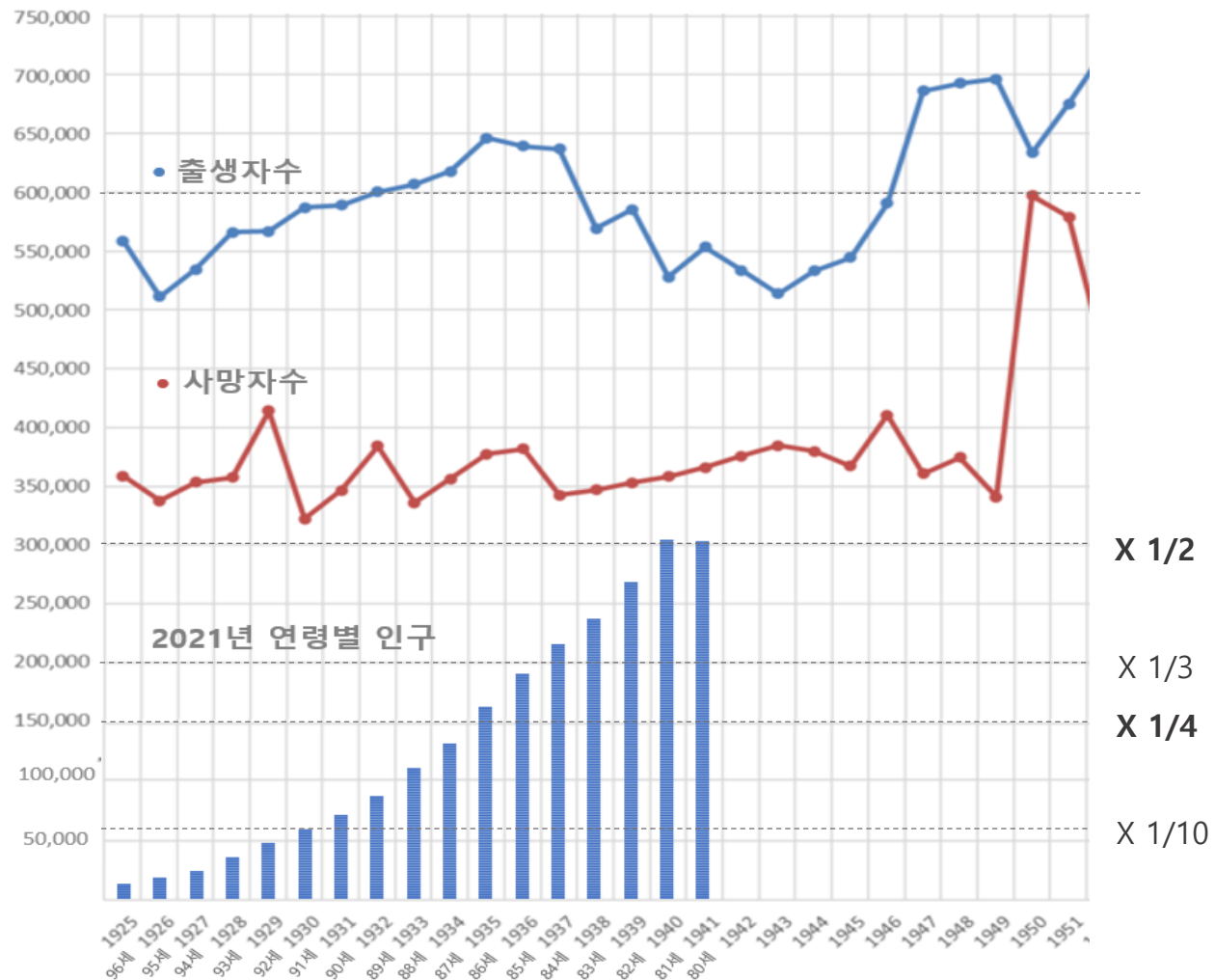
Ineligible for a clinical trials, so there is no strong evidence supporting the clinical value of standard cancer treatment.



Figure 1. Proportion of adult enrollments to the National Cancer Institute's National Clinical Trials Network by age at enrollment and enrollment year.

Octo-, nonagenarian in Dermographics

연도별 출생/사망자수 & 2021년 연령별 인구



연령별 사망, 사망률 2021년

	2021 전체		남자		여자	
	사망(명)	사망률 (십만명당)	사망(명)	사망률 (십만명당)	사망(명)	사망률 (십만명당)
80세 이상	158,739	7,847.3	64,277	9,462.5	94,462	7,030.7
80-84세	57,523	4,945.0	30,277	6,891.0	27,246	3,763.9
85-89세	55,126	9,137.8	22,077	11,982.4	33,049	7,887.0
90세 이상	46,090	17,981.3	11,923	21,418.6	34,167	17,027.7
90-94세	32,570	15,832.9	9,066	19,514.6	23,504	14,758.9
95-99세	11,313	25,694.4	2,450	29,918.2	8,863	24,729.4
100세 이상	2,207	33,533.4	407	39,902.0	1,800	32,365.4

Challenge in managing older patients with cancer

- Decreased life expectancy, Limited evidence of clinical trials, Competing comorbidities, Decreased tolerance to stress
 - ✓ Dose the expected benefits of treatment outweigh the risks?
 - ✓ What are patient's expectations?

Contents

- Comprehensive geriatric assessment
 - ✓ ASCO&NCCN guideline
 - ✓ Implement in practice
- Early stage lung cancer
 - ✓ Surgery
 - ✓ Radiotherapy
- Locally advanced lung cancer
 - ✓ Sequential or concurrent CRT
 - ✓ I/O consolidation
- Advanced lung cancer
 - ✓ Tyrosine kinase inhibitor
 - ✓ Immunotherapy

Practical Assessment and Management of Vulnerabilities in Older Patients Receiving Chemotherapy: ASCO Guideline for Geriatric Oncology

Supriya G. Mohile, William Dale, Mark R. Somerfield, Mara A. Schonberg, Cynthia M. Boyd, Peggy S. Burhenn, Beverly Canin, Harvey Jay Cohen, Holly M. Holmes, Judith O. Hopkins, Michelle C. Janelins, Alok A. Khorana, Heidi D. Klepin, Stuart M. Lichtman, Karen M. Mustian, William P. Tew, and Arti Hurria

Recommendations

1. In patients age 65 and older receiving chemotherapy, geriatric assessment (GA)—the evaluation of functional status, physical performance and falls, comorbid medical conditions, depression, social activity/support, nutritional status, and cognition—**should be used** to identify vulnerabilities or geriatric impairments that are not routinely captured in oncology assessments (Type: Evidence-based, benefits outweigh harms; Evidence quality: high; Strength of recommendation: strong).
2. While many tools are appropriate for assessment of each domain, the Expert Panel based its recommendations on evidence supporting their utility for predicting adverse outcomes and for ease of administration. In patients aged 65 and older receiving chemotherapy, validated and practical geriatric assessment (GA)-based tools can be used to predict adverse outcomes.
 - a. The evidence supports, **at a minimum, assessment of function, comorbidity, falls, depression, cognition, and nutrition.**
 - b. The Expert Panel recommends instrumental activities of daily living (IADLs) for function, a thorough history or validated tool to assess comorbidity, a single question for falls, the Geriatric Depression Scale (GDS) to screen for depression, the Mini-Cog or the Blessed Orientation-Memory-Concentration test (BOMC) to screen for cognitive issues, and assessment of unintentional weight loss to evaluate nutrition.
 - c. Either the Cancer and Aging Research Group (CARG) or Chemotherapy Risk Assessment Scale for High-Age Patients (CRASH) tool is best used to obtain specific estimates on risk of chemotherapy toxicity, while short tools such as Geriatric-8 or Vulnerable Elders Survey-13 (VES-13) can help to predict mortality. [Table 1](#) also provides alternatives to these options.

(Type: evidence-based, benefits outweigh harms; Evidence quality: high that GA tools predict chemotherapy toxicity and mortality; Evidence quality: moderate to recommend specific tools to evaluate GA domains such as function, comorbidity, depression, cognition, and nutrition. Strength of recommendations: moderate.).

Guidelines for geriatric oncology

VOLUME 36 · NUMBER 22 · AUGUST 1, 2018

JOURNAL OF CLINICAL ONCOLOGY

ASCO SPECIAL ARTICLE

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3. Based on the best clinical opinion of the Expert Panel, clinicians should use one of the validated tools listed at ePrognosis (<https://eprognosis.ucsf.edu>) to estimate life expectancy (LE) ≥ 4 years.

a. The Expert Panel especially recommends either the Schonberg or Lee Index (<https://eprognosis.ucsf.edu/leeschonberg.php>). The most common variables considered in these indices include age, sex, comorbidities (eg, diabetes, chronic obstructive pulmonary disease), functional status (eg, activities of daily living [ADLs], instrumental activities of daily living [IADLs], mobility), health behaviors and lifestyle factors (eg, smoking status, body mass index), and self-reported health.^{89-91,127,128}

b. Several indices have “presence of cancer” as a relevant variable, and answering no to this question will allow for estimation of “noncancer” life expectancy to consider competing risks of mortality.

(Type: informal consensus, benefits outweigh harms; Evidence quality: high that it predicts mortality, insufficient that it improves outcomes or improves decision making; Strength of recommendation: strong that it predicts mortality; weak that it improves outcomes or improves decision making).

Mortality Risk for Lee Index

Points	Risk of FIVE YEAR mortality	Risk of TEN YEAR mortality	Life Expectancy (years)
0 - 1	1% - 2%	2% - 5%	33.1 - 35.4
2 - 3	2% - 4%	7% - 10%	23.7 - 30.1
4 - 5	6% - 8%	15% - 23%	17.7 - 21.1
6 - 7	9% - 15%	34% - 43%	12.6 - 14.3
8 - 9	20%	52% - 58%	8.9 - 10
10 - 11	28% - 45%	70% - 82%	5.0 - 7.2
12 - 13	44% - 59%	83% - 91%	3.8 - 5.1
≥ 14	63%	93%	2.9

Patients that have >50% chance of death in a specific time interval have an estimated life expectancy less than that time interval. For example, a patient with a 60% mortality risk at 5 years has a life expectancy <5 years.

University of California San Francisco Search UCSF About UCSF

ePrognosis

HOME ABOUT CALCULATORS CANCER SCREENING DECISION TOOLS COMMUNICATION

Risk Calculator

- How old is your patient?
- What is the sex of your patient? Female Male
- What is your patient's BMI?
- Which best describes your patient's health in general?
- Does your patient have chronic lung disease, such as emphysema or chronic bronchitis? Yes No
- Has your patient ever had cancer (excluding minor skin cancers)? Yes No
- Does your patient have congestive heart failure? Yes No
- Does your patient have diabetes or high blood sugar? Yes No
- Which best describes your patient's cigarette use?
- Does your patient have difficulty walking 1/4 mile (several city blocks) without help from other people or special equipment? Yes No
- During the past 12 months, how many times was your patient hospitalized overnight?
- Because of a physical, mental or emotional problem, does your patient need the help of others in handling routine needs such as everyday household chores, doing necessary business, shopping, or getting around for other purposes? Yes No
- Because of a health or memory problem, does your patient have difficulty managing money - such as paying bills and keeping track of expenses? Yes No
- Because of a health or memory problem, does your patient have difficulty with bathing or showering? Yes No
- Because of a health problem, does your patient have difficulty pushing or pulling large objects like a living room chair? Yes No

Total Lee Index Points: 0
Total Schonberg Index Points: 0

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4. Delphi consensus panels of experts have established approaches for implementing GA-guided care processes in older adults with cancer.^{22,32}

- a. The Expert Panel recommends that clinicians apply the results of GA to develop an integrated and individualized plan for patients that informs treatment selection by helping to estimate risks for adverse outcomes (see Recommendation 2) and to identify nononcologic problems (see Recommendation 1) that may be amenable to intervention.
- b. Based on clinical experience and the results of formal expert consensus studies,^{22,32} the Expert Panel suggests that clinicians take into account GA results when recommending treatment and that the information be provided to patients and caregivers to guide decision making for treatment.⁶ In addition, clinicians should implement targeted, GA-guided interventions to manage nononcologic problems.
- c. Consistent with the results of formal modified Delphi consensus studies, the Expert Panel supports the specific high-priority GA-guided interventions outlined in Table 2.

(Type: informal consensus; Evidence quality: moderate; Strength of recommendation: moderate).

Geriatric Assessment Measure	Geriatric Assessment–Guided Interventions
Function and falls Instrumental activities of daily living deficit History of falls	Physical therapy and/or occupational therapy referrals to prescribe strength and balance training, assist device evaluation, home exercise program, and safety evaluation Fall prevention discussion Home safety evaluation
Comorbidity domain Comorbidity and polypharmacy considerations	Involve caregiver in discussions to assess risks of therapy and management of comorbidities Involve primary care physician and/or geriatrician in decision making for treatment and management of comorbidities; consider referral to geriatrician Review medication list and minimize medications as much as possible; consider involving a pharmacist Assess adherence to medications; have patient bring in medications to review
Cognition Screen positive on validated cognitive screen	Assess decision-making capacity and ability to consent for treatment Identification of health care proxy and involve proxy in decision making for treatment, including signing consent forms with patient Delirium risk counseling for patient and family Medication review to minimize medications with higher risk of delirium Consider further work-up with geriatrician or cognitive specialist
Depression Geriatric Depression Scale > 5	Consider referral for psychotherapy/psychiatry Consider cognitive-behavioral therapy Social work involvement Consider pharmacologic therapy
Nutrition Weight loss > 10%	Nutrition counseling Referral to nutritionist/dietician Assess need for extra support for meal preparation and institute support interventions if necessary (eg, caregiver, Meals-on-Wheels)

Older Adult Oncology, Version 1.2021

Featured Updates to the NCCN Guidelines

Efrat Dotan, MD^{1,*}; Louise C. Walter, MD^{2,*}; Ilene S. Browner, MD³; Katherine Clifton, MD⁴; Harvey Jay Cohen, MD⁵; Martine Extermann, MD, PhD⁶; Cary Gross, MD⁷; Sumati Gupta, MD⁸; Genevieve Hollis, MSN, CRNP⁹; Joleen Hubbard, MD¹⁰; Reshma Jagsi, MD, DPhil¹¹; Nancy L. Keating, MD, MPH¹²; Elizabeth Kessler, MD¹³; Thuy Koll, MD¹⁴; Beatriz Korc-Grodzicki, MD, PhD¹⁵; June M. McKoy, MD, MBA, JD, MPH¹⁶; Sumi Misra, MD¹⁷; Dominic Moon, MD¹⁸; Tracey O'Connor, MD¹⁹; Cynthia Owusu, MD, MS²⁰; Ashley Rosko, MD²¹; Marcia Russell, MD²²; Mina Sedrak, MD, MS²³; Fareeha Siddiqui, MD²⁴; Amy Stella, MD²⁵; Derek L. Stirewalt, MD²⁶; Ishwaria M. Subbiah, MD, MS²⁷; William P. Tew, MD¹⁵; Grant R. Williams, MD²⁸; Liz Hollinger, BSN, RN^{29,*}; Giby V. George, MD^{29,*}; and Hema Sundar, PhD^{29,*}

➤ Reasons to perform CGA

- ✓ **Reveal/detect reversible geriatric problems** not found by routine oncology care
- ✓ **Predict risk of toxicity**/adverse effects from cancer treatment or **decrease in QOL**, enabling more targeted use of supportive care measures
- ✓ Prognostic information that can be helpful in **estimating life expectancy** and making **treatment decision**
- ✓ Allows **targeted intervention**, which can **improve QOL** and **adherence to therapy**
- ✓ Helpful in improving communication

Guidelines for geriatric oncology

NCCN GUIDELINES® INSIGHTS

CE

Older Adult Oncology, Version 1.2021

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Consider consultation to a geriatric trained clinician

- Cognitive impairment
 - Dementia/delirium Decision-making capacity evaluation
 - Life expectancy, advance directive/advance care planning, guardianship (See NCCN Guidelines for Palliative Care)
- Functional or physical impairment, mobility issues, or disability
 - Falls evaluation and/or advice on falls prevention
 - Promote independent living or supportive living
- Multimorbidity including vision and hearing impairments
- Polypharmacy evaluation
- When considering a high-risk procedure, such as:
 - Chemotherapy and radiotherapy
 - Hematopoietic cell transplantation
 - Complex surgeries (eg, cystectomy)
- Presence of geriatric syndromes
 - Frailty, osteoporosis, depression, pressure ulcers, urinary incontinence, neglect or abuse, failure to thrive
- Weight loss (≥5% unintentional weight loss in last 3 months) and anorexia
- Caregiver support
- Assistance with social support resources

Screening tools for CGA: G8, VES-13

Table 1. Screening Tools Evaluated

Screening tool	No. of items	Original purpose	Original population intended	Score range	Original reference		
					Cutoff	Time required	Method of administration
aCGA ⁴⁰	15	To screen for who would benefit from geriatric assessment using abbreviated versions of established tools	Older adults with cancer	0-3 ADL; 0-4 IADL; 0-8 on MMSE; 0-4 on GDS-15	≥1 ADL and IADL; ≤6 on MMSE; and ≥2 on GDS-15	NR	Clinician interview
BFC ⁴¹	3	Criteria normally derived from geriatric assessment to define a frail population	Community-dwelling older adults	0-3	≥1	NR	Used by clinician to classify frailty status; not normally used as screening tool
FFC ^{42,43}	5	Criteria to define a frail population	Community-dwelling older adults	0-5	≥3	NR	Used by clinician to classify frailty status; not normally used as screening tool
G8⁴⁴	8	Identification of older adults with cancer who require geriatric assessment; derived from the MNA	Older adults with cancer	0-17	≤14	NR	By trained nurse or physician
GFI ⁴⁵	15	Screening for frailty and psychosocial issues	Community-dwelling older adults	0-15	≥4	NR	Clinician interview
KPS ⁴⁶	Single score	Evaluate patient's ability to tolerate chemotherapy	Adults with cancer	0-100	≤80%	NR	Assigned by clinician
PPT ⁴⁷	7-9	Assessing physical function by simulating ADL	Community-dwelling older adults	0-36	≤20	NR	By clinician
Rockwood CFS ⁴⁸	7	Measure frailty, and estimate death or need for institutional care	Community-dwelling older adults	1-9	≥2	NR	By clinician
SAOP2 ⁴⁹ screening tool	15	To determine when a multidisciplinary team consultation is required for a person with cancer	Older adults with cancer	NA	≥1	NR	Jointly completed by patient and clinical staff
TRST ⁵⁰	5	To screen for risk of dependence	Community-dwelling older adults presenting to ED	0-5	≥1	NR	Clinician/ED staff interview
Usual gait speed ⁵¹	As a single item	Assess physical functioning	Community-dwelling older adults	NA	<1 ms ⁻¹	NR	By clinician
VES-13 ⁵²	13	To screen for risk of health deterioration	Community-dwelling older adults	1-10	≥3	5 min	Self-administered

	Items	Possible answers (score)
A	Has food intake declined over the past 3 months due to loss of appetite, digestive problems, chewing or swallowing difficulties?	0 : severe decrease in food intake
		1 : moderate decrease in food intake
		2 : no decrease in food intake
B	Weight loss during the last 3 months	0 : weight loss > 3 kg
		1 : does not know
		2 : weight loss between 1 and 3 kgs
C	Mobility	0 : bed or chair bound
		1 : able to get out of bed/chair but does not go out
		2 : goes out
E	Neuropsychological problems	0 : severe dementia or depression
		1 : mild dementia or depression
		2 : no psychological problems
F	Body Mass Index (BMI (weight in kg) / (height in m ²))	0 : BMI < 19
		1 : BMI = 19 to BMI < 21
		2 : BMI = 21 to BMI < 23
		3 : BMI = 23 and > 23
H	Takes more than 3 medications per day	0 : yes
		1 : no
P	In comparison with other people of the same age, how does the patient consider his/her health status?	0 : not as good
		0.5 : does not know
		1 : as good
	Age	2 : better
		0 : >85
		1 : 80-85
		2 : <80
	TOTAL SCORE	0 - 17

Screening tools for CGA: G8, VES-13

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VES-13

- Age _____ SCORE : 1 POINT FOR AGE 73-84
3 POINTS FOR AGE ≥ 85
- In general compared to other people your age, would you say that your health is:
 - Poor* (1 POINT)
 - Fair* (1 POINT)
 - Good
 - Very good, or
 - ExcellentSCORE : 1 POINT FOR FAIR or POOR
- How much difficulty, on average, do you have with the following physical activities.

	No Difficulty	A little Difficulty	Some Difficulty	A Lot of Difficulty	Unable to do
a. stooping, crouching or kneeling?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
b. lifting or carrying objects as heavy as 10 pounds?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
c. reaching or extending arms above shoulder level?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
d. writing or handling and draping small objects?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
e. walking a quarter of a mile?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
f. heavy housework such as scrubbing floors or washing windows?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

SCORE : 1 POINT FOR EACH * RESPONSE IN Q3a THROUGH Q3f. MAXIMUM OF 2 POINTS
- Because of your health or a physical condition, do you have any difficulty
 - shopping for personal items (like toilet items or medicines)?

<input type="checkbox"/> YES → Do you get help with shopping?	<input type="checkbox"/> YES*	<input type="checkbox"/> NO
<input type="checkbox"/> NO		
<input type="checkbox"/> DON'T DO → Is that because of your health?	<input type="checkbox"/> YES*	<input type="checkbox"/> NO
 - managing money (like keeping track of expenses or paying bills)?

<input type="checkbox"/> YES → Do you get help with managing money?	<input type="checkbox"/> YES*	<input type="checkbox"/> NO
<input type="checkbox"/> NO		
<input type="checkbox"/> DON'T DO → Is that because of your health?	<input type="checkbox"/> YES*	<input type="checkbox"/> NO
 - walking across the room? USE OF CANE OR WALKER IS OK.

<input type="checkbox"/> YES → Do you get help with walking?	<input type="checkbox"/> YES*	<input type="checkbox"/> NO
<input type="checkbox"/> NO		
<input type="checkbox"/> DON'T DO → Is that because of your health?	<input type="checkbox"/> YES*	<input type="checkbox"/> NO
 - doing light housework (like washing dishes, straightening up, or light cleaning)?

<input type="checkbox"/> YES → Do you get help with light housework?	<input type="checkbox"/> YES*	<input type="checkbox"/> NO
<input type="checkbox"/> NO		
<input type="checkbox"/> DON'T DO → Is that because of your health?	<input type="checkbox"/> YES*	<input type="checkbox"/> NO
 - bathing or showering?

<input type="checkbox"/> YES → Do you get help with bathing or showering?	<input type="checkbox"/> YES*	<input type="checkbox"/> NO
<input type="checkbox"/> NO		
<input type="checkbox"/> DON'T DO → Is that because of your health?	<input type="checkbox"/> YES*	<input type="checkbox"/> NO

Screening tools for CGA: G8, VES-13

Table 3. Results of Diagnostic Accuracy Studies

Source	Vulnerable patients, %		Finding, No. of patients				Sensitivity, % (95% CI)	Specificity, % (95% CI)	PPV, % (95% CI)	NPV, % (95% CI)	PLR (95% CI)	NLR (95% CI)	AUC (95% CI)
	Screening	GA	TP	TN	FP	FN							
Geriatric-8													
Russo et al, ¹² 2018	74.0	62.0	156	54	53	19	89.0 (NR)	49.5 (NR)	73.9 (NR)	73.6 (NR)	NR	NR	0.80 (NR)
Yokom et al, ³⁰ 2018	63.0	78.6	NR	NR	NR	NR	73.0 (54.0-91.0)	80.0 (45.0-100.0)	94.0 (83.0-100.0)	40.0 (10.0-70.0)	NR	NR	NR
ONCODAGE study: Bellera et al, ²³ 2017; Soubeyran et al, ²⁴ 2014	68.4	80.2	880	183	101	271	76.5 (73.4-78.9)	64.4 (58.6-70)	89.7 (87.6-91.5)	40.3 (35.8-45.0)	2.15 (1.83-2.52)	0.36 (0.32-0.42)	0.80 (0.78-0.83)
Osborne et al, ¹³ 2017	22.5	30.9	21	92	17	26	44.7 (NR)	84.4 (NR)	55.3 (NR)	78 (NR)	NR	NR	NR
Pamoukdjian et al, ²⁸ 2017	88.4	93.7	NR	NR	NR	NR	90.1 (85.7-93.5)	74.3 (14.2-61.7)	95.4 (91.9-97.7)	19.4 (7.5-35.7)	1.39 (0.97-1.98)	0.28 (0.13-0.59)	0.79 (0.70-0.88)
Martinez-Tapia et al, ²⁷ 2016	NR	86.7	NR	NR	NR	NR	87.2 (84.3-89.7)	57.7 (47.3-67.7)	93.1 (90.7-95.0)	40.9 (32.6-49.6)	NR	NR	0.865 (0.835-0.896)
Dubruille et al, ³¹ 2015	72.0	80.0	NR	NR	NR	NR	79.2 (NR)	55.6 (NR)	NR	NR	NR	NR	0.749 (0.05) ^a
Kenig et al, ²⁶ 2015	85.0	73.0	NR	NR	NR	NR	97.0 (89.0-98.0)	44.0 (30.0-64.0)	83.0 (75.0-89.0)	84.0 (57.0-93.0)	NR	NR	0.71 (0.6-0.82) (SE, 0.06)
Hamaker et al, ³² 2014	61.0	92.0	NR	NR	NR	NR	69.0 (58.0-78.0)	79.0 (62.0-91.0)	89.0 (79.0-88.0)	50.0 (55.0-79.0)	NR	NR	NR
Pottel et al, ³⁶ 2014	69.0	75.0	NR	NR	NR	NR	81.1 (NR)	66.7 (NR)	NR	NR	NR	NR	0.82 (0.67-0.97)
Smets et al, ²⁹ 2014	60.0	48.0	151	139	53	19	87.0 (80.0-93.0)	64.0 (55.0-73.0)	69.0 (61.0-78.0)	84.0 (77-91)	NR	NR	NR
Velghe et al, ³⁵ 2014	76.0	88.0	NR	NR	NR	NR	89.0 (75.0-96.0)	100.0 (54.0-100.0)	NR	NR	NR	NR	0.95 (0.30) ^a
Vulnerable Elders Survey-13													
Yokom et al, ³⁰ 2018	35.7	78.6	NR	NR	NR	NR	46.0 (25.0-66.0)	100.0 (100.0-100.0)	100.0 (100.0-100.0)	32 (11.0-52.0)	NR	NR	NR
ONCODAGE study: Bellera et al, ²³ 2017; Soubeyran et al, ²⁴ 2014	60.2	80.2	NR	NR	NR	NR	69.0 (66.0-71.4)	74.3 (68.8-79.3)	91.6 (89.5-93.3)	37.0 (33.0-41.1)	2.67 (2.19-3.3)	0.42 (0.38-0.5)	0.79 (0.77-0.82)
Osborne et al, ¹³ 2017	60.0	30.9	11	113	0	44	20.0 (NR)	100.0 (NR)	100.0 (NR)	72.0 (NR)	NR	NR	NR
Kenig et al, ²⁶ 2015	56.0	73.0	NR	NR	NR	NR	69.0 (58.0-77.0)	81.0 (63-91)	91.0 (81.0-96.0)	52.0 (35.0-61.0)	NR	NR	0.75 (0.65-0.84) (SE, 0.05)
Okuyama et al, ³³ 2015	48.0	50.0	NR	NR	NR	NR	72.0 (NR)	79.0 (NR)	79.0 (NR)	72.0 (NR)	NR	NR	0.85 (NR)
Augschoell et al, ³⁷ 2014	41.5	70.0	30	20	2	24	56.0 (NR)	91.0 (NR)	94.0 (NR)	45.0 (NR)	NR	NR	0.73 (NR)
Kenig et al, ³⁸ 2014	45.3	59.4	NR	NR	NR	NR	60.0 (NR)	78.0 (NR)	81.0 (NR)	57.0 (NR)	NR	NR	0.76 (0.07) ^b
Pottel et al, ³⁶ 2014	38.8	75.0	NR	NR	NR	NR	49.0 (35.0-62.4)	91.7 (83.9-100)	NR	NR	NR	NR	0.69 (0.54-0.84)
Smets et al, ²⁹ 2014	48.0	48.0	150	156	49	43	67.0 (58.0-76.0)	70.0 (61.0-78.0)	67.0 (58.0-76.0)	70.0 (61.0-78.0)	NR	NR	NR

Recommended assessment tools for CGA

8 Domains of CGA

- | | |
|--|------------------|
| 1. Self-reported Function and Mobility | 5. Cognition |
| 2. Objective Function and Mobility | 6. Psychological |
| 3. Comorbidity | 7. Nutrition |
| 4. Social Functioning and Support | 8. Polypharmacy |

Domain	Assessment Tools ^b /Description
Self-reported Function and Mobility (OAO-C, 7 of 11)	Activities of Daily Living (ADLs) • Measures limitations in physical function activities, including bathing and dressing ▶ Katz Index of Independence in Activities of Daily Living (ADL)
	Instrumental Activities of Daily Living (IADLs) • Measures ability to complete activities required to maintain independence ranging from making telephone calls to money management ▶ OARS ▶ Lawton-Brody Instrumental Activities of Daily Living (IADL) Scale
	Falls (See OAO-D) • Number of falls within the last 6 months
Objective Function and Mobility (See OAO-D)	Time it takes for individuals to stand up, walk 10 feet, return to chair and sit back down Timed "Up and Go" (TUG) (See OAO-D)
	Assesses functional mobility Timed 10-Meter Walk Test (See OAO-D)
	Short Physical Performance Battery (SPPB) Evaluation of lower extremity functioning

The Lawton Instrumental Activities of Daily Living Scale

A. Ability to Use Telephone

- Operates telephone on own initiative; looks up and dials numbers..... 1
- Dials a few well-known numbers..... 1
- Answers telephone, but does not dial..... 1
- Does not use telephone at all..... 0

B. Shopping

- Takes care of all shopping needs independently 1
- Shops independently for small purchases..... 0
- Needs to be accompanied on any shopping trip 0
- Completely unable to shop 0

C. Food Preparation

- Plans, prepares, and serves adequate meals independently 1
- Prepares adequate meals if supplied with ingredients..... 0
- Heats and serves prepared meals or prepares meals but does not maintain adequate diet..... 0
- Needs to have meals prepared and served..... 0

D. Housekeeping

- Maintains house alone with occasion assistance (heavy work)..... 1
- Performs light daily tasks such as dishwashing, bed making..... 1
- Performs light daily tasks, but cannot maintain acceptable level of cleanliness 1
- Needs help with all home maintenance tasks..... 1
- Does not participate in any housekeeping tasks..... 0

E. Laundry

- Does personal laundry completely 1
- Launders small items, rinses socks, stockings, etc..... 1
- All laundry must be done by others 0

F. Mode of Transportation

- Travels independently on public transportation or drives own car..... 1
- Arranges own travel via taxi, but does not otherwise use public transportation 1
- Travels on public transportation when assisted or accompanied by another 1
- Travel limited to taxi or automobile with assistance of another..... 0
- Does not travel at all..... 0

G. Responsibility for Own Medications

- Is responsible for taking medication in correct dosages at correct time..... 1
- Takes responsibility if medication is prepared in advance in separate dosages 0
- Is not capable of dispensing own medication 0

H. Ability to Handle Finances

- Manages financial matters independently (budgets, writes checks, pays rent and bills, goes to bank); collects and keeps track of income..... 1
- Manages day-to-day purchases, but needs help with banking, major purchases, etc 1
- Incapable of handling money 0

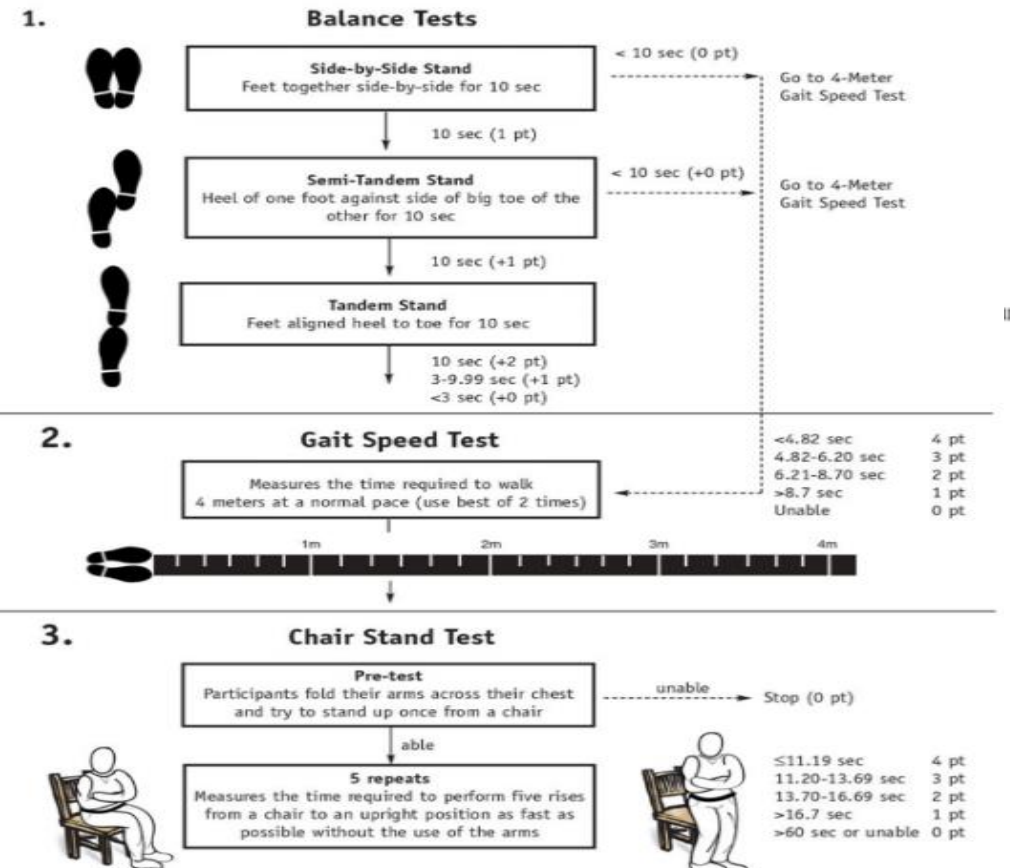
Recommended assessment tools for CGA

8 Domains of CGA

1. Self-reported Function and Mobility
- 2. Objective Function and Mobility**
3. Comorbidity
4. Social Functioning and Support
5. Cognition
6. Psychological
7. Nutrition
8. Polypharmacy

Domain	Assessment Tools ^b /Description
Self-reported Function and Mobility (OAO-C, 7 of 11)	Activities of Daily Living (ADLs) • Measures limitations in physical function activities, including bathing and dressing ▶ Katz Index of Independence in Activities of Daily Living (ADL)
	Instrumental Activities of Daily Living (IADLs) • Measures ability to complete activities required to maintain independence ranging from making telephone calls to money management ▶ OARS ▶ Lawton-Brody Instrumental Activities of Daily Living (IADL) Scale
	Falls (See OAO-D) • Number of falls within the last 6 months
Objective Function and Mobility (See OAO-D)	Time it takes for individuals to stand up, walk 10 feet, return to chair and sit back down Timed "Up and Go" (TUG) (See OAO-D)
	Assesses functional mobility Timed 10-Meter Walk Test (See OAO-D)
	Short Physical Performance Battery (SPPB) Evaluation of lower extremity functioning

Short Physical Performance Battery



Recommended assessment tools for CGA

8 Domains of CGA

- | | |
|--|------------------|
| 1. Self-reported Function and Mobility | 5. Cognition |
| 2. Objective Function and Mobility | 6. Psychological |
| 3. Comorbidity | 7. Nutrition |
| 4. Social Functioning and Support | 8. Polypharmacy |

Domain	Assessment Tools ^b /Description
Comorbidity	<ul style="list-style-type: none"> Assess the presence or absence of comorbidities <ul style="list-style-type: none"> Charlson Comorbidity Index (CCI) Cumulative Illness Rating Scale-Geriatric (CIRS-G)
	<ul style="list-style-type: none"> Assess different categories of organ dysfunction and non-relapsed mortality risk <ul style="list-style-type: none"> Hematopoietic Cell Transplantation-Specific Comorbidity Index (HCT-CI)
Social Functioning and Support (See OAO-C, 7 of 11)	<ul style="list-style-type: none"> Measure the availability of social support and engagement in physical or social activities <ul style="list-style-type: none"> MOS Social Support Survey
	<ul style="list-style-type: none"> Evaluate the self-reported availability of emotional/informational social support <ul style="list-style-type: none"> RAND Health Care Social Support Survey Instrument: Emotional/Informational Subscale
	<ul style="list-style-type: none"> Evaluate the self-reported availability of tangible physical social support <ul style="list-style-type: none"> RAND Health Care Social Support Survey: Tangible Subscale

Recommended assessment tools for CGA

8 Domains of CGA

1. Self-reported Function and Mobility
2. Objective Function and Mobility
3. Comorbidity
4. Social Functioning and Support
5. **Cognition**
6. **Psychological**
7. **Nutrition**
8. **Polypharmacy**

Domain	Assessment Tools ^b /Description
Cognition (See OAO-E)	<ul style="list-style-type: none"> • Evaluate the level of cognitive impairment, if any. <ul style="list-style-type: none"> ▶ Mini-Cog (See OAO-F) ▶ Mini-Mental State Examination (MMSE) ▶ Blessed Orientation Memory Concentration Test (BOMC)
Psychological	<ul style="list-style-type: none"> • Evaluates the level of depression and anxiety experienced in the last month <ul style="list-style-type: none"> ▶ Mental Health Inventory (MHI-17)
	<ul style="list-style-type: none"> • Evaluates the level of distress <ul style="list-style-type: none"> ▶ Distress thermometer (See NCCN Guidelines for Distress Management)
	<ul style="list-style-type: none"> • Evaluate for the risk for depression <ul style="list-style-type: none"> ▶ Geriatric Depression Scale-4 (GDS-4)

Domain	Assessment Tools ^b /Description
Nutrition (See OAO-C, 8 of 11)	Body Mass Index (BMI) Weight (kg)/ Height (m ²)
	Percent unintentional weight loss in last 6 months
	Mini-Nutritional Assessment (MNA) Validated self-reported tool that can identify older adults who are malnourished or at risk for malnutrition
Polypharmacy (See OAO-C, 8 of 11)	Medications Prescription and over-the-counter medication list

The Impact of CGA in clinical practice

Relevance of a systematic geriatric screening and assessment in older patients with cancer: results of a prospective multicentric study

C. Kenis¹, D. Bron², Y. Libert³, L. Decoster⁴, K. Van Puyvelde⁵, P. Scalliet⁶, P. Cornette⁷,

Background: To evaluate the large-scale feasibility and usefulness of geriatric screening and assessment in clinical oncology practice by assessing the impact on the detection of unknown geriatric problems, geriatric interventions and treatment decisions.

Patients and methods: Eligible patients who had a malignant tumour were ≥ 70 years old and treatment decision had to be made. Patients were screened using G8; if abnormal (score $\leq 14/17$) followed by Comprehensive Geriatric Assessment (CGA). The assessment results were communicated to the treating physician using a predefined questionnaire to assess the topics mentioned above.

Results: One thousand nine hundred and sixty-seven patients were included in 10 hospitals. Of these patients, 70.7% had an abnormal G8 score warranting a CGA. Physicians were aware of the assessment results at the time of treatment decision in two-thirds of the patients ($n = 1115$; 61.3%). The assessment detected unknown geriatric problems in 51.2% of patients. When the physician was aware of the assessment results at the time of decision making, geriatric interventions were planned in 286 patients (25.7%) and the treatment decision was influenced in 282 patients (25.3%).

SCREENING	Instrument	Score	<i>n</i>	%	95% CI
Geriatric profile	G8 (0–17) (<i>n</i> = 1967)	Absence of a geriatric profile: score >14	576	29.3	27.3–31.3
		Presence of a geriatric profile: score ≤ 14	1391	70.7	68.7–72.7

Conclusion: Geriatric screening and assessment in older patients with cancer is feasible at large scale and has a significant impact on the detection of unknown geriatric problems, leading to geriatric interventions and adapted treatment.

Table 4. Questionnaire for the treating physician

	<i>n</i>	%	95% CI
Questionnaire completed by the treating physician (<i>n</i> = 1967)	1820	92.5	91.4–93.7
Physician aware of the results of the assessment at the time of treatment decision ^a (<i>n</i> = 1820)	1115	61.3	59.0–63.5
Period 1: 10/2009–05/2010 (<i>n</i> = 661)	336	50.8	47.0–54.6
Period 2: 06/2010–12/2010 (<i>n</i> = 624)	412	66.0	62.3–69.7
Period 3: 01/2011–07/2011 (<i>n</i> = 535)	367	68.6	64.7–72.5
Patients with unknown geriatric problems detected (<i>n</i> = 1820)	931	51.2	48.9–53.5
Patients with interventions planned based on assessment ^b (<i>n</i> = 1115)	286	25.7	23.1–28.2
Planned interventions related to: (<i>n</i> = 286)			
Nutrition	162	56.6	50.9–62.4
Depression	107	37.4	31.8–43.0
Fatigue	107	37.4	31.8–43.0
Pain	99	34.6	29.1–40.1
Functionality	93	32.5	27.1–38.0
Falls	64	22.4	17.6–27.2
Cognition	60	21.0	16.3–25.7
Social status	59	20.6	15.9–25.3
Influence of assessment on treatment decision ^b (<i>n</i> = 1115)	282	25.3	22.7–27.8

Randomized clinical trials of geriatric assessment

Use of a Comprehensive Geriatric Assessment for the Management of Elderly Patients With Advanced Non-Small-Cell Lung Cancer: The Phase III Randomized ESOGIA-GFPC-GECP 08-02 Study

Romain Corre, Laurent Greillier, Hervé Le Caër, Clarisse Audigier-Valette, Nathalie Baize, Henri Bérard,

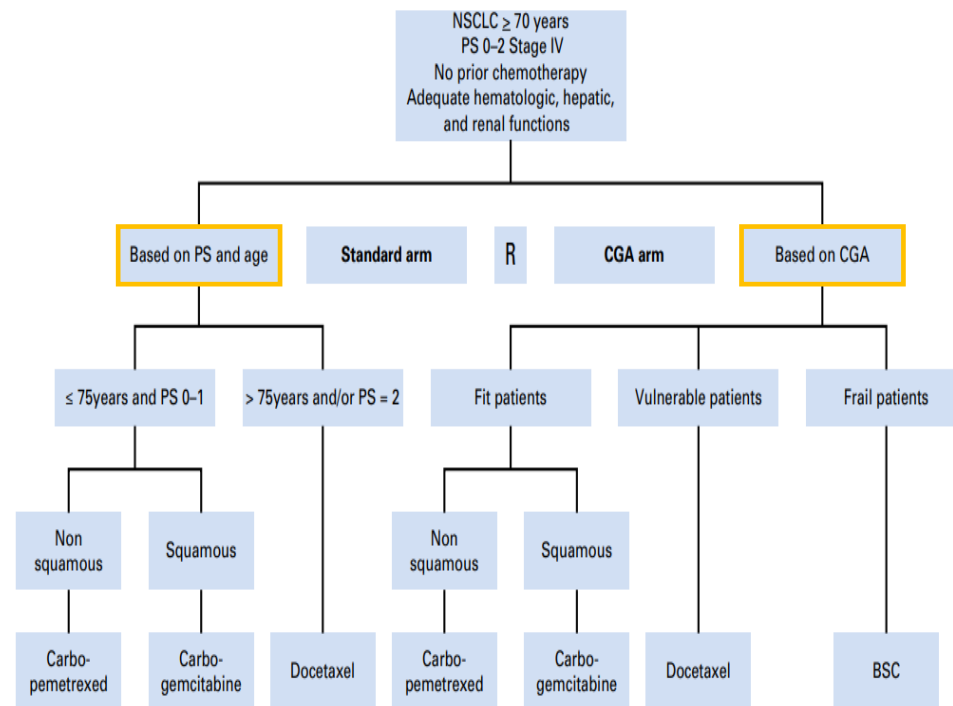


Table 4. Grade 3 or 4 Toxicities

Toxicity	% of Patients		P
	Standard Arm (n = 251)	CGA Arm (n = 243)	
All grades	93.4	85.6	.01
Grade 3-4	71.3	67.9	.41

Table 3. Treatments and Outcomes

Treatment and Outcome	Standard Arm (n = 251)	CGA Arm (n = 243)	P (Log-Rank Test)
Treatment allocation, No. (%)			< .001
Monotherapy	163 (64.9)	76 (31.3)	
Doublet	88 (35.1)	111 (45.7)	
BSC		56 (23.0)	
Median TFFS, months			.32
All	3.2	3.1	
Doublet	4.4	4.8	
Monotherapy	2.9	2.6	
BSC	—	1.3	
Reasons for treatments failures, No. (%)			
Missing data	14	15	
Progression	156 (65.8)	158 (69.3)	.42
Toxicity	28 (11.8)	11 (4.8)	.01
Toxicity except for BSC in the CGA arm	28 (11.8)	11 (6.3)	.06
Withdrawal of consent	9 (3.8)	7 (3.1)	.67
Death	31 (13.1)	32 (14.0)	.76
Other	13 (5.5)	20 (8.8)	.17
Median PFS, months			.59
All	3.7	3.4	
Doublet	4.7	4.8	
Monotherapy	3.1	2.7	
BSC	—	1.3	
Median OS, months			.87
All	6.4	6.1	
Doublet	8.6	10.0	
Monotherapy	5.7	4.9	
BSC	—	2.8	
Mean life expectancy adjusted on QoL, months	4.3	4.4	.51

Randomized clinical trials of geriatric assessment

Table 3. Randomized Controlled Trials of Geriatric Assessment Under Way

First Author and Location	Design	Population	Intervention Delivery	Management Strategy	Outcomes
Hurria, City of Hope	2:1 patient randomization (n = 600)	Age 65+ with any stage solid tumor Malignancies starting a new chemotherapy regimen (any line)	Study nurse practitioner in collaboration with the primary oncologist and clinic nurse	Established protocol for referral to the multidisciplinary team based on multidisciplinary team input and triggers based on geriatric assessment results	Four primary end points: chemotherapy toxicity (grade 3+), rate of hospitalization, change in functional status, change in psychosocial status
Soubeyran, 28 regional coordination units for geriatric oncology (mix of sites)	Patient randomization (n = 1,200)	Age 70+ with most solid tumor malignancies candidate for first-/second- line medical treatment	Geriatrician with nurse follow-up	Established protocol based on expert input	Coprietary end point of overall survival and dimensions of quality of life, response, progression-free survival, other quality of life, chemotherapy toxicity, health care utilization
Puts, multicenter study of centers in Canada	Patient randomization (n = 350)	Aged 70+ with most solid tumor malignancies starting first-/second- line chemotherapy	Geriatric oncology with nurse follow-up	Established protocol based on Delphi consensus and guidelines	Quality of life cost-effectiveness, function, chemotherapy toxicity, satisfaction, cancer treatment changes, survival
Mohile, community oncology practices affiliated with the University of Rochester NCORP Research Base	Two studies: cluster randomization by oncology practice (n = 700) and (n = 528)	Aged 70+ with advanced solid tumor malignancies	Study 1: chemotherapy toxicity (grade 3+), survival, function Study 2: communication, satisfaction, patient and caregiver quality of life, health care utilization	Established protocol based on Delphi consensus panel and guidelines	Chemotherapy toxicity (grade 3+), survival, function Communication, satisfaction, patient, and caregiver quality of life, health care utilization

Abbreviation: NCORP, National Cancer Institute Community Oncology Research Program.

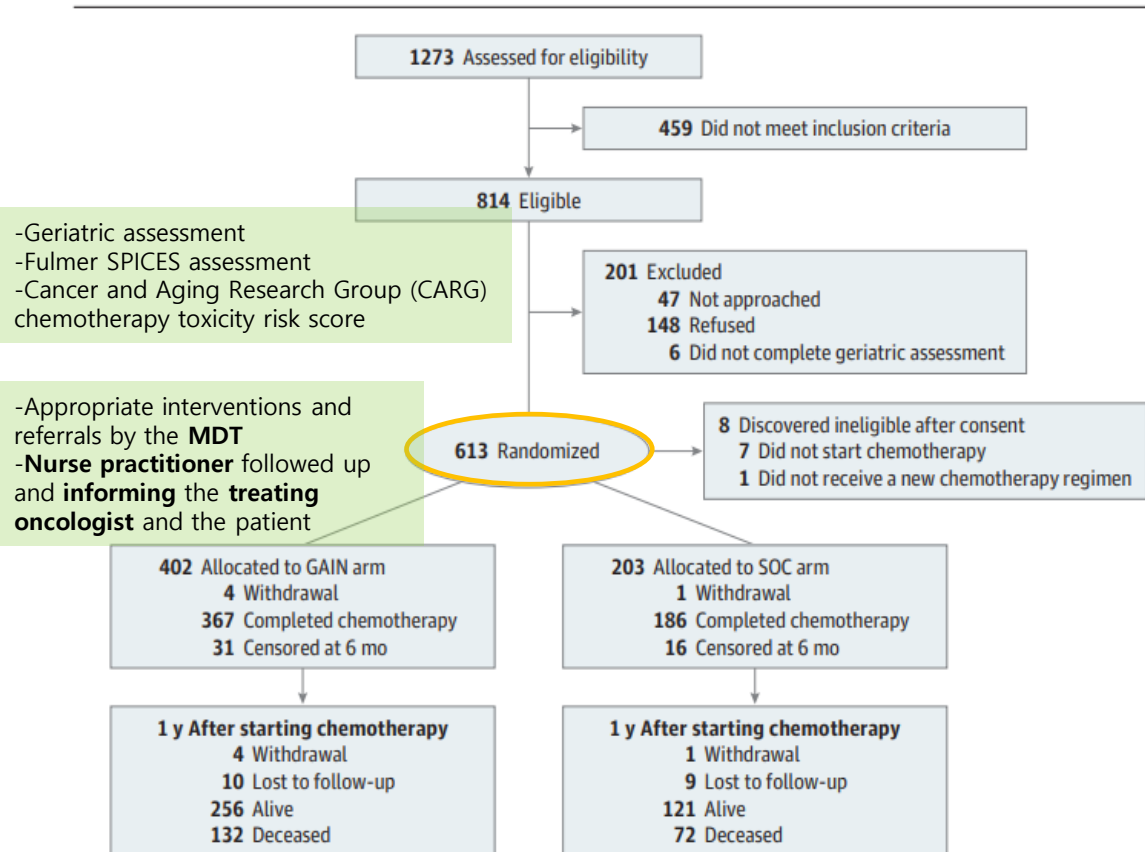
The effect of CGA in clinical practice: advanced stage

JAMA Oncology | Original Investigation

Geriatric Assessment-Driven Intervention (GAIN) on Chemotherapy-Related Toxic Effects in Older Adults With Cancer A Randomized Clinical Trial

Daneng Li, MD; Can-Lan Sun, PhD; Heeyoung Kim, MPH; Enrique Soto-Perez-de-Celis, MD; Vincent Chung, MD; Marianna Koczywas, MD;

Figure 1. CONSORT Flow Diagram



- **65 years and older** with a solid malignant neoplasm, Starting a new chemotherapy regimen, and completed a GCA
- Results were sent to treating oncologists for consideration
- Followed up until chemotherapy completion or 6 months after initiation

GA Domains	GAIN		SOC	
	Recommended	Implemented	Recommended	Implemented
All Domains	3971	3050	2029	254
Specific Domains				
Functional status	900	615	481	58
Comorbidities	287	201	143	0
Psychological status	508	414	246	61
Social activity	152	127	83	0
Social support	217	165	132	24
Nutrition	404	288	210	68
Cognition	59	49	32	0
Polypharmacy	317	311	151	3
Spiritual well-being	78	13	26	0
Clinical symptoms	541	421	296	21
Other issues*	508	446	229	19

Abbreviations: GAIN, Geriatric Assessment INtervention; SOC, standard of care; GA, geriatric assessment.

*Other issues included high toxicity score, lack of advance directive, and patient does not have PCP.

eTable 3. Number of Recommended and Implemented Intervention/Referrals by Study Arm

The effect of CGA in clinical practice: advanced stage

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Daneng Li, MD; Can-Lan Sun, PhD; Heeyoung Kim, MPH; Enrique Soto-Perez-de-Celis, MD; Vincent Chung, MD; Marianna Koczywas, MD;

- **65 years and older** with a solid malignant neoplasm, Starting a new chemotherapy regimen, and completed a GCA Results were sent to treating oncologists for consideration Followed up until chemotherapy completion or 6 months after initiation

Table 2. Grade 3 or Higher Chemotherapy-Related Toxic Effects Comparison Between GAIN and SOC Arms

Toxic effects	No. (%)			P value
	GAIN (n = 402)	SOC (n = 203)	Total (n = 605)	
Patients with grade 3 or higher chemotherapy-related toxic effects [95% CI]	203 (50.5) [45.6-55.4]	123 (60.6) [53.9-67.3]	326 (53.9) [49.9-57.9]	.02
Hematologic only	45 (11.2) [8.1-14.3]	39 (19.2) [13.8-24.6]	84 (13.9) [11.1-16.6]	.003
Nonhematologic only	74 (18.4) [14.6-22.2]	54 (26.6) [20.5-32.7]	128 (21.2) [17.9-24.4]	.007
Both hematologic and nonhematologic	84 (20.9) [16.9-24.9]	30 (14.8) [9.9-19.7]	114 (18.8) [15.7-22.0]	.64

Table 3. Secondary Outcomes Comparisons Between GAIN and SOC Arms

Outcome	No. (%) [95% CI]			P value ^a
	GAIN (n = 402)	SOC (n = 203)	Total (n = 605)	
Absolute change in AD status ^b	114 (28.4) [24.0-32.8]	27 (13.3) [8.6-18.0]	141 (23.3) [19.9-26.7]	<.001
Emergency department visit	110 (27.4) [23.0-31.7]	62 (30.5) [24.2-36.9]	172 (28.4) [24.8-32.0]	.41
Unplanned hospitalization	89 (22.1) [18.1-26.2]	39 (19.2) [13.8-24.6]	128 (21.2) [17.9-24.4]	.41
Average length of stay, d				
Mean (SD)	5.9 (4.2)	6.8 (5.6)	6.2 (4.7)	NA
Median (range)	5 (1-23)	5 (1-26)	5 (1-26)	.60 ^c
Unplanned readmission	17 (19.1) [10.9-27.3]	8 (20.5) [7.8-33.2]	25 (19.5) [12.7-26.4]	.85
Early chemotherapy discontinuation	216 (53.7) [48.9-58.6]	118 (58.1) [51.3-64.9]	334 (55.2) [51.2-59.2]	.30
Chemotherapy dose modifications ^d	218 (54.2) [49.4-59.1]	95 (46.8) [39.9-53.7]	313 (51.7) [47.8-55.7]	.08

The **6-month and 12-month survival** probabilities : 84% and 66% for the GAIN arm 83% and 64% for the SOC arm, respectively (**log-rank P value = .55**)

The effect of CGA in clinical practice: advanced stage

Evaluation of geriatric assessment and management on the toxic effects of cancer treatment (GAP70+): a cluster-randomised study

Supriya G Mohile, Mostafa R Mohamed, Huiwen Xu, Eva Culakova, Kah Poh Loh, Allison Magnuson, Marie A Flannery, Spencer Obrecht,

- Cluster-randomised trial
- Patients aged > **70 years** with incurable solid tumours or lymphoma
- At least one **impaired geriatric assessment domain** & Starting a new regimen Ctx
- Intervention (Provide CGA summary and management recommendations)
- vs usual care (No information provided to oncologist)

Primary outcome: Grade 3-5 toxic effect over 3months

	All patients (n=718)	Geriatric assessment intervention group (n=349)	Usual care group (n=369)
Age, years	77.2 (5.4)	77.2 (5.7)	77.2 (5.2)
70-79	494 (69%)	244 (70%)	250 (68%)
80-89	204 (28%)	94 (27%)	110 (30%)
≥90	18 (3%)	10 (3%)	8 (2%)
Missing	2 (<1%)	1 (<1%)	1 (<1%)
Gender			
Male	405 (56%)	203 (58%)	202 (55%)
Female	311 (43%)	145 (42%)	166 (45%)
Cancer type			
Breast	56 (8%)	19 (5%)	37 (10%)
Gastrointestinal	246 (34%)	132 (38%)	114 (31%)
Genitourinary	109 (15%)	56 (16%)	53 (14%)
Gynaecological	43 (6%)	29 (8%)	14 (4%)
Lung	180 (25%)	64 (18%)	116 (31%)
Lymphoma	46 (6%)	23 (7%)	23 (6%)
Other	38 (5%)	26 (7%)	12 (3%)

Cancer stage	Geriatric assessment intervention group (n=349)	Usual care group (n=369)
III	77 (11%)	42 (12%)
IV	628 (87%)	324 (88%)
Other	13 (2%)	10 (3%)

Previous chemotherapy	Geriatric assessment intervention group (n=349)	Usual care group (n=369)
Yes	185 (26%)	104 (30%)
No	164 (47%)	265 (72%)

Number of impaired geriatric assessment domains	Geriatric assessment intervention group (n=349)	Usual care group (n=369)
0	4.5 (1.6)	4.6 (1.6)
1	4.4 (1.5)	4.4 (1.5)

Impaired geriatric assessment domains*	Geriatric assessment intervention group (n=349)	Usual care group (n=369)
Physical performance	669 (93%)	314 (90%)
Polypharmacy	584 (81%)	287 (82%)
Comorbidity	484 (67%)	236 (68%)
Functional status	412 (57%)	200 (57%)
Nutrition	439 (61%)	211 (60%)
Cognition	261 (36%)	140 (40%)
Social support	194 (27%)	111 (32%)
Psychological status	205 (29%)	107 (30%)

Data are mean (SD) or n (%). Missing data for any variable were less than 5%.
*See appendix (pp 3-6) for further detail.

Table 1: Patient baseline characteristics

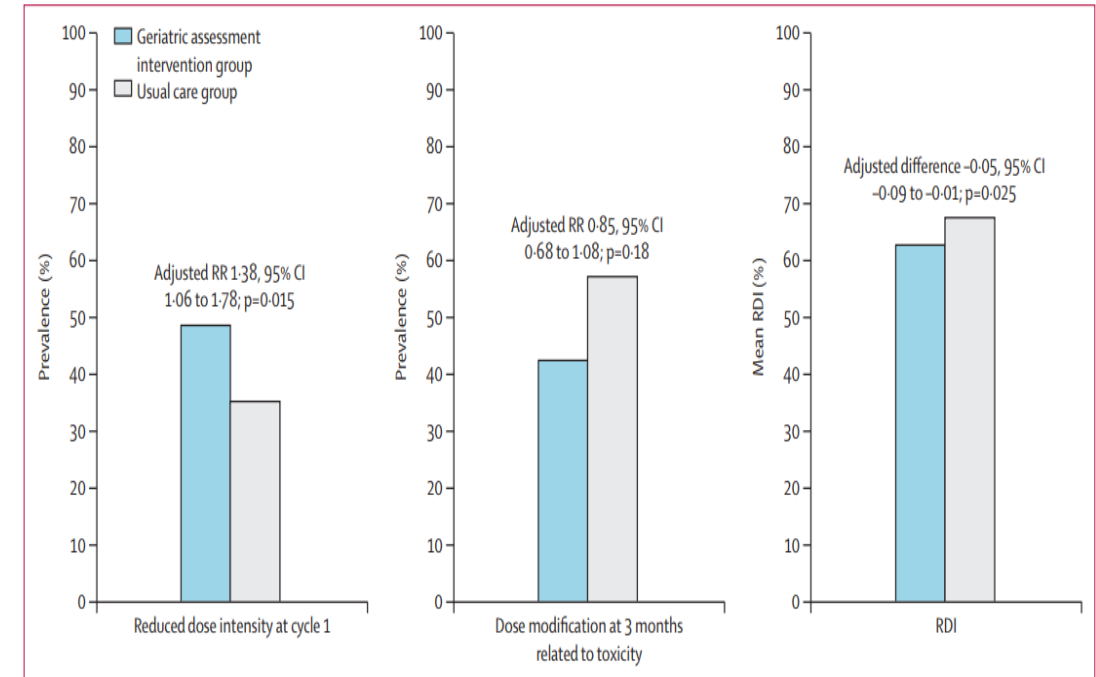


Figure 3: Treatment intensity by study group

RDI=relative dose intensity; The ratio of the total dose actually delivered to standard dose [not planned dose]

The effect of CGA in clinical practice: advanced stage

Evaluation of geriatric assessment and management on the toxic effects of cancer treatment (GAP70+): a cluster-randomised study

Supriya G Mohile, Mostafa R Mohamed, Huiwen Xu, Eva Culakova, Kah Poh Loh, Allison Magnuson, Marie A Flannery, Spencer Obrecht,

- Cluster-randomised trial
- Patients aged > **70 years** with incurable solid tumours or lymphoma
- At least one **impaired geriatric assessment domain** & Starting a new regimen Ctx
- Intervention (Provide CGA summary and management recommendations)
- vs usual care (No information provided to oncologist)

Primary outcome: Grade 3-5 toxic effect over 3months

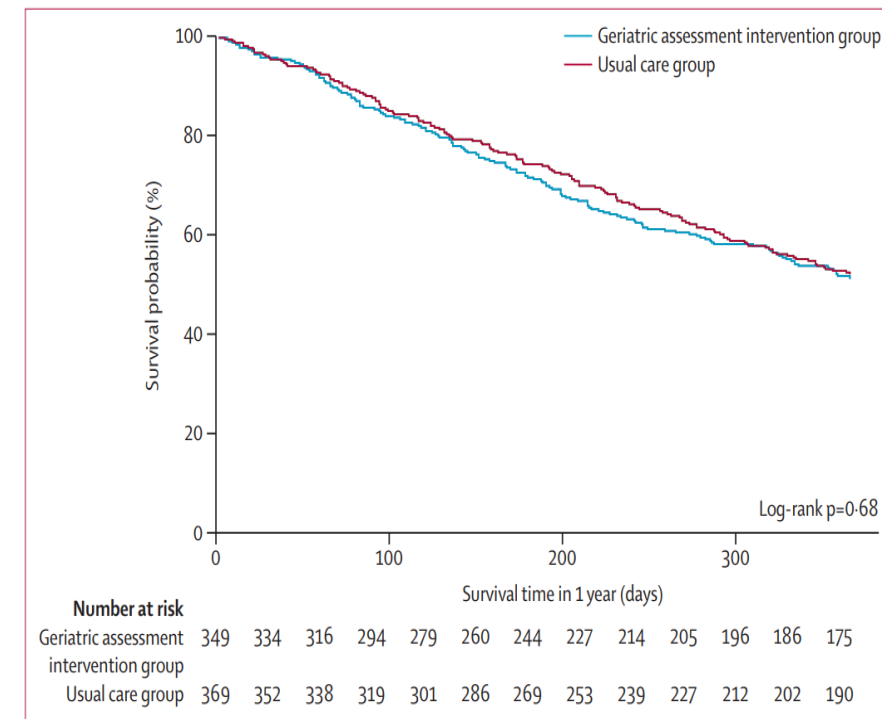
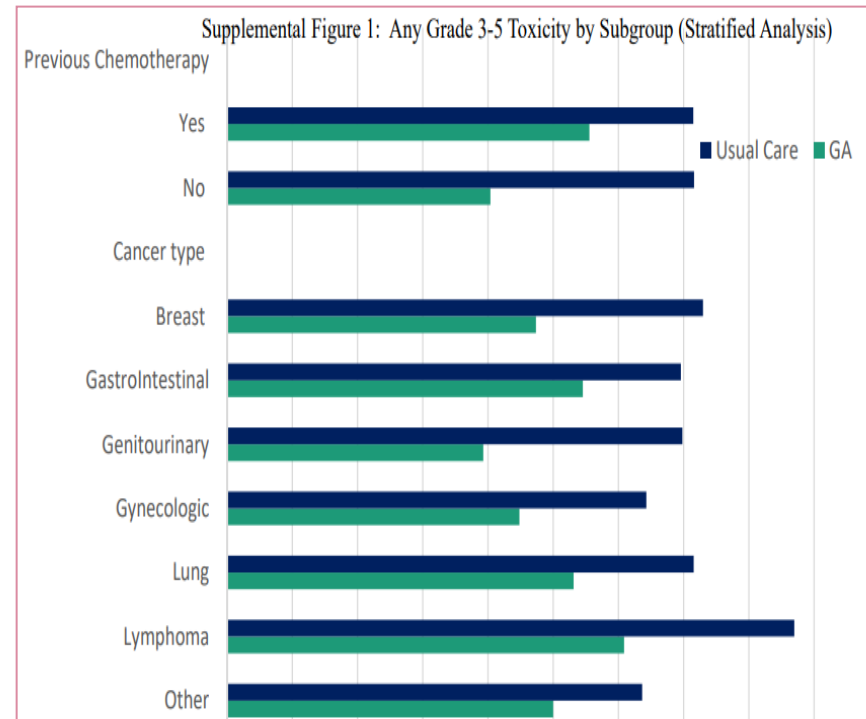
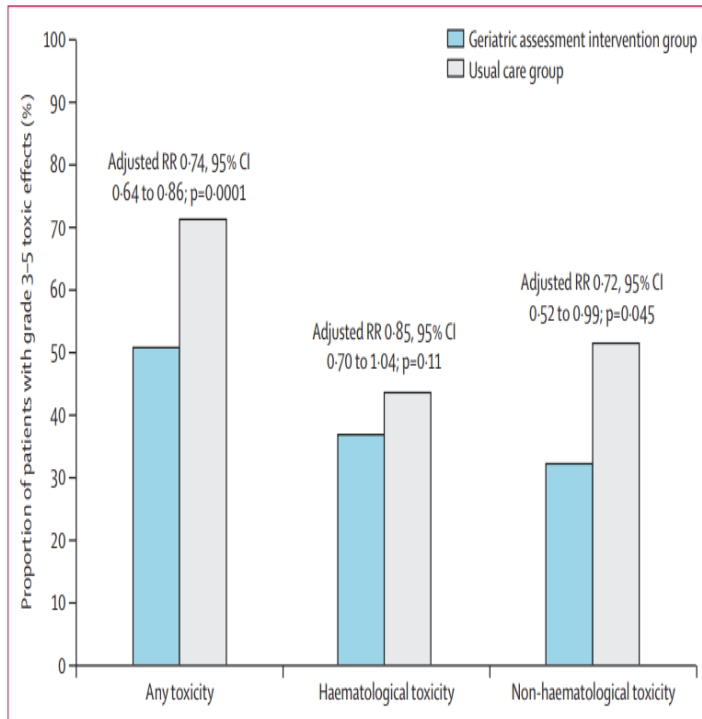


Figure 2: Prevalence of any grade 3-5 Common Terminology Criteria for Adverse Events toxic effects over 3 months

Figure 4: Survival over 1 year by study group

The effect of CGA in clinical practice: advanced stage lung cancer

A Geriatric Assessment Intervention to Reduce Treatment Toxicity Among Older Adults With Advanced Lung Cancer: A Subgroup Analysis From a Cluster Randomized Controlled Trial

Carolyn J. Presley^{1*}, Mostafa R. Mohamed², Eva Culakova³, Marie Flannery⁴,

TABLE 1 | Patient Characteristics by Study Arm

	All patients (N = 180)	Intervention arm (N = 64)	Usual care arm (N = 116)	P-values
Age (mean [standard deviation])	76.3 (5.1)	76.3 (5.3)	76.2 (4.9)	0.88
70-79	138 (76.7%)	46 (71.9%)	92 (79.3%)	0.12*
80-89	37 (20.6%)	17 (26.6%)	20 (17.2%)	
≥90	4 (2.2%)	0 (0.0%)	4 (3.5%)	
Missing	1 (0.6%)	1 (1.6%)	0 (0.0%)	
Sex				0.34
Male	108 (60.0%)	41 (64.1%)	67 (57.8%)	
Female	71 (39.4%)	22 (34.4%)	49 (42.2%)	
Cancer stage and lung cancer type				0.05*
Stage III NSCLC	30 (16.7%)	16 (25.0%)	14 (12.1%)	
Stage IV NSCLC	148 (82.2%)	48 (75.0%)	100 (86.2%)	
ES-SCLC	2 (1.1%)	0 (0.0%)	2 (1.7%)	
Prior chemotherapy	28 (15.6%)	7 (10.9%)	21 (18.1%)	0.16
Treatment Regimen (Chi-square test)				0.38
Chemo platinum doublet	134 (74.4%)	45 (70.3%)	89 (76.7%)	
Chemo+ immunotherapy	21 (11.7%)	8 (12.5%)	13 (11.2%)	
Single agent chemo	21 (11.7%)	8 (12.5%)	13 (11.2%)	
Other**	4 (2.2%)	3 (4.7%)	1 (0.8%)	

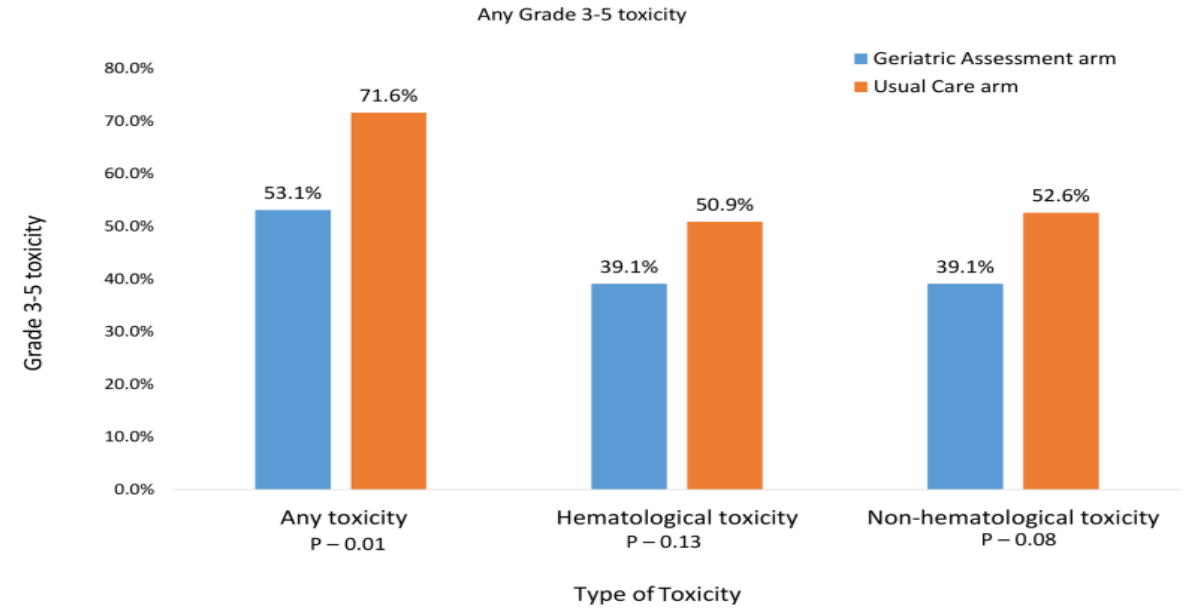


TABLE 2 | GAP Study Lung Cancer Treatment Secondary Outcomes by Study Arm.

	All patients (n = 180)	GA arm (n = 64)	Usual care arm (n = 116)	P values
Unplanned Hospitalization	62 (34.4%)	18 (28.1%)	44 (37.9%)	0.19
Dose delay	55 (30.6%)	18 (28.1%)	37 (31.9%)	0.60
Subsequent dose reduction	40 (22.2%)	8 (12.5%)	32 (27.6%)	0.02
Early discontinuation of treatment	37 (20.6%)	14 (21.9%)	23 (19.8%)	0.74
Reduced dose intensity at cycle 1	77 (42.8%)	36 (56.3%)	41 (35.3%)	<0.01
Overall Survival at 6 months*	124 (68.9%)	45 (70.3%)	79 (68.1%)	0.76
Overall Survival at 1 year*	82 (45.6%)	31 (48.4%)	51 (44.0%)	0.56

*Censoring is not considered.

The effect of CGA in clinical practice: advanced stage

Effects of a Geriatric Assessment Intervention on Patient-Reported Symptomatic Toxicity in Older Adults With Advanced Cancer

Eva Culakova, PhD, MS¹; Supriya G. Mohile, MD, MS²; Luke Peppone, PhD, MPH^{1,2}; Erika Ramsdale, MD, MS²;

- Secondary analysis of the GAP70+ trial to assess the effect of the GA intervention on **patient-reported symptomatic toxicities**

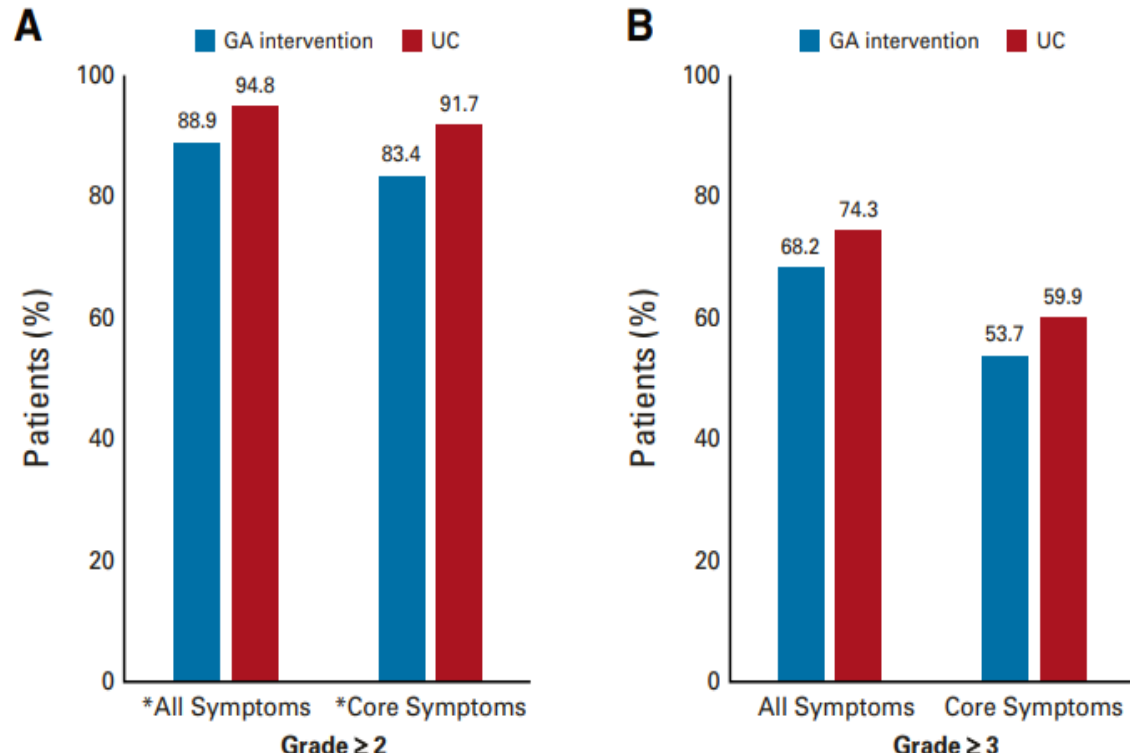


FIG 4. Effect of the GA intervention on patient-reported symptomatic toxicity reported over 6 months: (A) grade ≥ 2 and (B) grade ≥ 3 . * $P < .05$. GA, geriatric assessment; UC, usual care.

Symptom Items	Grade ≥ 2 (moderate or higher) Baseline-Adjusted				Grade ≥ 3 (severe or very severe) Baseline-Adjusted			
	% With Toxicity		ARR (95% CI) ^a	P^a	% With Toxicity		ARR (95% CI)	P^a
UC (n = 327)	GA (n = 296)	UC (n = 327)			GA (n = 296)			
Fatigue	52.9	45.6	0.862 (0.735 to 1.011)	.068	30.3	24.0	0.792 (0.638 to 0.984)	.035
Decreased appetite	34.9	35.5	1.018 (0.770 to 1.345)	.903	16.8	18.9	1.125 (0.670 to 1.888)	.656
Pain	29.1	26.7	0.919 (0.728 to 1.159)	.474	12.2	9.8	0.801 (0.540 to 1.188)	.270
Insomnia	31.5	27.4	0.869 (0.724 to 1.043)	.132	9.5	9.1	0.962 (0.734 to 1.261)	.780
Constipation	30.9	29.1	0.941 (0.746 to 1.186)	.604	15.6	10.1	0.650 (0.455 to 0.929)	.018
Shortness of breath	31.5	22.0	0.697 (0.515 to 0.944)	.020	16.2	8.8	0.542 (0.424 to 0.693)	<.001
Numbness/tingling	24.8	20.6	0.832 (0.608 to 1.139)	.252	9.5	7.8	0.820 (0.520 to 1.291)	.391
Nausea	16.8	14.5	0.864 (0.637 to 1.171)	.345	3.1	2.7	0.884 (0.367 to 2.128)	.783
Concentration problems	18.0	17.2	0.955 (0.663 to 1.377)	.805	4.0	3.0	0.765 (0.290 to 2.016)	.588
Memory problems	18.7	17.9	0.960 (0.610 to 1.510)	.859	3.7	4.7	1.289 (0.600 to 2.770)	.516
Diarrhea	28.7	28.4	0.987 (0.714 to 1.364)	.938	8.3	10.1	1.228 (0.808 to 1.864)	.336

NOTE. ARR and P values are evaluated by generalized estimating equation model. P value $< .05$ are bold.

TABLE 2. Symptomatic Toxicity in GA Intervention Versus UC

The effect of CGA in clinical practice: advanced stage

Geriatric assessment in the management of older patients with cancer – A systematic review (update)

Marije Hamaker^{a,*}, Cecilia Lund^b, Marthe te Molder^c, Pierre Soubeyran^d, Hans Wildiers^e,

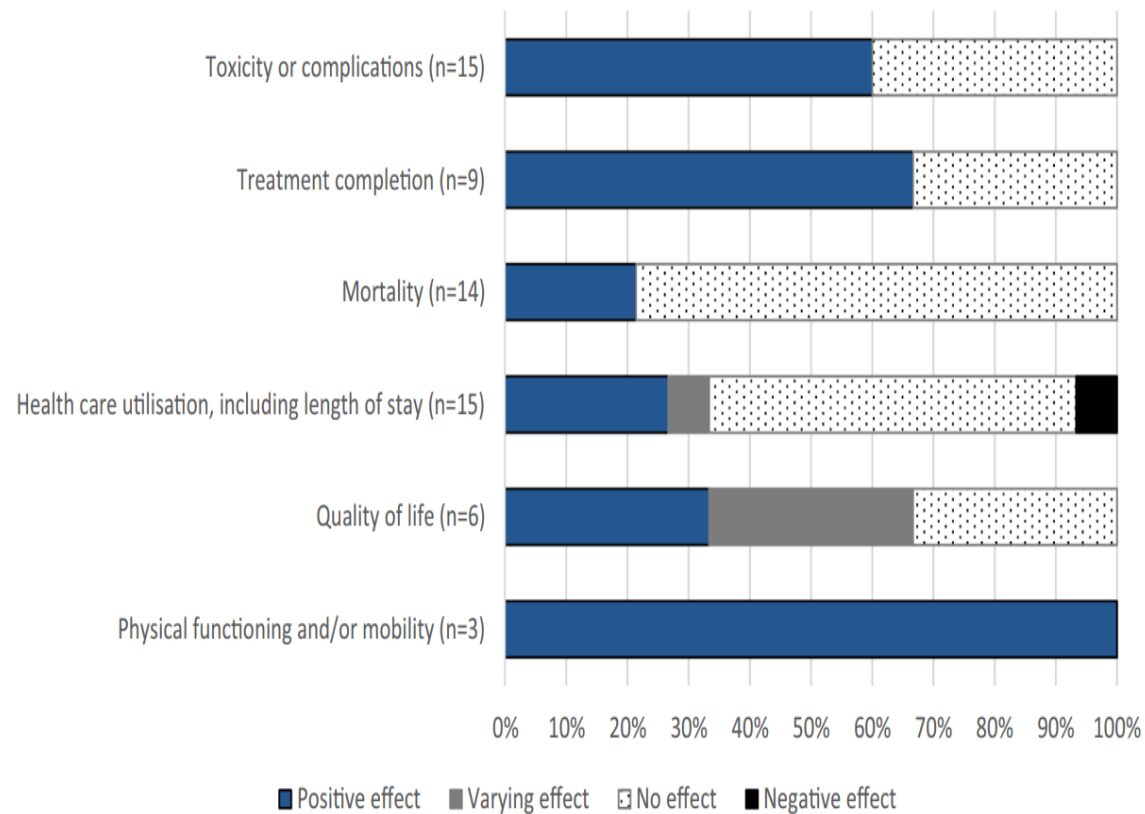


Fig. 4. Summary of **the effect of geriatric assessment** on course of treatment and outcome. N represents the number of studies assessing each outcome.

- Systemic review of Sixty-five publications from 61 studies
 - Oncologic **treatment plan** was **altered in 31%** of patients (range 7–56%)
 - **Non-oncologic interventions** were recommended in over **70%** of patients.

➤ Conclusion

- A geriatric assessment can change oncologic treatment plans, leads to non-oncologic interventions, and improve communication about care planning and ageing-related issues.
- It can **decrease toxicity/complications** and **improve treatment completion and patient-centred outcomes**

The effect of CGA in early stage cancer

Geriatric assessment in the management of older patients with cancer – A systematic review (update)

Marije Hamaker^{a,*}, Cecilia Lund^b, Marthe te Molder^c, Pierre Soubeyran^d, Hans Wildiers^e,

- Systemic review of Sixty-five publications from 61 studies
- Oncologic **treatment plan** was **altered in 31%** of patients (range 7–56%)
- **Non-oncologic interventions** were recommended in over **70%** of patients.

Table 2
Studies assessing the effect of geriatric assessment on treatment outcome.

Author	Study design				Type of cancer treatment	Duration of follow-up	n=	Effect on course of treatment and outcomes					
	Type of assessment*	Assessment included in oncologic decision-making	Intervention/follow-up included	Control population**				Toxicity or complications	Treatment completion	Mortality	Health care utilisation, including length of stay	Quality of life	Physical functioning and/or mobility
Kalsi [55]	C	Yes	Yes	HC	CT	6 months	135	=	+	=			
Nadaraja [26]	C	Yes	Yes	R	CT	6 months	96	=	=	=			
Singh [69]	C	No	Yes	HC	Surgery	Discharge	?				+		
Dumontier [12]	C	No	Yes	R	CT	12 months	160			=	=		
Hempenius [49,50]	C	No	Yes	R	Surgery	3 months	260	=		=		=	
Ommundsen [61]	C	No	Yes	R	Surgery	30 days	122	=		=	=		
Puts [64,71]	C	No	Yes	R	CT	3 months	58			+	=	=	=
Soo [34]	C	?	Yes	R	CT	6 months	154		+		+	+	+
Corre [44]	O	Yes	No	R	CT	12 months	494	+	+	=			
Mohile [23,24]	O	Yes	Yes	R	CT	12 months	718	+	+	=		±	+
Lund [22]	O	No	Yes	R	CT	End of treatment	142	=	+	=	=	+	+
Magnuson [57]	O	No	Yes	R	Various	3 months	71	=	=	=			
Fletcher [46]	M	Yes	No	MC	Various	?	149	+	+		-		
Derman [10]	M	Yes	Yes	HC	CT	Discharge	247	+		+	+		
Pattinson [63]	M	Yes	Yes	HC	Various	6 months	97			+	±		
Li [20]	M	Yes	Yes	R	CT	12 months	605	+	=	=	=		
Odetto [60]	M	Yes	Yes	R	Surgery	?	38	+					
Mak [58]	M	No	Yes	MC	Surgery	30 days	39	+					
Ho [51]	M	No	Yes	R	Surgery	discharge	?	+			+		
Rao [65]	M	No	Yes	R	Various	3 months	99			=		±	
Santos [30]	M	?	Yes	MC	Various	12 months	300	+		=	=	±	

* Geriatric consultation (C) refers to the assessment as used in standard geriatric care, performed by a geriatrician; an assessment by the oncology team (O) refers to an assessment performed by the cancer specialist/health care provider working with the cancer specialist; multidisciplinary team evaluation (M) refers to a geriatric assessment performed by two or more (para)medical health care professionals.

** HC historic controls, MC matched controls, R randomisation, CT chemotherapy, ? Unclear/not reported.

+ indicates a positive effect on this outcome for the intervention arm; – indicates a negative effect for the intervention arm; = indicates no (significant) effect for this outcome; ± indicates contradicting results with positive effect on one but not all outcome measures.

The effect of CGA in early stage lung cancer

- Geriatric nutritional risk index and survival outcome
 $GNRI = 14.89 \times ALB(g/dL) + 41.7 \times [current\ BW\ (kg) / 22 \times height\ (m)^2]$

Univariate and multivariate Cox proportional hazards regression analysis of overall survival, cancer-specific survival, and relapse-free survival.

Variables *	Overall survival		Cancer-specific survival		Relapse-free survival	
	HR (95% CI)	P value	HR (95% CI)	P value	HR (95% CI)	P value
(B) Multivariate analysis						
Age, yr	1.05 (1.01–1.08)	.009	1.05 (1.01–1.09)	.009		
Sex (female vs male)	0.31 (0.12–0.80)	.015				
TNM stage (IIA/IIB/IIIA vs IA/IB)	3.54 (1.88–6.69)	<.001	7.11 (3.18–15.90)	<.001	3.68 (2.19–6.18)	<.001
Pleural invasion (PL2/3 vs PLO/1)	3.85 (1.75–8.44)	<.001	2.98 (1.24–7.13)	.014	2.68 (1.36–5.25)	.004
Lymphatic invasion (yes vs no)					2.28 (1.29–4.04)	.005
GNRI (high vs low)	0.37 (0.19–0.71)	.003	0.47 (0.23–0.97)	.041	0.38 (0.23–0.62)	<.001

- Pretreatment Physical and Geriatric Parameters with Treatment Tolerance

	Surgery (n = 104) Treatment Intolerance n = 49 (47%) Univariable		SABR (n = 56) Treatment Intolerance n = 21 (38%) Univariable	
	OR (90% CI)	p-Value	OR (90% CI)	p-Value
SNAQ score Adequate nutritional status (≤1) Malnourished (>1)	Reference 2.84 (0.91–8.86)	0.07	Reference 1.56 (0.47–5.12)	0.47
SPPB Higher level of functioning (>9) Lower level of functioning (≤9)	Reference 4.14 (1.45–11.87)	0.01	Reference 2.38 (0.42–13.39)	0.33
G8 Fit (>14) Frail (≤14)	Reference 3.79 (1.38–10.37)	0.01	Reference 0.36 (0.05–2.50)	0.30
GFI Fit (<4) Frail (≥4)	Reference 3.40 (1.26–9.21)	0.02	Reference 0.32 (0.06–1.71)	0.18

Treatment intolerance: **complications** classified as ClavienDindo grade 2 or higher, at least one **readmission**, with in postOp 30days, and/or a postoperative hospital length of stay > 5 days.

SNAQ = short nutritional assessment questionnaire; SPPB = short physical performance battery; GFI = Groningen frailty index

Contents

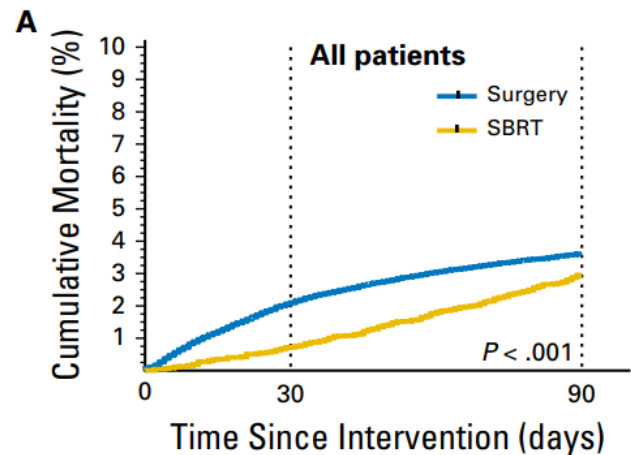
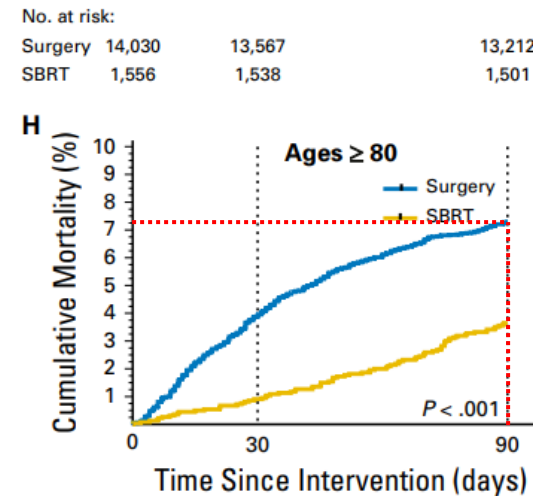
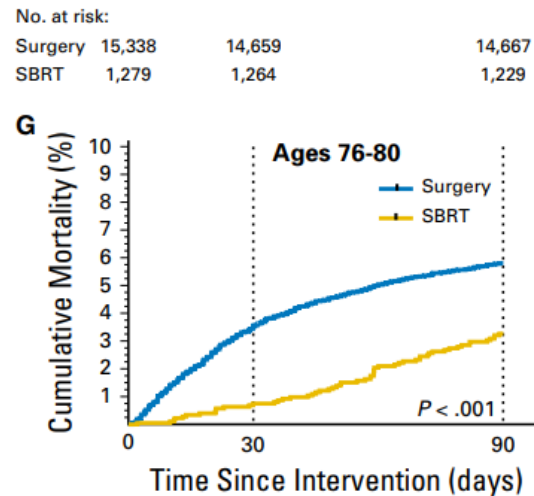
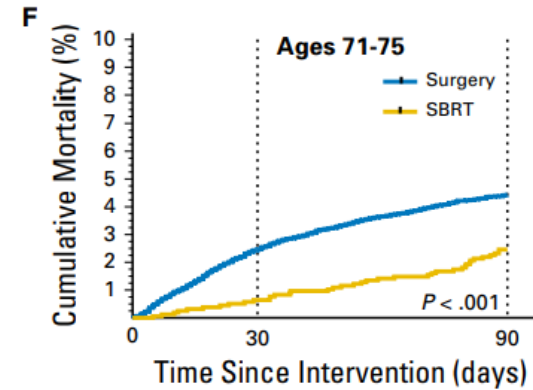
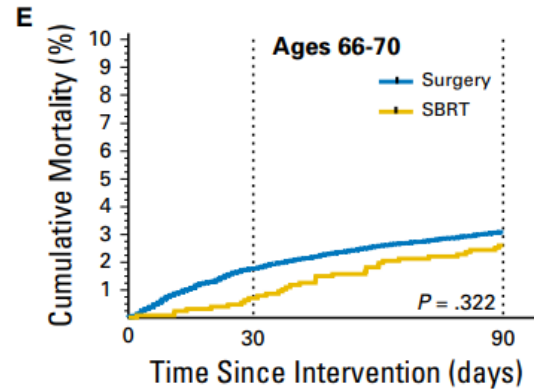
- Comprehensive geriatric assessment
 - ✓ ASCO&NCCN guideline
 - ✓ Implement in practice
- **Early stage lung cancer**
 - ✓ **Surgery**
 - ✓ **SBRT**
- Locally advanced lung cancer
- Advanced lung cancer
 - ✓ Tyrosine kinase inhibitor
 - ✓ Immunotherapy

Post-Treatment mortality in early stage NSCLC

➤ cT1-T2a, N0, M0 NSCLC diagnosed between 2004 and 2013 from National Cancer Database

Table 1. Descriptive Statistics Comparing Patients Undergoing Surgery Versus SBRT (N = 84,839)

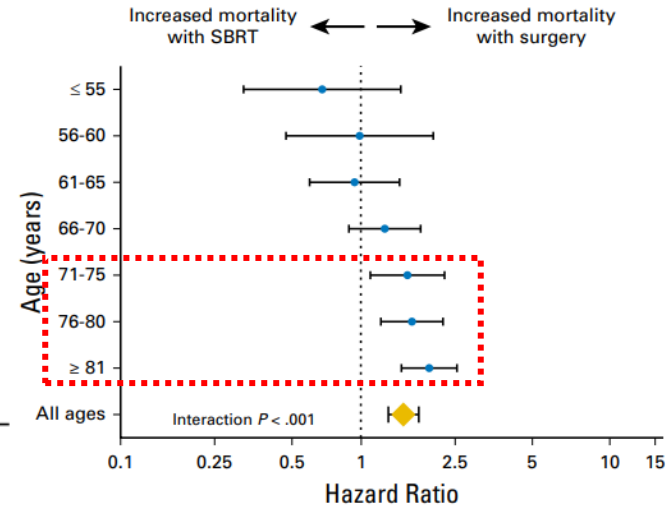
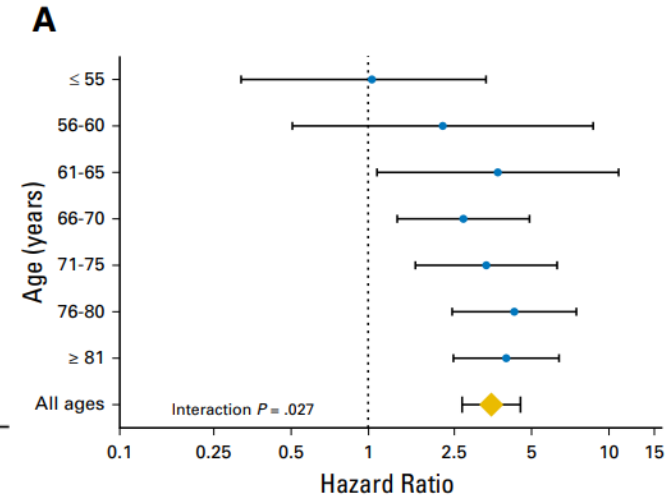
Characteristic	Surgery (n = 76,623)		SBRT (n = 8,216)		P
	No.	%	No.	%	
Age, years					< .001
≤ 55	9,816	12.8	241	2.9	
56-60	8,472	11.1	416	5.1	
61-65	12,069	15.8	800	9.7	
66-70	15,338	20.0	1,279	15.6	
71-75	14,030	18.3	1,556	18.9	
76-80	10,761	14.0	1,720	20.9	
≥ 81	6,137	8.0	2,204	26.8	



No. at risk:				
Surgery	76,623	74,439	72,823	
SBRT	8,216	8,122	7,892	

No. at risk:				
Surgery	10,761	10,309	10,004	
SBRT	1,720	1,702	1,652	

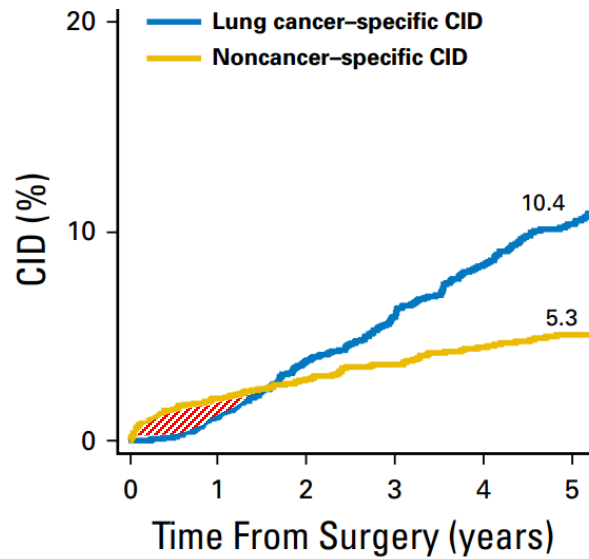
No. at risk:				
Surgery	6,137	5,851	5,608	
SBRT	2,204	2,176	2,103	



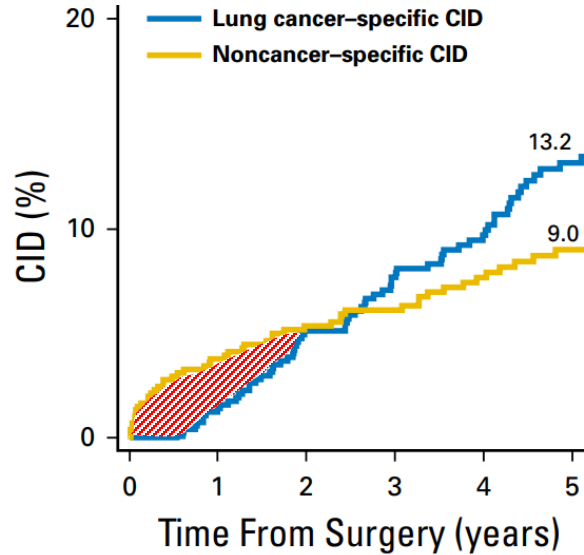
Impact of increasing age on mortality of stage I NSCLC

➤ Retrospective analysis of 2,186 NSCLC stage I patients undergone curative-intent resection from 2000 to 2011

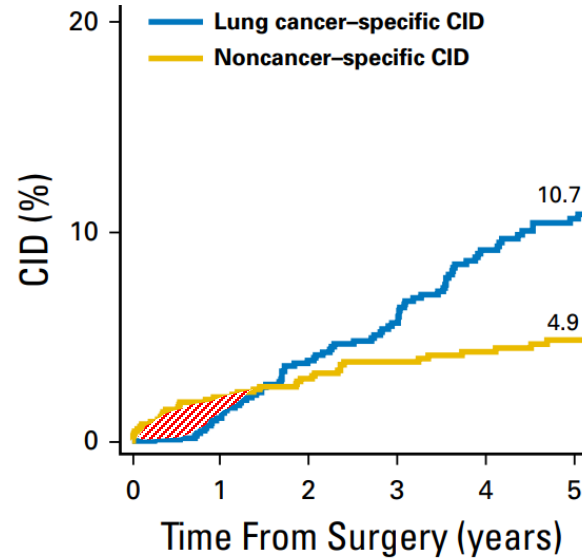
A Study population: N=2,168



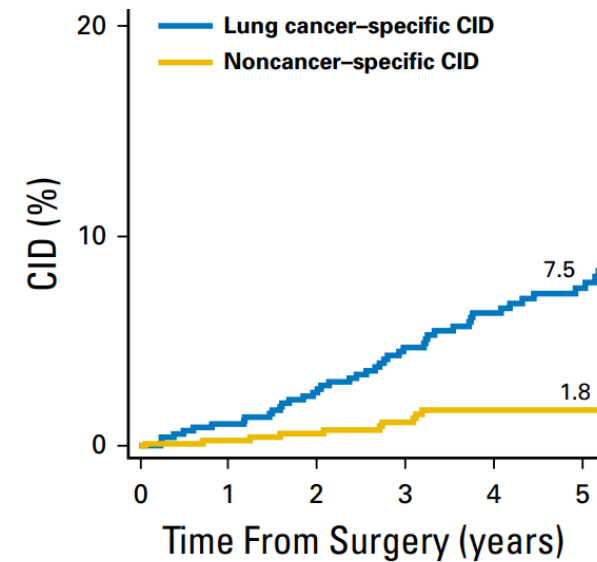
B ≥75 years of age, N=638



C 65-74 years of age, N=894



D < 65 years old, N=654



CID: cumulative incidence of death

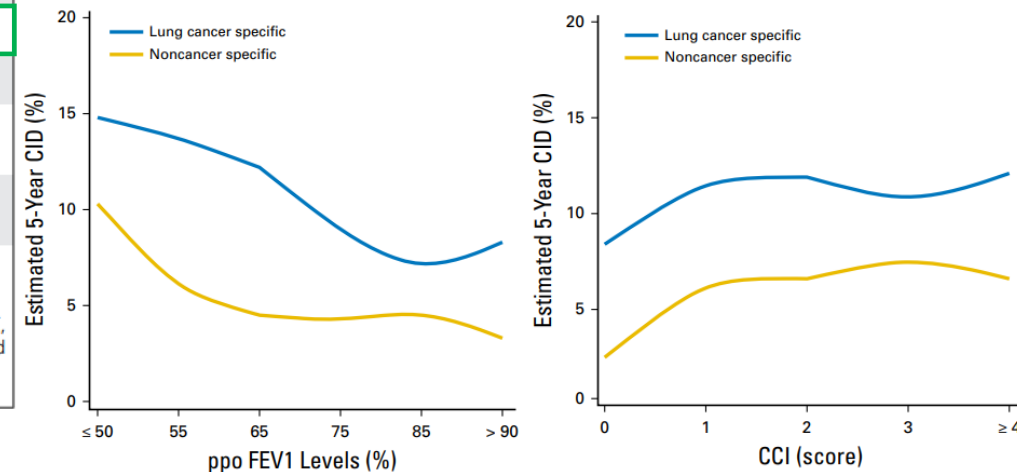
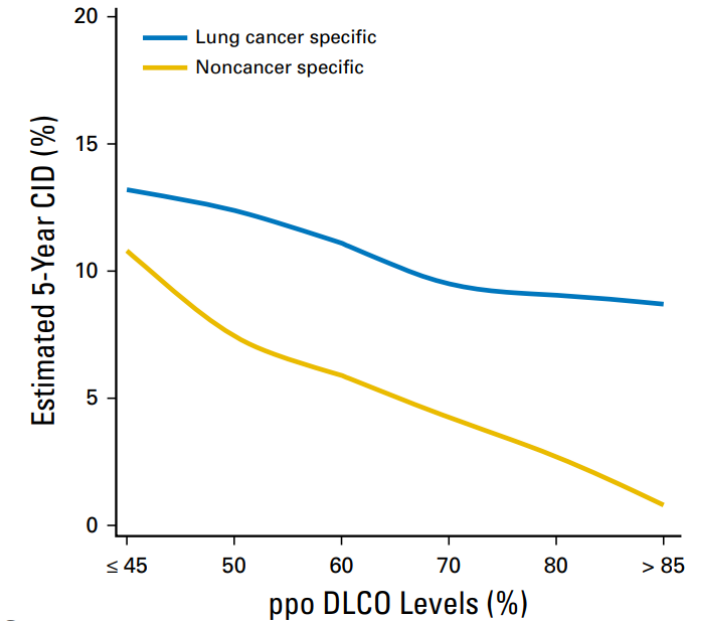
Risk factors for cancer and noncancer-specific mortality

➤ Retrospective analysis of 2,186 NSCLC stage I patients undergone curative-intent resection from 2000 to 2011

Table 3. Multivariable Analysis for Short- and Long-Term Outcomes

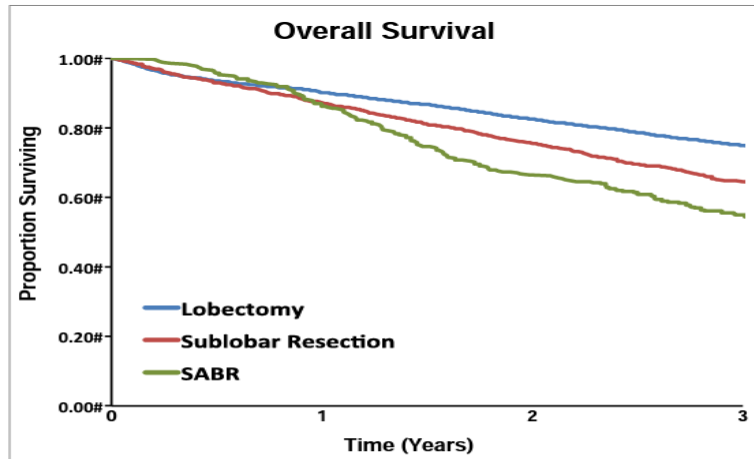
Variable	Short-Term Outcome						Long-Term Outcome								
	Severe Morbidity			1-Year Mortality			Lung Cancer-Specific Mortality			Noncancer-Specific Mortality			Overall Survival		
	OR	95% CI	<i>P</i>	OR	95% CI	<i>P</i>	SHR	95% CI	<i>P</i>	SHR	95% CI	<i>P</i>	HR	95% CI	<i>P</i>
Age at diagnosis (per 1-year increase)				1.04	1.01 to 1.07	.015				1.05	1.03 to 1.08	< .001	1.05	1.04 to 1.06	< .001
Male sex (v female)				1.76	1.10 to 2.79	.017				1.92	1.31 to 2.83	.001	1.38	1.17 to 1.63	< .001
Former smoker (v never)							1.7	1.07 to 2.70	.026				1.17	0.89 to 1.54	.3
Current smoker (v never)							1.82	1.04 to 3.19	.037				1.59	1.14 to 2.22	.007
COPD history (v no history)	1.61	1.12 to 2.31	.01												
CVD history (v no history)										1.68	1.12 to 2.52	.012			
BMI (per 1-index increase)															
CCI (per 1-index increase)													1.14	1.07 to 1.21	< .001
ppo FEV1 (per 1% increase)							0.99	0.98 to 1.00	.002				0.99	0.99 to 1.00	.019
ppo DLCO (per 1% increase)	0.97	0.96 to 0.98	< .001	0.96	0.95 to 0.98	< .001				0.96	0.95 to 0.98	< .001	0.99	0.98 to 0.99	< .001
Serum Cr (per 1 mg/dL increase)	1.48	1.03 to 2.12	.032												
Tumor size on CT scan (per 1-cm increase)				1.63	1.30 to 2.03	< .001	1.44	1.27 to 1.64	< .001				1.27	1.17 to 1.38	< .001
Sublobar resection (v lobectomy)	0.58	0.37 to 0.90	.014	2.54	1.51 to 4.26	< .001	2.06	1.53 to 2.79	< .001	1.53	1.03 to 2.28	.034	1.74	1.45 to 2.10	< .001
C-index (95% CI)	0.686 (0.641 to 0.732)			0.771 (0.729 to 0.813)			0.668 (0.631 to 0.706)			0.769 (0.731 to 0.813)			0.709 (0.688 to 0.731)		

NOTE. Statistically significant *P* values are indicated by boldface.
Abbreviations: BMI, body mass index; C-index, concordance index; CCI, Charlson comorbidity index; COPD, chronic obstructive pulmonary disease; Cr, creatinine; CT, computed tomography; CVD, cardiovascular disease; DLCO, diffusion capacity of lung for carbon monoxide; FEV1, forced expiratory volume in 1 second; HR, hazard ratio; OR, odds ratio; ppo, predicted postoperative; SHR, subhazard ratio.



Lobectomy vs sublobar resection

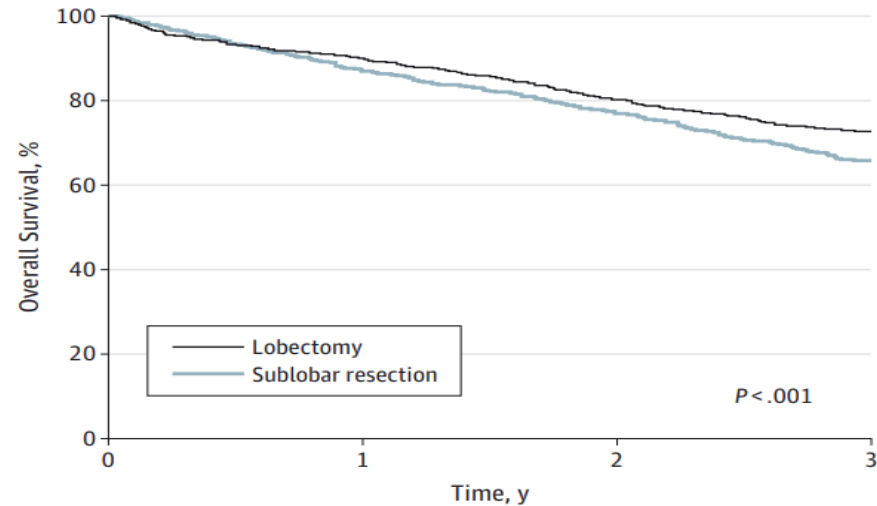
- SEER-Medicare database from 2003 through 2009, **>66 years older** NSCLC, Pathologic confirm, **T<5cmN0**
 - 9093 patients, Median age 75 years
 - Lobectomy in 7215 patients (79.3%), sublobar resection in 1496 (16.5%), and SABR in 382 (4.2%)



Independent variables for PSM:
Age, sex, CCI, O2 supply, T-stage, PET staging, Mediastinal sampling

Figure. Outcomes for Propensity Score-Matched Cohorts

A Lobectomy vs Sublobar Resection



No at Risk	0	1	2	3
Lobectomy	7215	6517	5957	4771
Sublobar Resection	1496	1303	1131	860
SABR	382	332	253	132

AHRs comparing sublobar resection and lobectomy: **1.32 [95% CI 1.20-1.44]; P < .001**

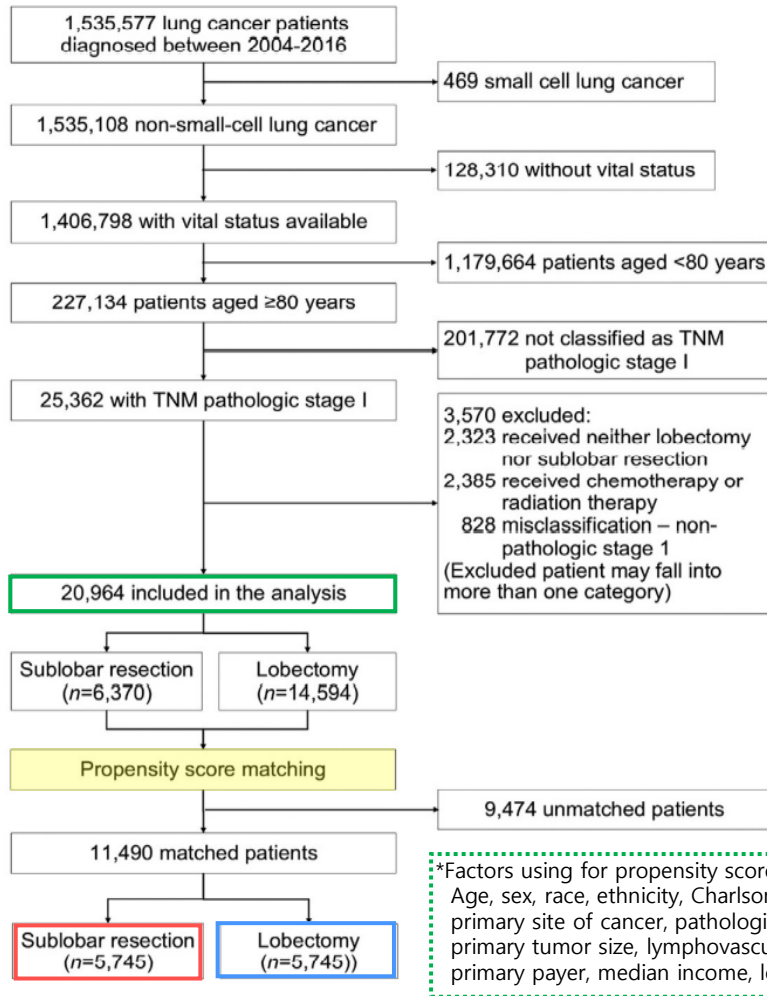
Table 5. Propensity Score-Matching Sensitivity Analysis

Comparison	Overall Survival	
	AHR (95% CI) ^a	P Value
Sublobar Resection vs Lobectomy		
Main analysis (1077 matched pairs) ^b	1.36 (1.17-1.58)	<.001
Stricter match (1057 matched pairs) ^c	1.20 (1.03-1.39)	.02
Less strict match (1496 matched pairs) ^d	1.25 (1.08-1.45)	.004

Comparison	Overall Survival			Lung Cancer Specific Survival		
	AHR ¹	95%CI	P	AHR ¹	95%CI	P
Sublobar Resection v Lobectomy						
Tumors ≤ 2 cm	1.43	(1.25-1.62)	<.001	1.64	(1.32-2.04)	<.001
Age ≥ 75 Years	1.18	(1.04-1.33)	0.01	1.26	(1.02-1.55)	0.03

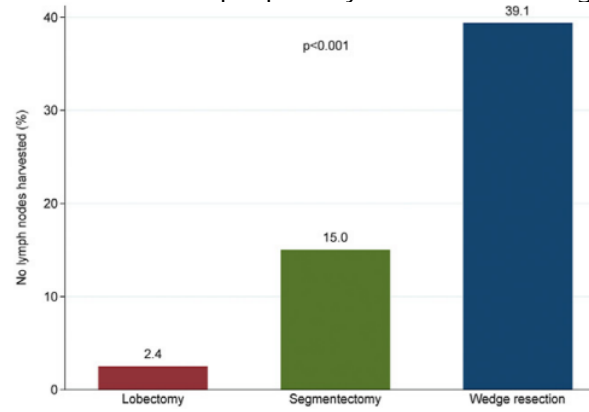
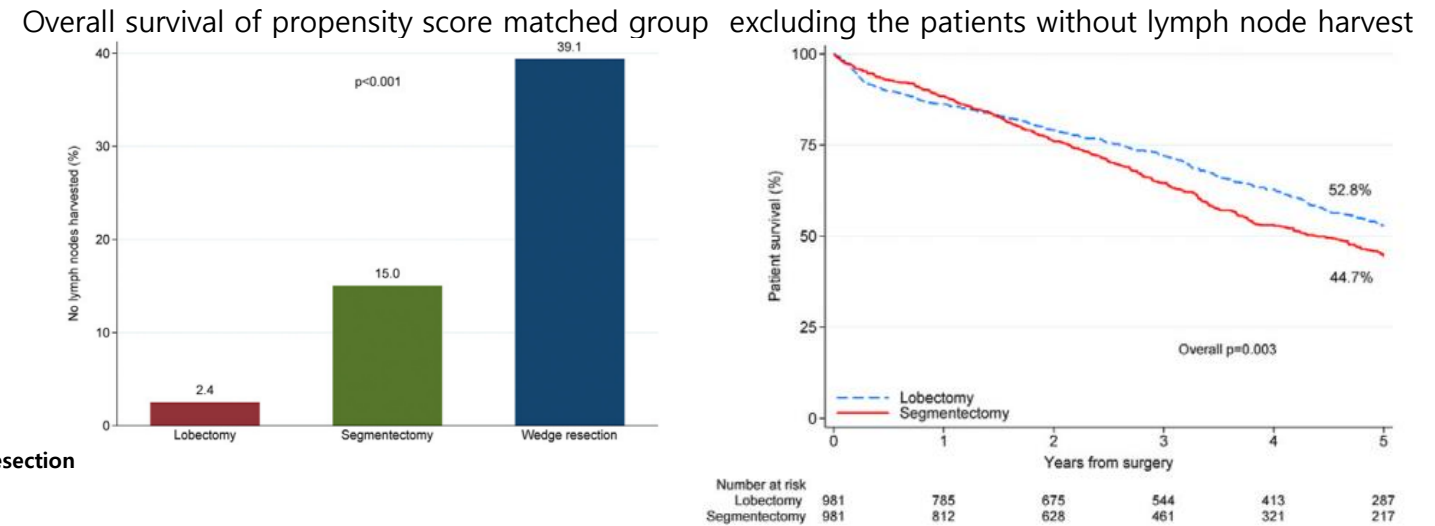
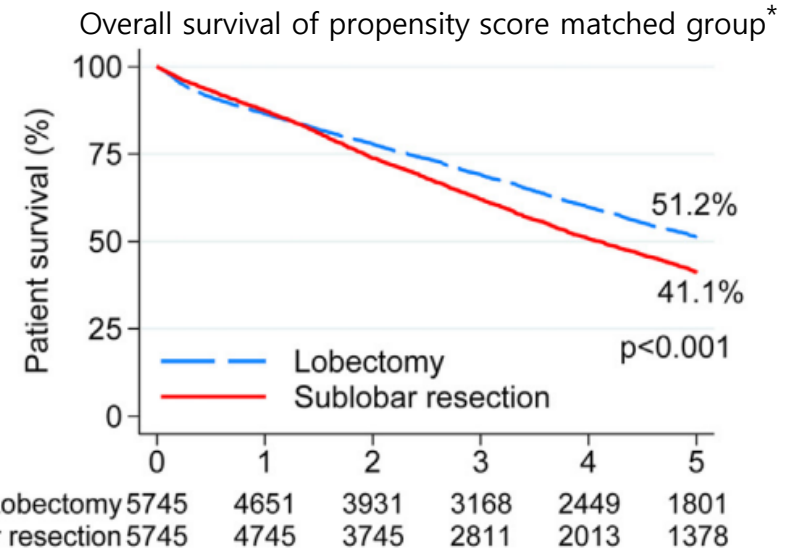
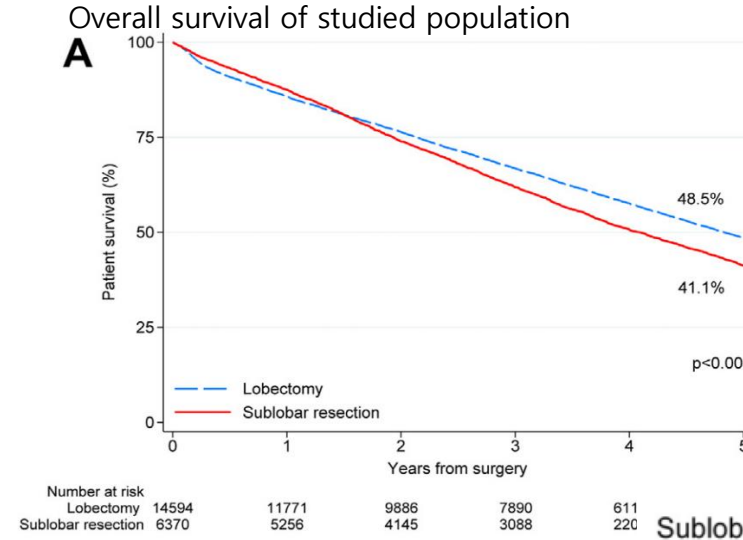
Lobectomy vs sublobar resection in elderly patients

➤ **Octogenarians Stage I** (AJCC 7th, T size ≤5cm) NSCLC, data from National Cancer Database from 2004 to 2016



*Factors using for propensity score matching:
Age, sex, race, ethnicity, Charlson-Deyo score
primary site of cancer, pathologic stage,
primary tumor size, lymphovascular invasion
primary payer, median income, location

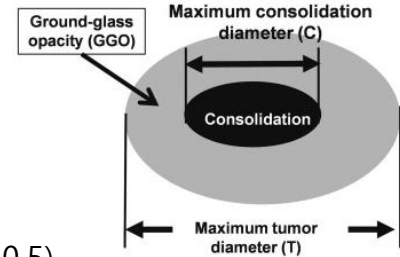
**No data about PFT and the reason for sublobar resection



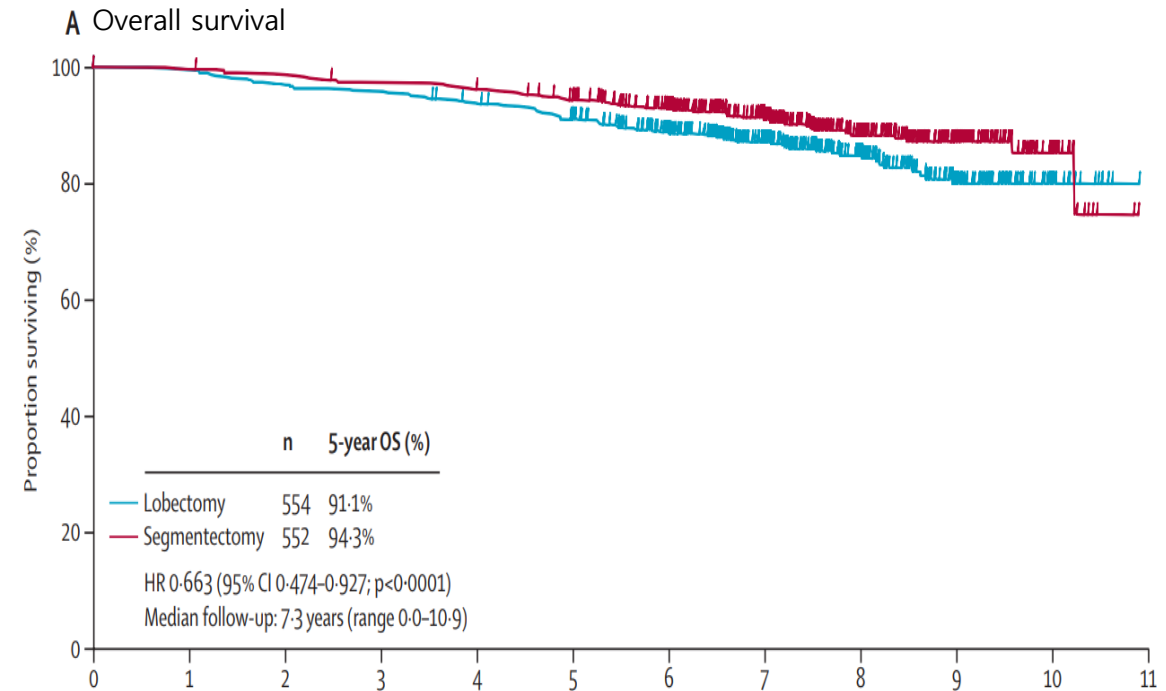
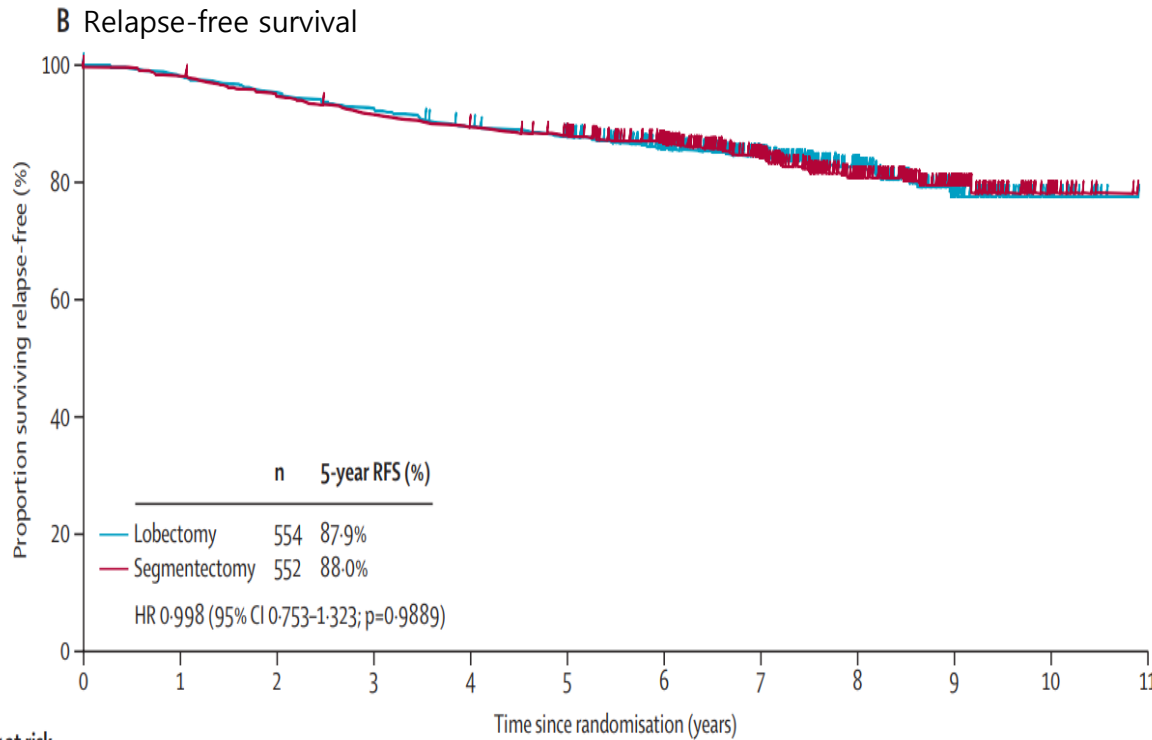
Lobectomy vs segmentectomy resection in small peripheral NSCLC

Segmentectomy versus lobectomy in small-sized peripheral non-small-cell lung cancer (JCOG0802/WJOG4607L): a multicentre, open-label, phase 3, randomised, controlled, non-inferiority trial

Hisashi Saji, Morihito Okada, Masahiro Tsuboi, Ryu Nakajima, Kenji Suzuki, Keiju Aokage, Tadashi Aoki, Jiro Okami, Ichiro Yoshino, Hiroyuki Ito,



- Multicenter RCT (JCOG0802)
IA NSCLC (T size $\leq 2\text{cm}$, consolidation to tumor ratio >0.5)
Randomly assigned 1:1 to receive either lobectomy or segmentectomy



Number at risk (number censored)

	0	1	2	3	4	5	6	7	8	9	10	11
Lobectomy	554 (0)	542 (1)	527 (0)	512 (0)	492 (3)	477 (6)	409 (57)	310 (93)	184 (121)	85 (91)	22 (63)	0 (22)
Segmentectomy	552 (0)	541 (1)	521 (1)	503 (1)	491 (0)	477 (6)	426 (45)	304 (112)	181 (112)	89 (90)	21 (67)	0 (21)

Number at risk (number censored)

	0	1	2	3	4	5	6	7	8	9	10	11
Lobectomy	554 (0)	550 (1)	537 (0)	530 (0)	525 (3)	495 (6)	426 (57)	322 (97)	190 (125)	90 (92)	23 (67)	0 (23)
Segmentectomy	552 (0)	549 (1)	543 (1)	534 (1)	528 (0)	512 (6)	457 (47)	332 (118)	202 (122)	104 (96)	25 (78)	0 (24)

Lobectomy vs segmentectomy resection in small peripheral NSCLC

Segmentectomy versus lobectomy in small-sized peripheral non-small-cell lung cancer (JCOG0802/WJOG4607L): a multicentre, open-label, phase 3, randomised, controlled, non-inferiority trial



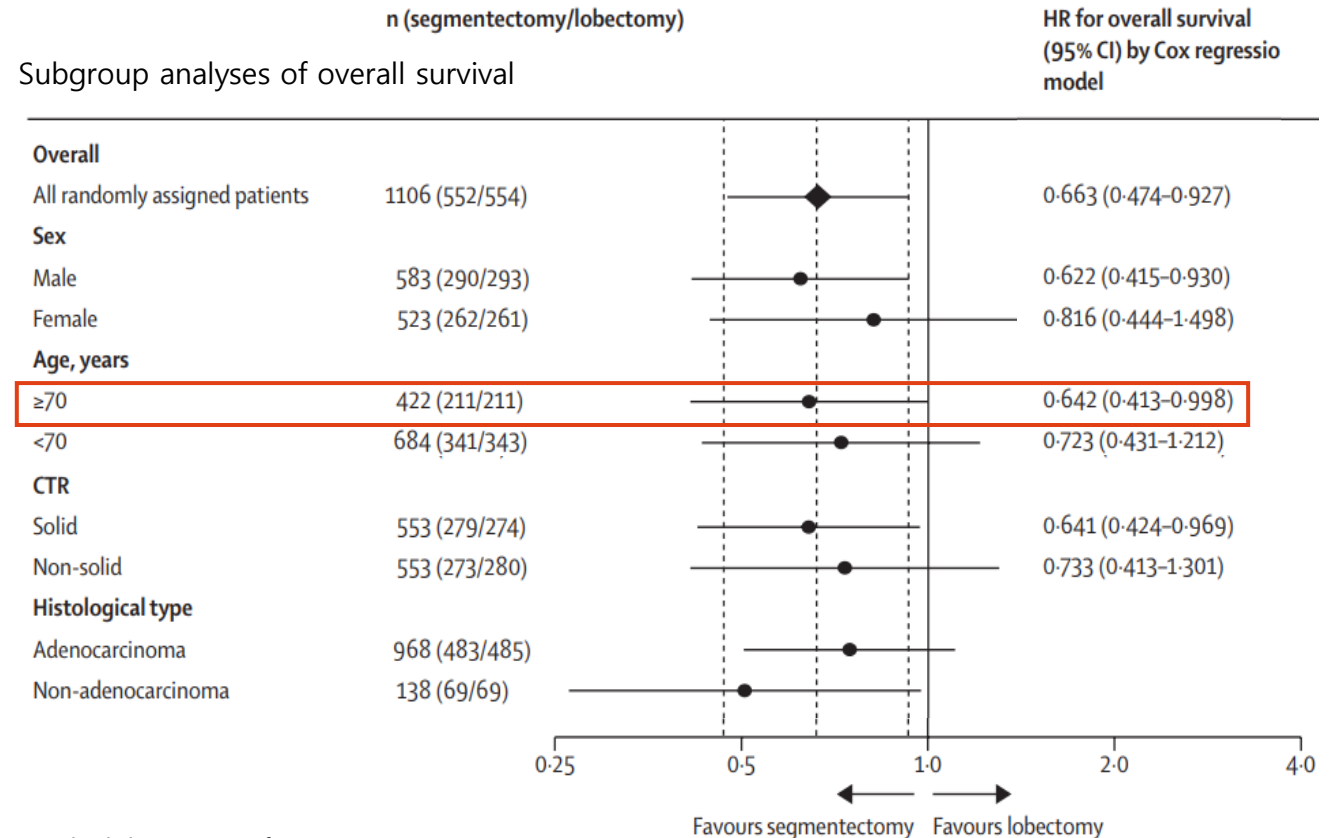
Hisashi Saji, Morihito Okada, Masahiro Tsuboi, Ryu Nakajima, Kenji Suzuki, Keiju Aokage, Tadashi Aoki, Jiro Okami, Ichiro Yoshino, Hiroyuki Ito,

- Multicenter RCT (JCOG0802)
IA NSCLC (T size ≤2cm , consolidation to tumor ratio >0.5)
 Randomly assigned 1:1 to receive either lobectomy or segmentectomy

	Lobectomy group (n=554)	Segmentectomy group (n=552)
Total deaths	83	58
Lung cancer death	28	26
Other death	52	27
Other cancer (including second primary lung cancer)	31	12
Non-malignant disease	21	15
Respiratory disease	8	4
Cerebrovascular disease	7	2
Cardiovascular disease	4	4
Other diseases	2	5
Unknown	3	5

141 patients died during the follow-up period. *At median follow-up of 7.3 years (range 0.0–10.9).

Table 2: Summary of causes of death during follow-up*



Among the patients with replese

18 (49%) of 37 patients in the lobectomy group,
35 (68%) of 51 patients in the segmentectomy group alive at 5-year F/U,

* Eligibility : Age of 20-85 years,
 Median age of enrolled patients: 67 (35-85) in lobectomy, 67 (32-83) in segmentectomy

Lobectomy vs segmentectomy resection in small peripheral NSCLC

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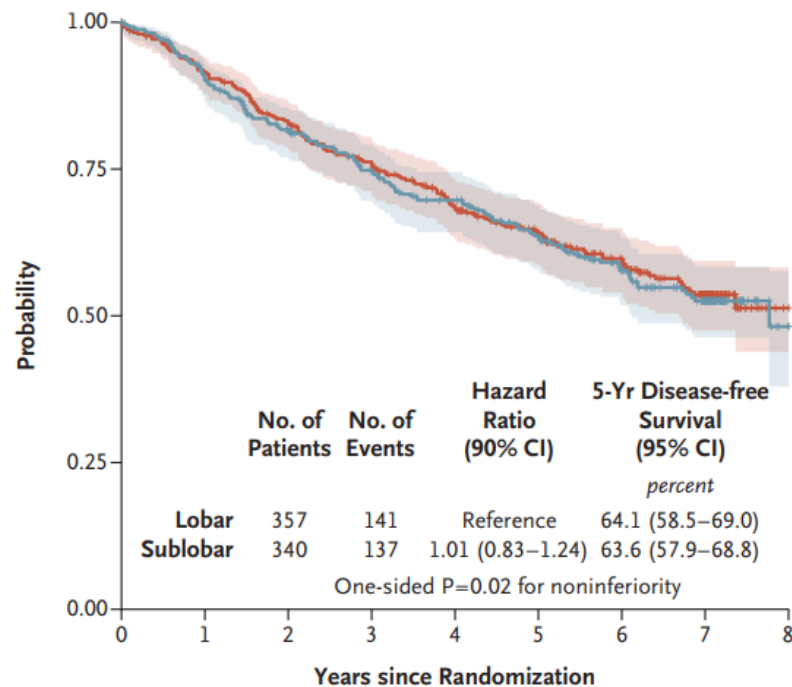
VOL. 388 NO. 6

Lobar or Sublobar Resection for Peripheral Stage IA Non-Small-Cell Lung Cancer

Nasser Altorki, M.D., Xiaofei Wang, Ph.D., David Kozono, M.D., Ph.D., Colleen Watt, B.S.,

➤ Peripheral lung nodule <2cm(solid portion), **N0**, not pure GGN, multicenter RCT (CALGB 140503 Alliance)

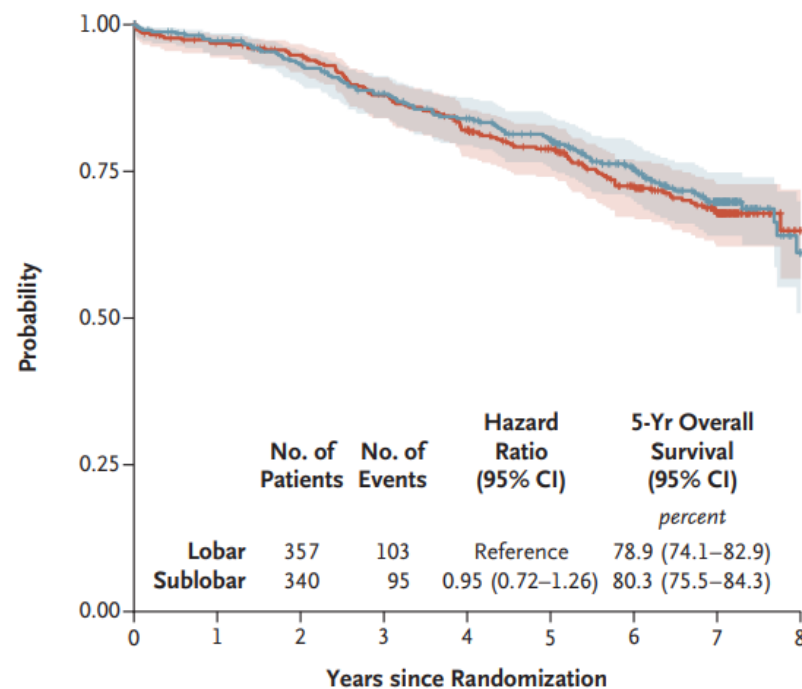
A Disease-free Survival



No. at Risk

	0	1	2	3	4	5	6	7	8
Lobar	357	310	276	246	209	175	132	80	5
Sublobar	340	291	254	222	201	172	123	78	6

B Overall Survival



No. at Risk

	0	1	2	3	4	5	6	7	8
Lobar	357	337	322	297	270	240	192	142	14
Sublobar	340	320	298	276	258	236	185	127	19

Lobectomy vs segmentectomy resection in small peripheral NSCLC

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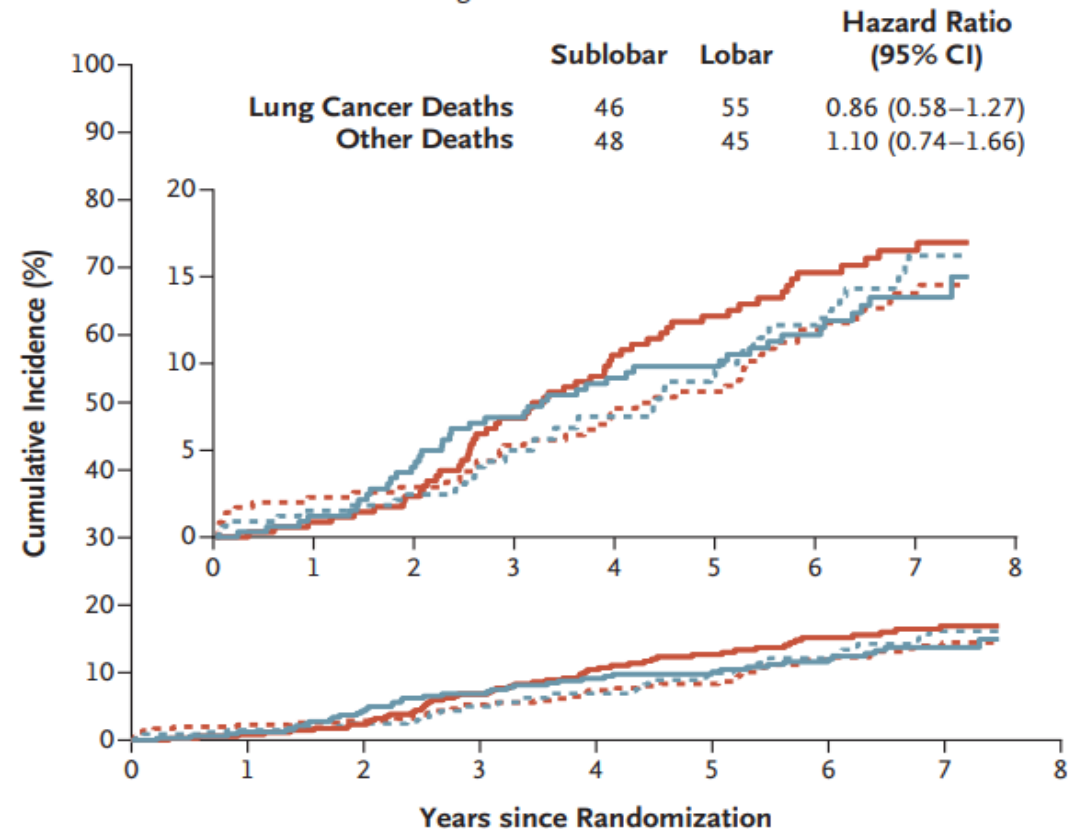
➤ Peripheral lung nodule <2cm(solid portion), **N0**, not pure GGN, multicenter RCT (CALGB 140503 Alliance)

Table 2. Patterns of Recurrence and death

Type of Recurrence	Sublobar Resection (N=336)	Lobar Resection (N=351)	Difference (95% CI)* <i>percentage points</i>
	<i>number (percent)</i>	<i>number (percent)</i>	
Overall	102 (30.4)	35 (10.0)	3.4 (1.0 to 8.3)
Locoregional recurrence	45 (13.4)	35 (10.0)	3.4 (1.0 to 8.3)
Regional recurrence only	6 (1.8)	9 (2.6)	-0.8 (-3.2 to 1.6)
Any distant recurrence	51 (15.2)	59 (16.8)	-1.6 (-7.1 to 3.9)
New primary lung cancer	60 (17.9)	52 (14.8)	3.0 (-2.5 to 8.6)
Lung cancer deaths	46	55	
Other cause deaths	48	45	

B Cause of Death

— Lobar resection — Sublobar resection
— Lung cancer death - - - Other death



Lobectomy vs segmentectomy resection in small peripheral NSCLC

The NEW ENGLAND
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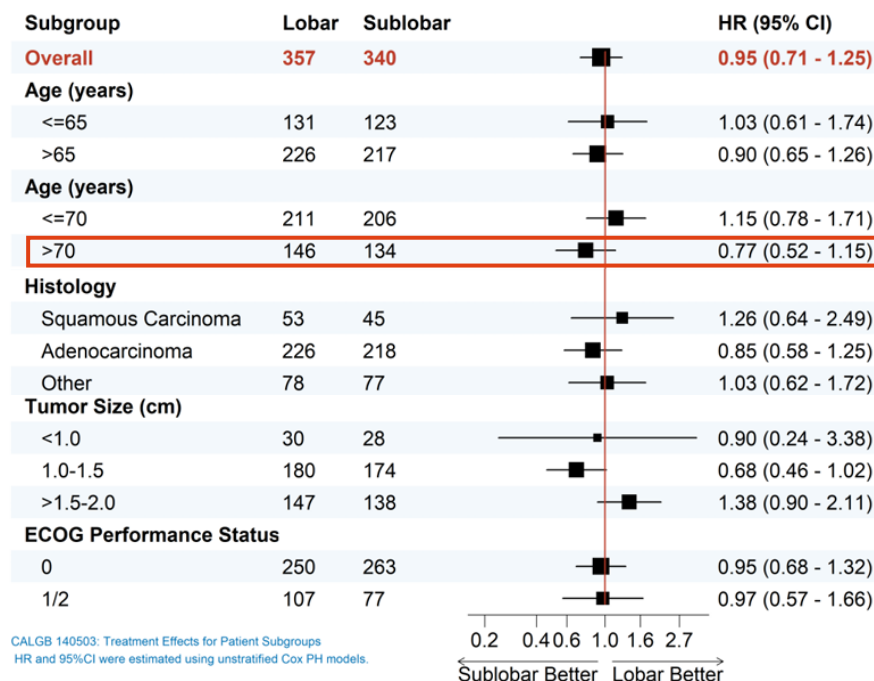
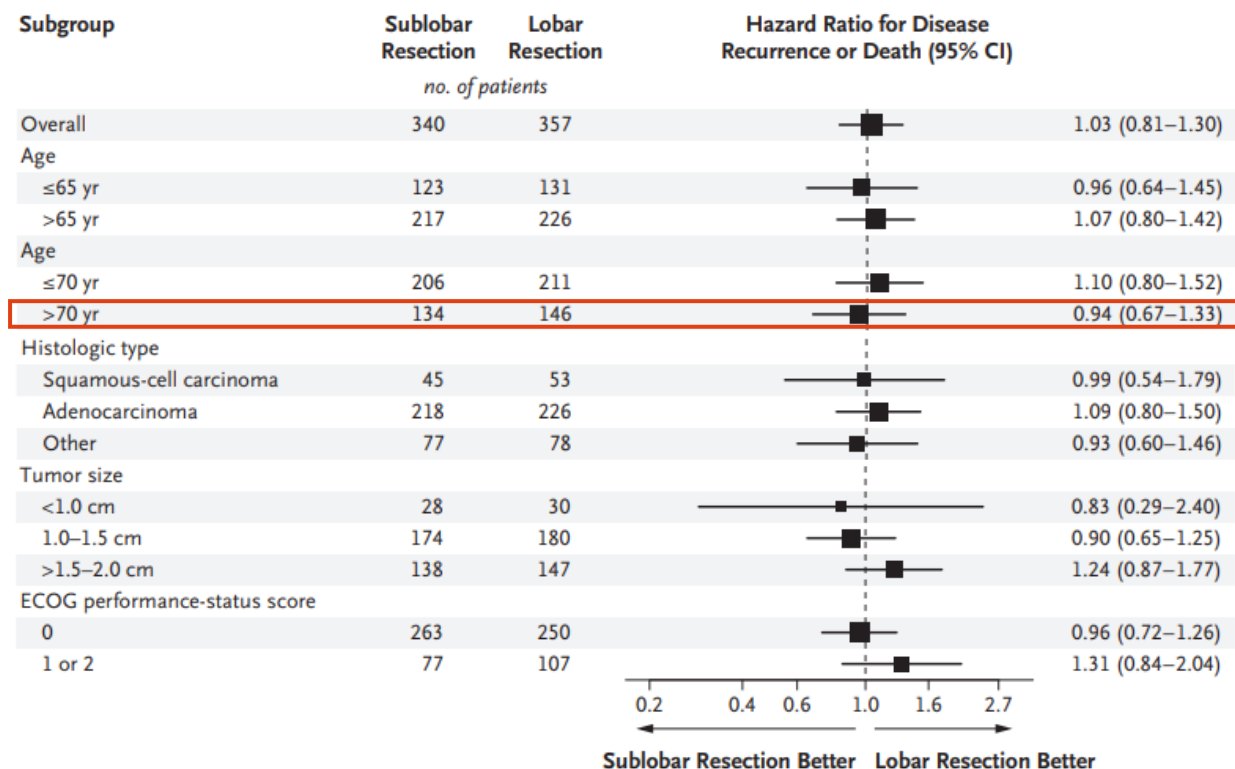
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Lobar or Sublobar Resection for Peripheral Stage IA Non-Small-Cell Lung Cancer

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- Peripheral lung nodule <2cm(solid portion), **N0**, not pure GGN, multicenter RCT (CALGB 140503 Alliance)

Figure 2. Exploratory Subgroup Analysis of Disease-free Survival.



CALGB 140503: Treatment Effects for Patient Subgroups
HR and 95%CI were estimated using unstratified Cox PH models.

Real-world treatment pattern of early lung cancer in elderly patients

- Insurance claim data about surgery and SBRT, from 2008 to 2016 in Korea

Table 1 Demographics of very elderly (≥80 years old) lung cancer patients

Characteristic	Treatment, No. (%)		
	Total (N = 1,684)	Surgery (N = 1,262)	SBRT (N = 422)
Mean age, years	82.3 ± 2.5	82.0 ± 2.2	83.2 ± 3.1
Sex			
Male	1,207 (71.7)	904 (71.6)	303 (71.8)
Female	477 (28.3)	358 (28.4)	119 (28.2)
Chemotherapy ^a			
No	1,540 (91.4)	1,152 (91.3)	388 (91.9)
Yes	144 (8.6)	110 (8.7)	34 (8.1)
Year of treatment			
2008	64	58 (90.6)	6 (9.4)
2009	83	72 (86.7)	11 (13.3)
2010	105	89 (84.8)	16 (15.2)
2011	111	90 (81.1)	21 (18.9)
2012	186	139 (74.7)	47 (25.3)
2013	219	154 (70.3)	65 (29.7)
2014	255	188 (73.7)	67 (26.3)
2015	297	212 (71.4)	85 (28.6)
2016	364	260 (71.4)	104 (28.6)

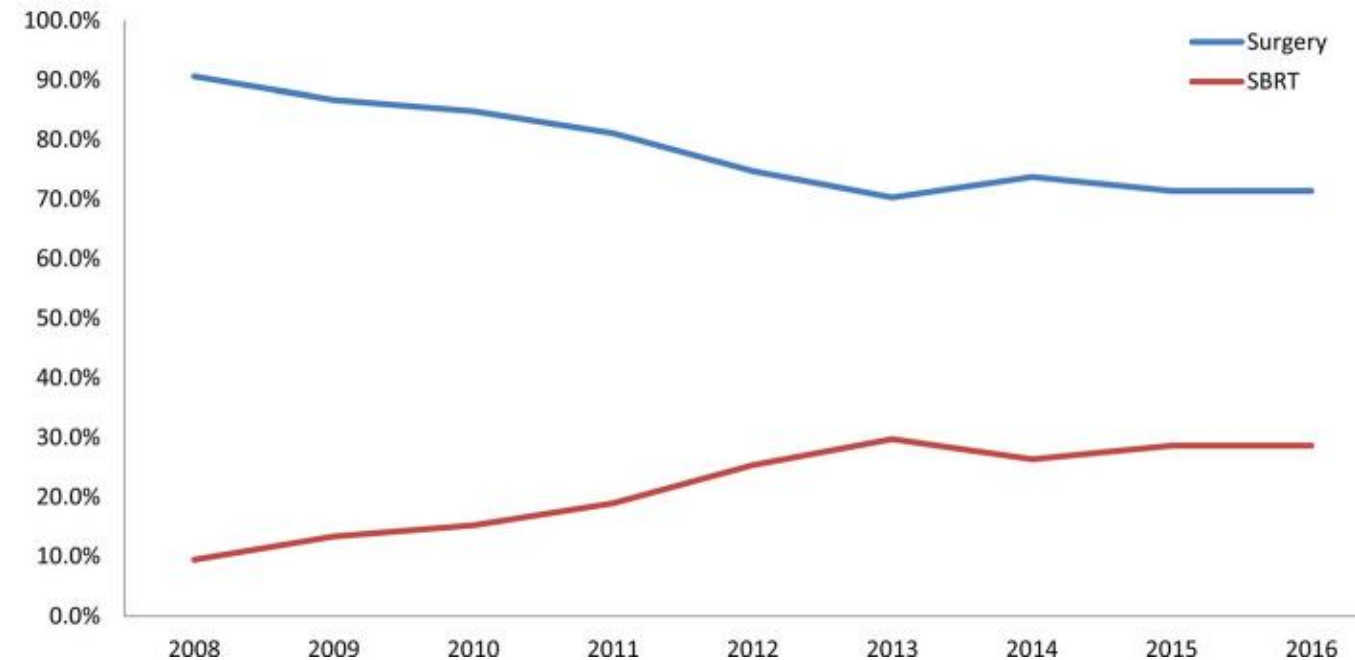


Fig. 1 Practice changes in local treatment patterns in very elderly (≥80 years old) patients diagnosed with early-stage lung cancer. The proportion of patients who underwent stereotactic body radiation therapy (SBRT) increased gradually as a local treatment modality in the old age group over the year ($p < 0.001$)

Complication and mortality of treatment in elderly NSCLC patients

- Systematic review and meta-analysis of literatures

Outcome of **surgery in elderly patients** with early stages NSCLC

Study	Patient		Stage	Complication	Mortality	Survival
	Age	No				
Endoh et al 2013	>75	295		18.6%	2.7%	68% (5yr)
Dominguez 2007	≥80	379		48%	6.3%	30% (F/U 2.3yr)
Voltolini 2009	≥80	96		17.7%	9.4%	60% (5yr)
Berry et al 2011	≥80	193		46%	3.6%	56% (3yr)
Zhang et al 2012	≥80	52		44.2%	3.8%	19.1 (5yr)
Okami et al 2009	≥80	367	I	8.4%	2%	55% (5yr)
Miura et al 2015	≥80	49		6%	4.1%	53.1% (5yr)
Mun et al 2008	≥80	55	I	25.6%	3.6%	65.9 (5yr)
Brock et al 2004	≥80	68	I	44%	8.8%	34% (5yr)
Port et al 2011	≥80	121		28.9%	1.2%	56.6% (5yr)

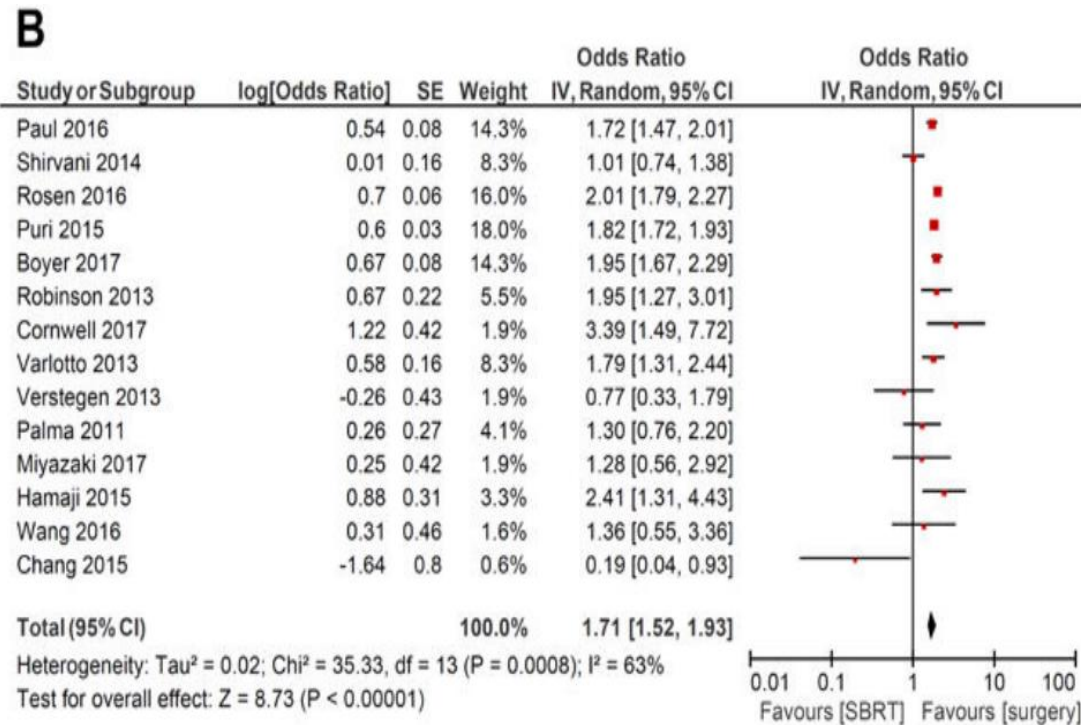
*Some excerpts (The patient is over 75 years old and published after 2000)

Outcome of SBRT in elderly patients with early stages NSCLC

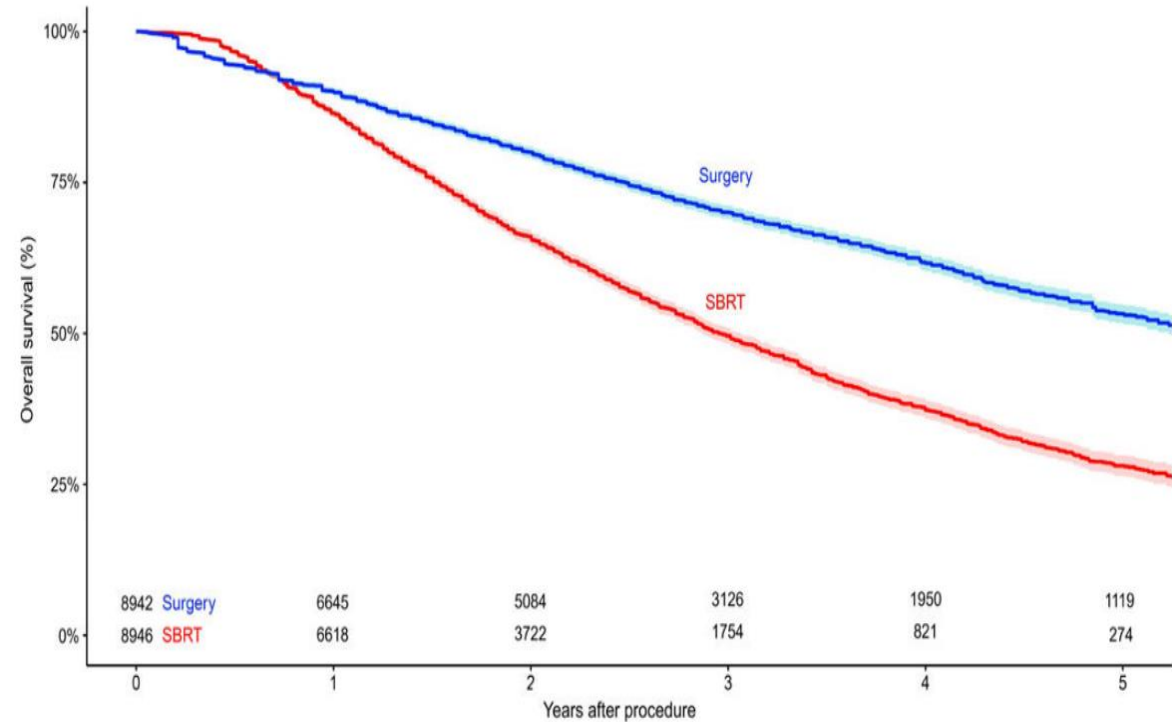
Study	Patient		Stage	Complication	Mortality	Survival
	Age	No				
Haasbeeket at el	>75	193	I	2.1%	0%	45%(3yr)
Van Zyp et al	≥80	38	I	2.6%	0%	44% (2yr)
Takeda et al	≥80	109		0.9%	0.9%	53% (3yr)
Cannon et al	≥80	193		10.%	0%	35% (2yr)
Hayashi et al	≥85	20		10 %	0%	40.7% (4yr)
Palma et al	≥75	60	I	0%	1.7%	42% (3yr)
Nanda et al	≥70	258		NR	NR	40% (3yr)

The survival outcome of SBRT, as second best treatment

- Systemic review and meta-analysis of **23 studies used propensity score matching**



Forest plot of the odds ratio (OR) of **overall survival in matched patients**



Reconstructed Kaplan-Meier graph of overall **survival using aggregated data from matched patients** with early-stage non-small cell lung cancer who underwent stereotactic body radiation therapy (SBRT) versus surgery

The outcome of SBRT, as second best treatment of early lung cancer

- **Stage I/II, N0 NSCLC patients who refused surgery**, data from National Cancer Database from 2004 to 2016

Appendix A. Definitions for Variable "Reason for No Surgery" in the National Cancer

Database

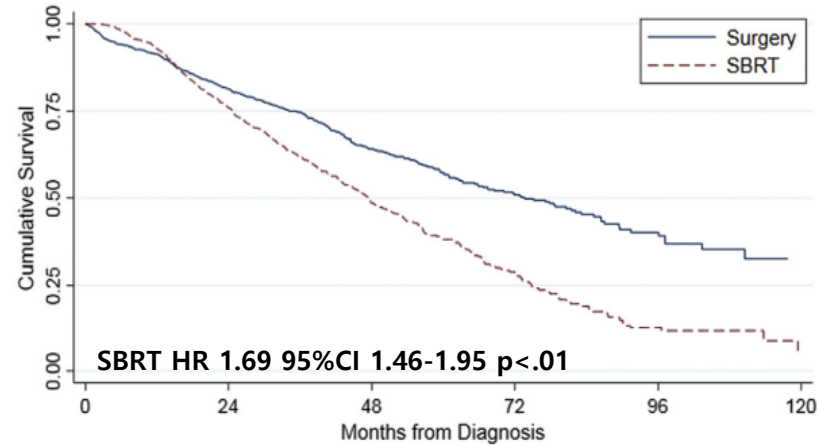
National Cancer Database Definition	Inclusion/Exclusion in Present Study
Surgery of the primary site was performed	Included in surgery cohort
Surgery of the primary site was not performed because it was not part of the planned first course of treatment	Excluded
Surgery of the primary site was not recommended/performed because it was contraindicated due to patient risk factors (comorbid conditions, advanced age, etc.)	Excluded
Surgery of the primary site was not performed because the patient died prior to planned or recommended surgery	Excluded
Surgery of the primary site was not performed; it was recommended by the patient's physician, but was not performed as part of the first course of therapy. No reason was noted in patient record.	Excluded
Surgery of the primary site was not performed; it was recommended by the patient's physician, but this treatment was refused by the patient, the patient's family member, or the patient's guardian. The refusal was noted in patient record.	Included in SBRT cohort
Surgery of the primary site was recommended, but it is unknown if it was performed.	Excluded
Unknown whether surgery of the primary site was recommended or performed	Excluded

N=127,644

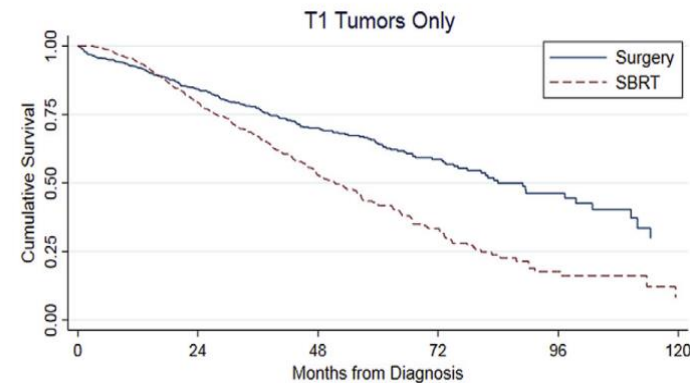
Propensity Score matching

N=1359

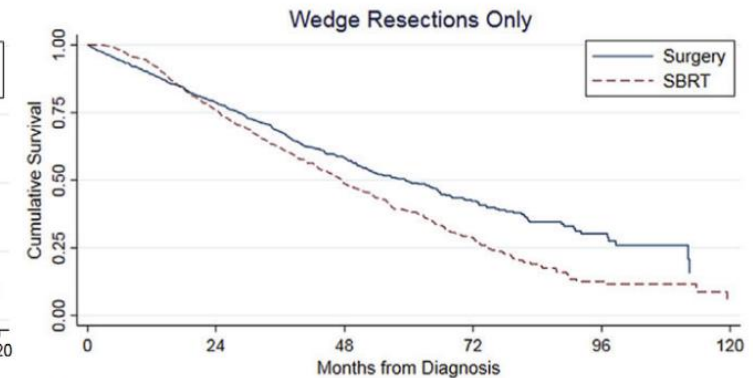
Kaplan-Meier survival for propensity-matched analysis



Number at risk	0	24	48	72	96	120
Surgery	1093	678	305	134	41	9
SBRT	1051	647	242	71	13	2



Number at risk	0	24	48	72	96	120
Surgery	794	511	229	99	30	8
SBRT	753	493	188	58	12	2



Number at risk	0	24	48	72	96	120
Surgery	1095	689	303	111	23	3
SBRT	1051	647	242	71	13	2

The outcome of SBRT in elderly stage I NSCLC

➤ Retrospective analysis in **old patients** using propensity score match

	Inclusion	Data	Statistics	N	Median Age (RT/Op)	T stage		Pathologic Confirm	Median F/U	OS (5yr)		P
						cT1	cT2			RT	Op	
D. Palma, 2011	Age≥75, stage I	Amsterdam Cancer Registry	Propensity matched	60/60	79/79	39(65%)	21(35%)	47%	50.1/35.5mo	OS (3yrs) 42% 60%		0.615
Shirvani SM, 2012	Age≥66 Stage I	SEER, US	Propensity matched	99/99	78/78	Median size 25±10 mm		100%	3.2 yr	HR (95% CI) 0.71 (0.45-1.12)		0.14
Shirvani SM, 2014	Age≥65, T<5cmN0	SEER, US	Propensity matched	251/251	≥75(53%/68%)	205(82%)	46(18%)	100%	-	Adjusted HR 1.01 (0.74-1.38)		0.94
Matsuo, 2014	Stage I T<5cmN0	Single center, China	Propensity matched	53/53	76/76	Median size 22/20 mm		100%	6.7/5.3 yr	40.4%	55.6%	0.124
Dong, 2019	Age≥70, Stage I	Single center, Japan	Propensity matched	35/35	76/74	28(80%)	7(20%)	89%	43mo.	59.5%	72.9%	0.22
N. Tomita, 2021	cT1-2aN0 7 th TNM	Single center, Japan	Propensity matched	120/120	76/76	93(77%)	27(23%)	100%	66/69mo	64%	71%	0.41

The result of clinical trials: SBRT in operable NSCLC

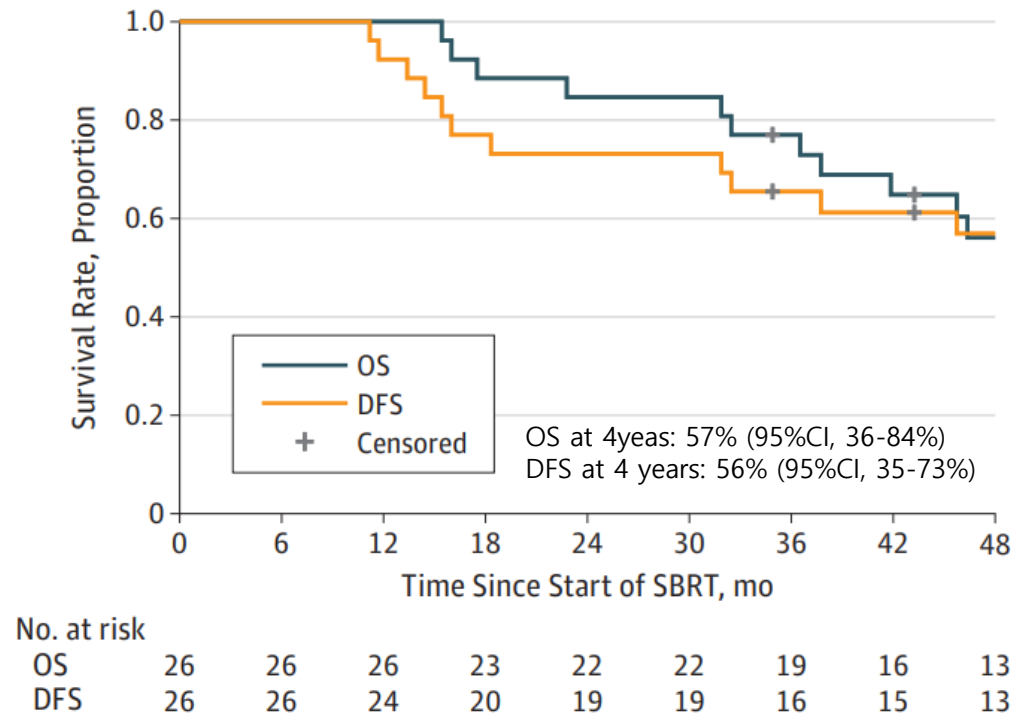
- NRG oncology **RTOG 0618 Trial**, Single-arm phase 2
T1-2(<5cm) N0M0, peripheral located, **operable NSCLC**

Table. Pretreatment Characteristics of 26 Patients in NRG Oncology RTOG 0618

Characteristic	Value
Age, median (range), y	72.5 (54-88)
FEV ₁ percent predicted, median (range)	72.5 (38-136)
Sex, No. (%)	
Male	15 (58)
Female	11 (42)
Zubrod performance status, No. (%)	
0	19 (73)
1	7 (27)
Stage, No. (%)	
IA	23 (88)
IB	3 (12)
Histologic type, No. (%)	
Squamous cell carcinoma	5 (19)
Adenocarcinoma	12 (46)
Non-small cell carcinoma not otherwise specified	9 (35)

* **Stage IA: Tumor size <3cm**, 1B Tumor size <5cm
 Median f/u: 48.1 months (range, 15.4-73.7 months)

Figure 2. Overall Survival (OS) and Disease-Free Survival (DFS)



Local control : 96% (95%CI, 83-100%) upto 4 years of median f/u

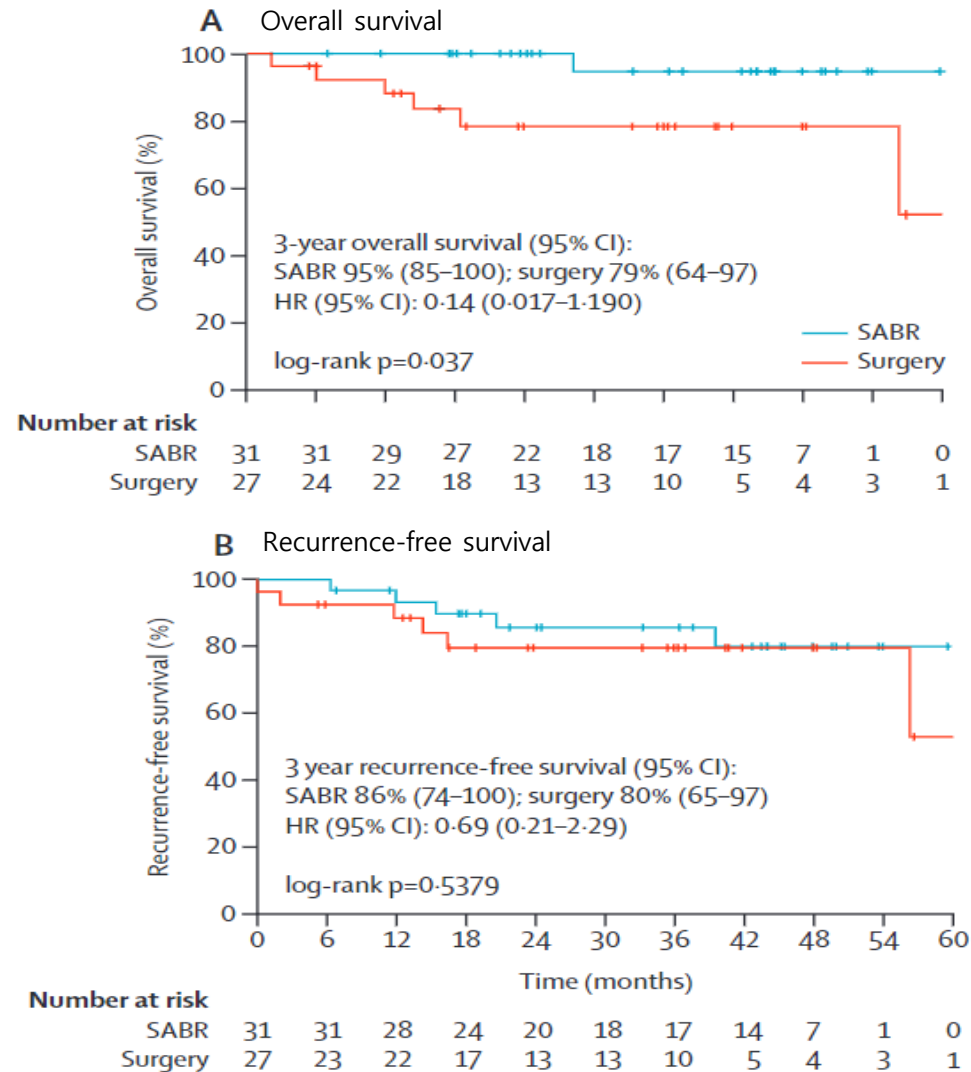
The result of clinical trials: SBRT in operable NSCLC

➤ Pooled analysis of two randomised trials (STARS, ROSEL)

T1-2a(<4cm, 7th edition) N0M0, operable NSCLC, 1:1 ratio to SABR or lobectomy with MLND

	SABR group (n=31)	Surgery group (n=27)	p value
Sex			0.73
Male	14 (45%)	11 (41%)	
Female	17 (55%)	16 (59%)	
Age (years)			
Mean (SD)	67.3 (9.2)	67.3 (8.2)	..
Median (range)	67.1 (43-82)	66.7 (51-85)	0.69
WHO performance status			0.31
0	21 (68%)	21 (78%)	
1	10 (32%)	5 (19%)	
2	0 (0%)	1 (4%)	
Histology before randomisation			0.62
Adenocarcinoma	16 (52%)	13 (48%)	
Squamous	5 (16%)	7 (26%)	
Other	2 (6%)	1 (4%)	
Unknown	8 (26%)*	6 (22%)*	
Tumour stage			0.41
T1a	16 (52%)	18 (67%)	
T1b	11 (35%)	8 (30%)	
T2a	4 (13%)	1 (4%)	

Table: Patient characteristics



The result of clinical trials: SBRT in operable NSCLC

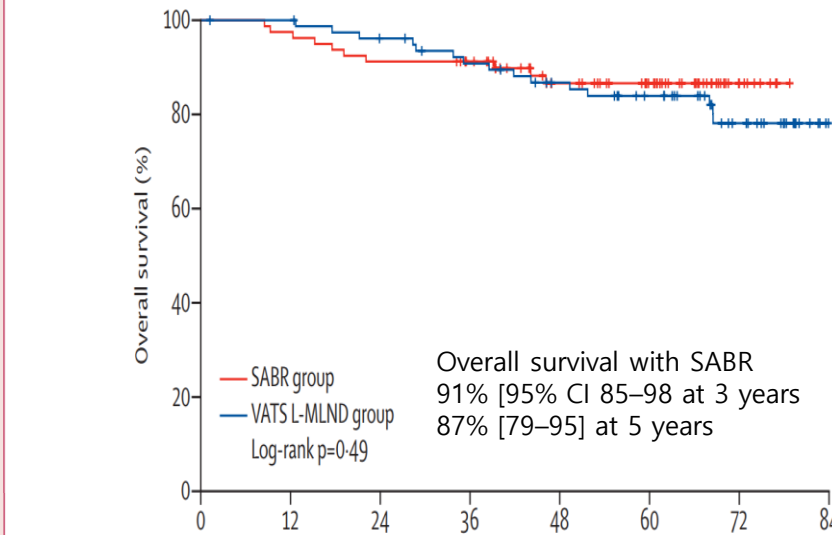
- Single arm, prospective trial of SBRT in operable stage I, with prespecified comparison to surgery (**Revised STARS**)

Tumor size <3cm, N0M0, operable NSCLC

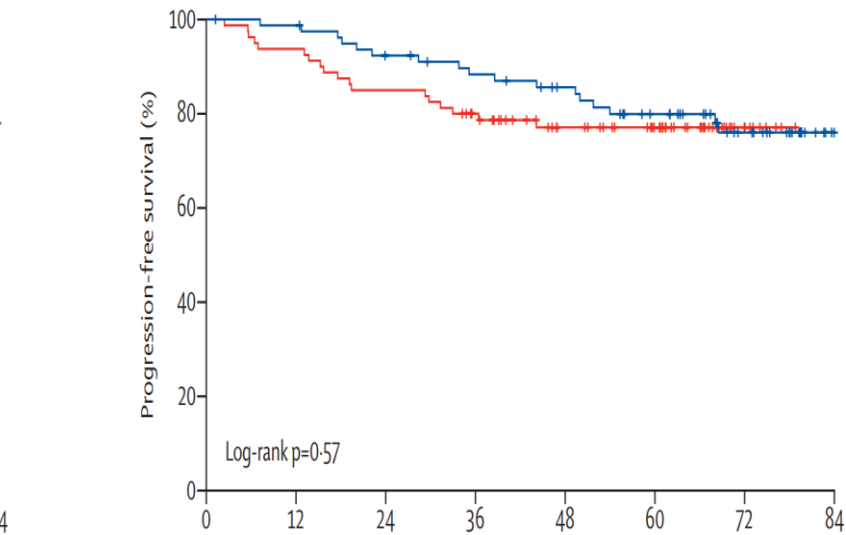
Propensity-matching analysis in prospectively registered **surgical cohort** in MD Anderson

Patients (n=80)	
Age, years	68.8 (7.9)
Sex	
Male	44 (55%)
Female	36 (45%)
Zubrod performance status	
0	55 (69%)
1	25 (31%)
Histology	
Squamous cell carcinoma	13 (16%)
Adenocarcinoma	63 (79%)
NSCLC, not otherwise specified	4 (5%)
Tumour stage	
T1aN0M0	52 (65%)
T1bN0M0	28 (35%)
Tumour size, cm	1.83 (0.56)
Tumour location	
Central	26 (33%)
Peripheral	54 (67%)
Baseline smoking status	
Current	16 (20%)
Former	50 (63%)
Never	14 (18%)
Baseline FEV ₁ , % predicted	85.8% (19.1)
Baseline FVC, % predicted	94.4% (16.5)
Baseline DLCO, % predicted	81.4% (16.9)

Table 1: Baseline characteristics



	Number at risk (number censored)						
	0	12	24	36	48	60	72
SABR group	80 (0)	78 (0)	73 (0)	69 (4)	51 (15)	39 (12)	11 (28)
VATS L-MLND group	80 (0)	79 (1)	74 (2)	68 (2)	61 (4)	54 (5)	37 (14)



	Number at risk (number censored)						
	0	12	24	36	48	60	72
SABR group	80 (0)	75 (0)	68 (0)	60 (4)	45 (13)	35 (10)	9 (26)
VATS L-MLND group	80 (0)	78 (1)	71 (2)	66 (2)	60 (4)	51 (5)	35 (14)

SBRT vs surgery for early stage NSCLC, can RCT provide a solution?

- Challenges faced by RCT: Surgery vs. SBRT may be too much of a leap of faith to undergo randomization

SABRTooth: a randomised controlled feasibility study of stereotactic ablative radiotherapy (SABR) with surgery in patients with peripheral stage I nonsmall cell lung cancer considered to be at higher risk of complications from surgical resection

Design and methods: SABRTooth was a UK multicentre randomised controlled feasibility study targeting patients with peripheral stage I NSCLC considered to be at higher risk of surgical complications. 54 patients were planned to be randomised 1:1 to SABR or surgery. The primary outcome was monthly average recruitment rates.

Results: Between July 2015 and January 2017, 318 patients were considered for the study and 205 (64.5%) were deemed ineligible. Out of 106 (33.3%) assessed as eligible, 24 (22.6%) patients were randomised to SABR (n=14) or surgery (n=10). A key theme for nonparticipation was treatment preference, with 43 (41%) preferring nonsurgical treatment and 19 (18%) preferring surgery. The average monthly recruitment rate was 1.7 patients against a target of three. 15 patients underwent their allocated treatment: SABR n=12, surgery n=3.

Conclusions: We conclude that a phase III RCT randomising higher risk patients between SABR and surgery is not feasible in the National Health Service. Patients have pre-existing treatment preferences, which was a barrier to recruitment. A significant proportion of patients randomised to the surgical group declined and chose SABR. SABR remains an alternative to surgery and novel study approaches are needed to define which patients benefit from a nonsurgical approach.

Kevin N Franks et al. *Eur Respir J.* 2020 Nov 12;56(5):2000118.

- Ongoing phase 3 trials comparing SBRT and surgery

	Stage	Radiographic finding	Tumor location	Pulmonary function test	Comparative arm	Estimated enrollment	Primary outcome
STABLE-MATES NCT02468024	T<4cm N0 *	Solid/GGO>50%	Peripheral (>2cm from prox. Bronchus)	Major criteria FEV1 ≤ 50% or DLCO ≤ 50% Minor (more than 2) FEV1 or DLCO 51-60%, Age ≥ 75 , PulHTN, LVEF < 40%, Hypoxia or hypercapnia, mMRC ≥ 3	Sublobar resection	670	OS (3yrs)
VALOR NCT02984761	T<5cm N0 *		Peripheral (>1cm from prox. bronchus)	FEV1 ≥ 40% DLCO ≥ 40%	Surgery (lobectomy or segmentectomy)	272	OS (upto 10yrs)

*Mandatory pathological assessment of any lymph nodes >10mm with a SUV >2.5 seen on FDG- PET/CT

SBRT vs surgery, what should we consider?

- **Societal Guidelines for High-Risk** Descriptors for Preoperative Pulmonary Assessment for Lung Resections

PFT High-Risk Cutoffs

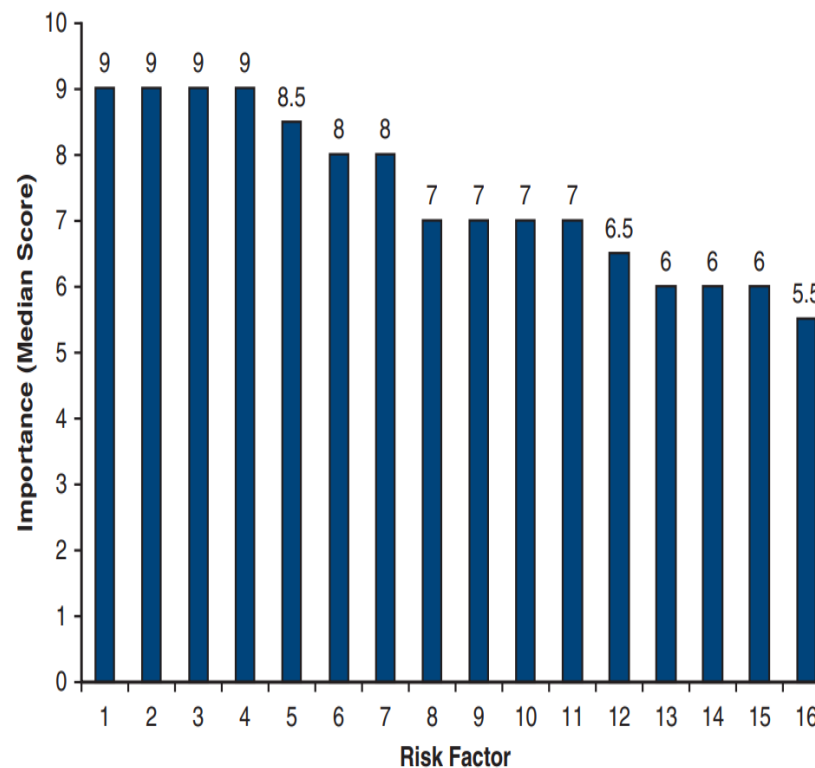
Society	Year	FEV1	DLCO
ERS/ESTS ⁷⁰	2009	< 80% pred or ppo < 30%	< 80% pred or ppo < 30%
ACCP ⁵	2013	ppo < 30% CPET indicated ppo 30%-60% low-technology exercise testing indicated	ppo < 30% CPET indicated ppo 30%-60% low-technology exercise testing indicated
ACCP/STS ⁴	2012	ppo < 40%	ppo < 40%
AATS ²	2021	NR (very important)	ppo < 30% (most important)

Exercise Testing Cutoffs for High Risk for Resection

Society	Walk Test	Stair Climbing	CPET
ERS/ESTS ⁷⁰	Not recommended for screening	Ascent height < 22 m	Peak VO ₂ < 10 mL/kg/min or 35%
ACCP ⁵	Shuttle walk < 400 m	Stair climb < 22 m	Peak VO ₂ < 10 mL/kg/min or 35% pred
ACCP/STS ⁴	NR	NR	Peak VO ₂ < 10 mL/kg/min
AATS ²	6 minutes < 500 m (very important)	< 40 steps or 10 m ascent height (very important)	peak VO ₂ < 35% (important)

1층 평균 높이: 4m, 1층 평균 계단 수: 20여개

- The risk factors of surgery: **Surgeon's choice**



Risk Factor	Rank
Use of Home O2, Underlying severe Lung Disease	1
Frailty	2
DLCO (PPO DLCO)	3
Functional status	4
FEV1 (PPO FEV1)	5
Pulmonary hypertension	6
ESLD (cirrhosis)	7
Cardiac evaluation	8
Psychiatry/Neurocognitive	9
Low technology tests	10
Independent Living	11
Sarcopenia	12
High technology tests	13
Age	14
BMI, Obesity	15
Creatinine	16

Factors can be detected and managed by CGA

SBRT vs surgery for early stage NSCLC, what should we consider?

- In elderly patients, **patient's life expectancy**, comorbidities, frailty and **patient preferences** should be considered

	Advantage	Disadvantage	Other consideration
Surgery	<ul style="list-style-type: none">• Direct and complete removal of tumor• Adjuvant chemotherapy or radiation after nodal upstaging by mediastinal LN dissection	<ul style="list-style-type: none">• High post-treatment mortality• Low QoL	<ul style="list-style-type: none">• Minimal invasive procedure(VATS)• Comorbidities (CVA, DM, etc)
SBRT	<ul style="list-style-type: none">• Fair loco-regional control rate• Limited toxicity	<ul style="list-style-type: none">• Less effective in central lesion, large tumor	

- In patients who fit and have willing to undergo surgery, Surgery(lobectomy) is optimal and standard treatment
 - In case, Tumor size less than 2cm, sub-lobar resection may provide good prognosis especially in older patients
- SBRT is second best treatment option for patients who cannot undergo surgery or refuse surgery
 - In T1N0 stage, small number of trials showed comparable outcomes in operable early NSCLC patients
But more large prospective studies are needed to confirm the results
- Geriatric assessment could be used for screening of high-risk patients

Contents

- Comprehensive geriatric assessment
 - ✓ ASCO&NCCN guideline
 - ✓ Implement in practice
- Early stage lung cancer
 - ✓ Operation
 - ✓ SBRT
- **Locally advanced lung cancer**
 - ✓ **Sequential or concurrent CRT**
 - ✓ **I/O consolidation**
- Advanced lung cancer
 - ✓ Tyrosine kinase inhibitor
 - ✓ Immunotherapy

Sequential or concurrent CRT in elderly patients

- cCRT is associated with improved survival and better locoregional control versus sCRT, as the preferred treatment strategy for stage III, unresectable NSCLC
- Patients can receive sCRT instead of cCRT for several reasons, including **concerns about the tolerability** of cCRT, **advanced age** or **frailty, comorbidities, volume** and **location of disease**, and access to radiation facilities in a timely fashion.



NCCN Guidelines Version 2.2023 Non-Small Cell Lung Cancer

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PRINCIPLES OF RADIATION THERAPY

Locally Advanced NSCLC (Stage II–III)

- **Concurrent chemotherapy/RT is recommended for patients with inoperable stage II (node-positive) and stage III NSCLC.**⁴⁷⁻⁵⁰
- **RT interruptions and dose reductions for manageable acute toxicities should be avoided by employing supportive care.**
- **Sequential chemotherapy/RT or RT alone is appropriate for frail patients unable to tolerate concurrent therapy.**^{51,52}

51. J Natl Cancer Inst 1996;88:1210-1215
52. Radiother Oncol 2011;100:76-85

Concurrent CRT in elderly patients

Pooled Analysis of Individual Patient Data on Concurrent Chemoradiotherapy for Stage III Non-Small-Cell Lung Cancer in Elderly Patients Compared With Younger Patients Who Participated in US National Cancer Institute Cooperative Group Studies

Thomas E. Stinchcombe, Ying Zhang, Everett E. Vokes, Joan H. Schiller, Jeffrey D. Bradley, Karen Kelly, Walter J.

➤ **N=3,600** Individual patient **data from 16 phase II or III trials** conducted by US NCI-supported cooperative groups of CCRT alone or with consolidation or induction chemotherapy for stage III NSCLC 1990 to 2012

Table 1. Patient Demographic and Clinical Characteristics

Characteristic	No. (%)		P‡
	Age (years)		
	≥ 70* (n = 832)	< 70† (n = 2,768)	
Treatment paradigm			.10
Concurrent only	337 (40)	1,077 (39)	
Induction → concurrent	179 (22)	697 (25)	
Concurrent → consolidation	316 (38)	994 (36)	

*Age range, 70 to 86 years.

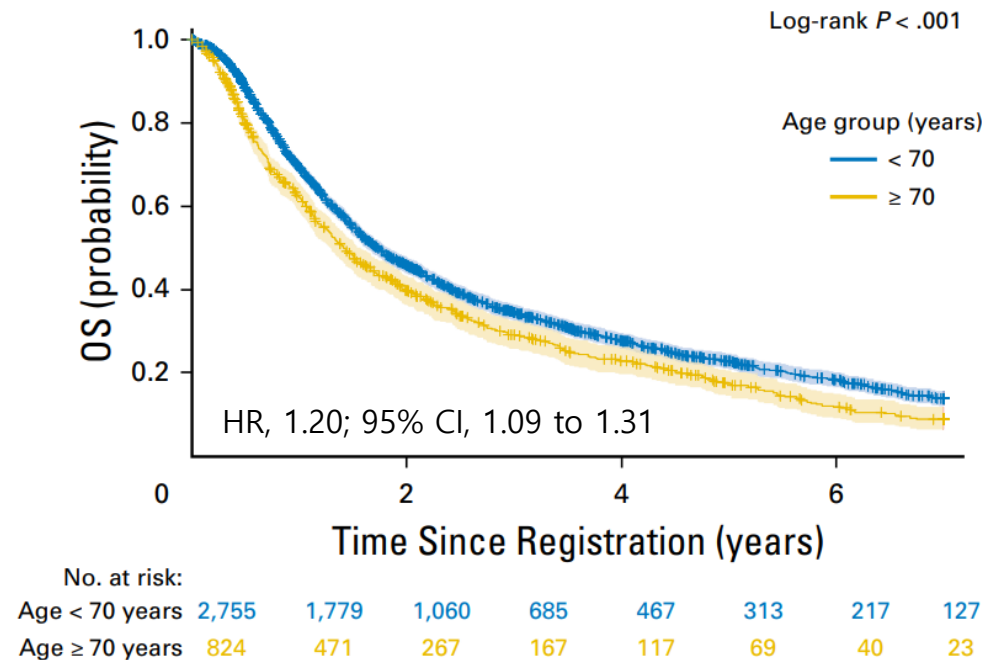
†Age range, 20 to 69 years.

‡ χ^2 test.

Table 2. Rate of AEs Among Older and Younger Patients

AE Category	Age (years)		P*
	≥ 70 (%) (n = 832)	< 70 (%) (n = 2,768)	
All grade ≥ 3	86	84	.04
Hematologic grade ≥ 3	65	61	.04
Nonhematologic grade ≥ 3	68	62	< .01
Grade 5	9	4	< .01
Treatment-related deaths†	3	2	.12

A



Sequential or concurrent CRT in elderly patients

Toxicity and survival outcomes in older adults receiving concurrent or sequential chemoradiation for stage III non-small cell lung cancer in Alliance trials (Alliance A151812)



Ronald J. Maggiore ^{a,*,1}, David Zahrieh ^{b,c,*,1}, Ryan P. McMurray ^{b,c}, Josephine L. Feliciano ^d, Pamela Samson ^e,

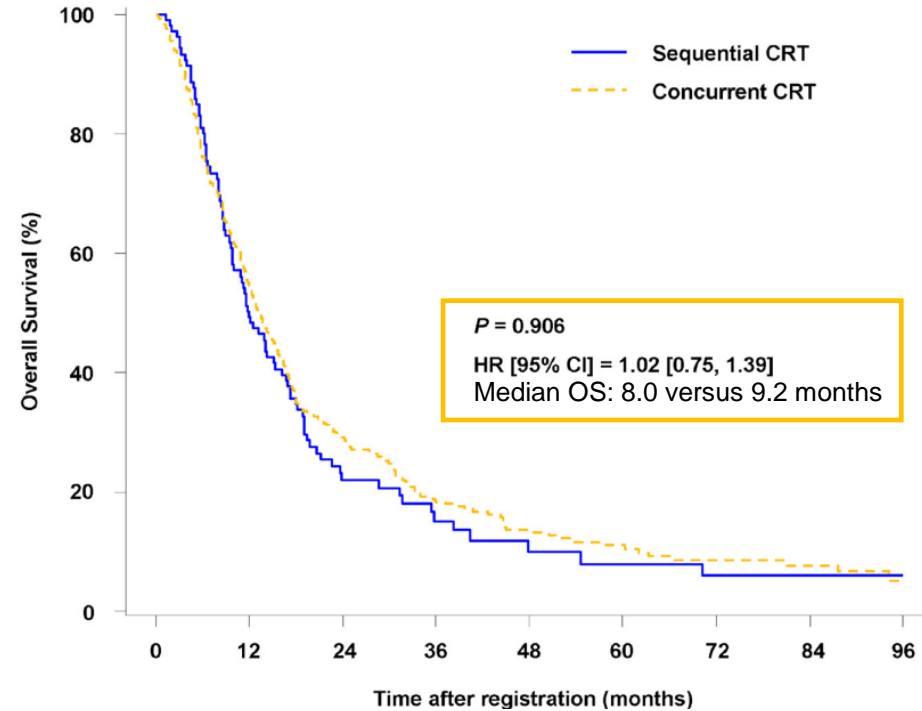
➤ Pooled analysis of patients, **age >65 years** from **6 first-line stage III NSCLC CRT trials**
CALGB 8433, 8831, 9130, 30106, 30407, 39801, Enrollment from **1984~2005**

Baseline characteristics

	Treatment regimen		Total (N = 400)	P-value ^a
	Sequential CRT (N = 106)	Concurrent CRT (N = 294)		
Age, years, n (%)				0.429
≥65 and <70	57(53.8%)	144(49.0%)	201(50.3%)	
≥70	49(46.2%)	150(51.0%)	199(49.8%)	
ECOG PS, n (%)				0.999
0	48 (45.3%)	135(45.9%)	183(45.8%)	
≥1	58 (54.7%)	159 (54.1%)	217 (54.3%)	

Toxicity Profile for Sequential and Concurrent Chemoradiation Therapy (CRT).

Toxicity Outcomes	Sequential CRT (N = 106)	Concurrent CRT (N = 294)	P-value ^a
Grade 3+ Adverse Event (AE)			
Any Time			
Hematologic	83(78.3%)	229(77.9%)	0.947
Non-hematologic	63(59.4%)	229(77.9%)	<0.001
All	92(86.8%)	277(94.2%)	0.018



adjustment for age, sex, ECOG PS, BMI, pretreatment weight loss, stage, and cisplatin-based therapy

Sequential or concurrent CRT in elderly patients

Benefit of Concurrent Versus Sequential Chemoradiotherapy in Elderly Patients With Stage III Non-Small Cell Lung Cancer

Marleen E. Logtenberg,¹ Ben Tomlow,² Elisabeth A. Kastelijns,¹

➤ Retrospective cohort study, from six hospitals in the Netherlands, **2008 and 2014**

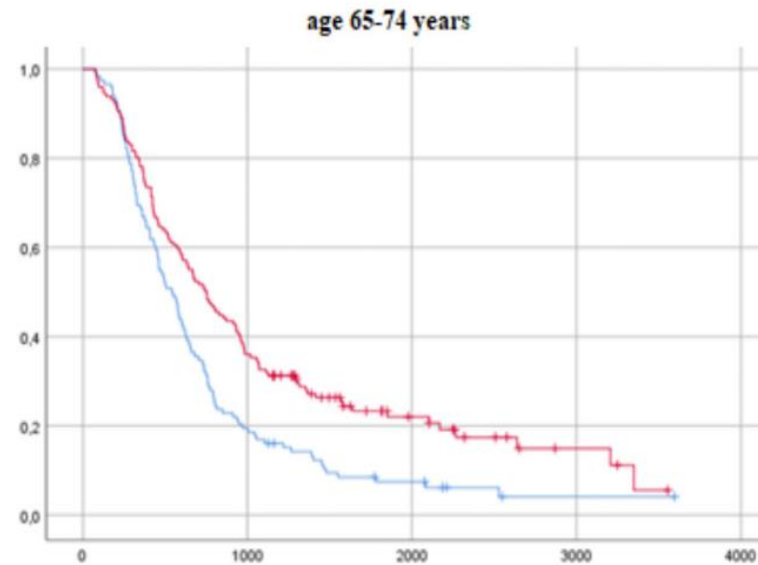
Odds Ratios of Occurrence of CTCAE Grade 3-5 Toxicity in Patients With Stage III NSCLC Treated

Toxicity ChemoradiotherapyStage III NSCLC	OR (95% CI)	P-value
Age		
Younger than 65 yrs	Reference	0.011
65-75 yrs	1.49 (1.08-2.07)	0.015
Older than 75 yrs	0.77 (0.46-1.29)	0.32
Treatment		
Chemoradiotherapy concurrent versus sequential	1.49 (1.08-2.06)	0.014

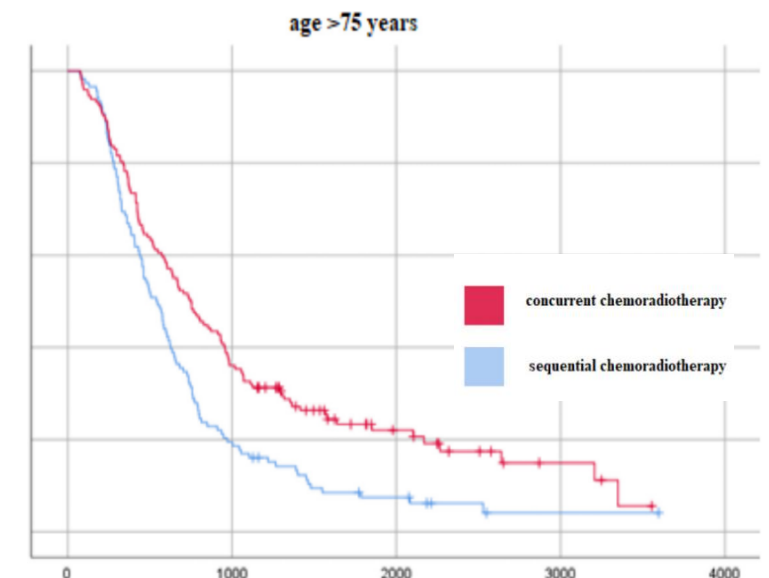
Patient Characteristics

Variables	Stage III (n = 553)		P-value	Missing
	Concurrent Chemoradiotherapy	Sequential Chemoradiotherapy		
N (%)	442 (59)	308 (41)		
Age				0
Average (SD)	62 (±9)	66 (±9)	.36	
<65 (%)	267 (67)	130 (33)	<.001	
65-74 (%)	148 (56)	118 (44)		
>75 (%)	27 (31)	60 (69)		
Performance				12
ECOG 0	278	141	<.001	
ECOG 1	129	139		
ECOG 2	23	20		
ECOG 3	3	3		
ECOG 4	2	0		
Stage				0
IIIA	333	176	<.001	
IIIB	109	132		

Kaplan Meier curve of patients aged 65-74 years, follow up in days.



Kaplan Meier curve of patients aged ≥75 years, follow up in days.



I/O consolidation after CCRT in elderly patients in clinical data

Durvalumab After Concurrent Chemoradiotherapy in Elderly Patients With Unresectable Stage III Non-Small-Cell Lung Cancer (PACIFIC)

Mark A. Socinski,¹ Mustafa Özgüroğlu,² Augusto Villegas,³ Davey Daniel,⁴

➤ Exploratory post-hoc analyses of PACIFIC according to an age threshold of **70 years**

➤ PACIFIC trial enrolment stratified according to a **65-year age** threshold

	≥65 years		<65 years	
	HR	95% CI	HR	95% CI
PFS	0.74	0.54-1.01	0.43	0.32-0.57
OS	0.76	0.55-1.06	0.62	0.44-0.86

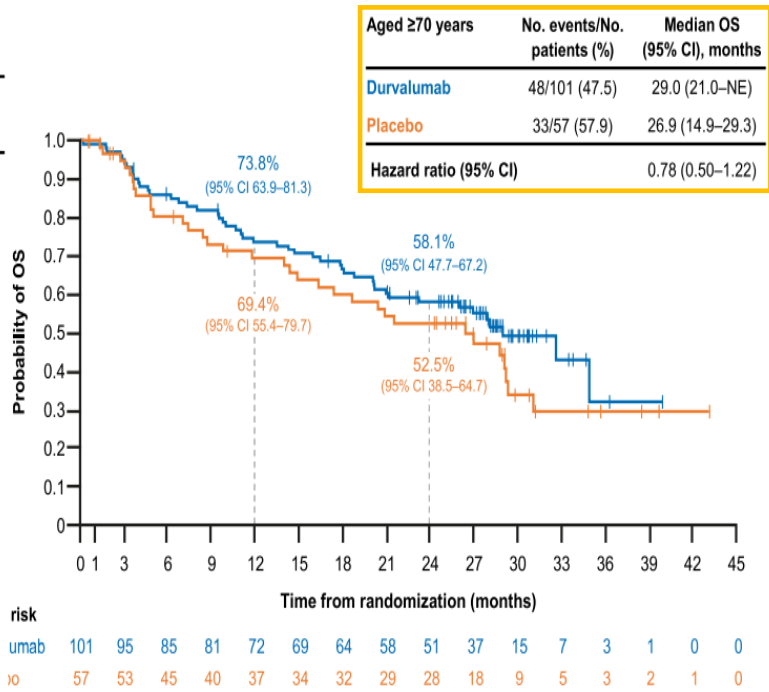
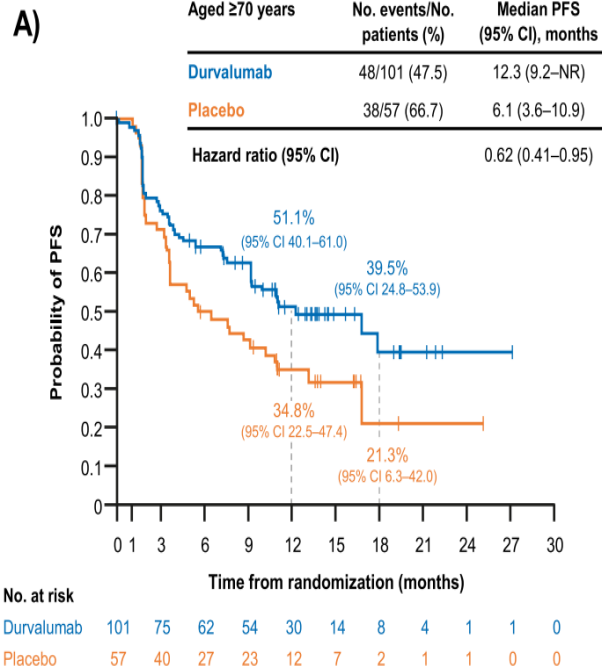


Table 3 Adverse Events in Patients Aged ≥70 Years and <70 Years

AE Category ^a	Aged ≥70 Years		Aged <70 Years	
	Durvalumab (N = 101)	Placebo (N = 55)	Durvalumab (N = 374)	Placebo (N = 179)
Any-grade all-causality AEs, n (%)	100 (99.0)	53 (96.4)	360 (96.3)	169 (94.4)
Grade 3/4	42 (41.6)	14 (25.5)	113 (30.2)	52 (29.1)
Outcome of death	11 (10.9)	7 (12.7)	10 (2.7)	8 (4.5)
Leading to discontinuation	22 (21.8)	9 (16.4)	51 (13.6)	14 (7.8)
Serious AEs, n (%)	43 (42.6)	14 (25.5)	95 (25.4)	40 (22.3)
Immune-mediated AEs, n (%) ^a	20 (19.8)	8 (14.5)	96 (25.7)	11 (6.1)
AEs leading to dose delay, n (%)	51 (50.5)	16 (29.1)	152 (40.6)	56 (31.3)
Pneumonitis/radiation pneumonitis ^b				
Any grade ^c	33 (32.7)	18 (32.7)	128 (34.2)	40 (22.3)
Grade 1	10 (9.9)	6 (10.9)	57 (15.2)	19 (10.6)
Grade 2	13 (12.9)	5 (9.1)	59 (15.8)	17 (9.5)
Grade 3	8 (7.9)	3 (5.5)	9 (2.4)	3 (1.7)
Grade 5	2 (2.0)	4 (7.3)	3 (<1)	1 (<1)
Leading to discontinuation	9 (8.9)	5 (9.1)	21 (5.6)	5 (2.8)

Real world data of I/O consolidation after CRT

ORIGINAL ARTICLE

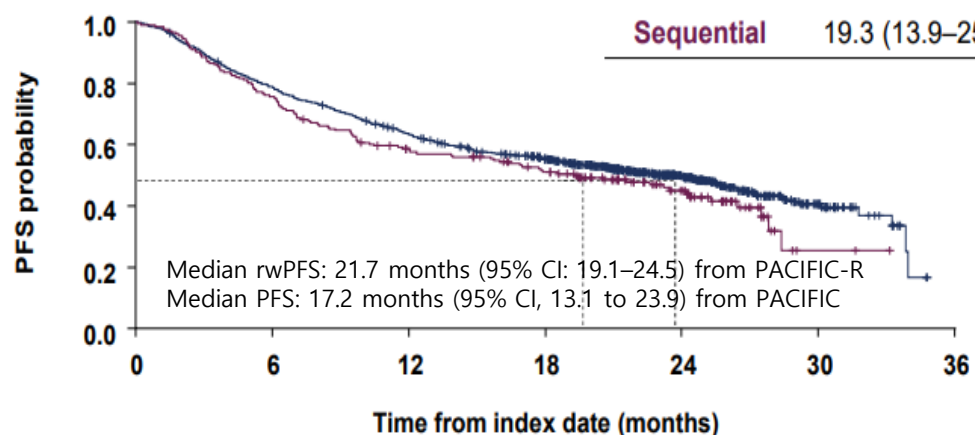
Treatment Characteristics and Real-World Progression-Free Survival in Patients With Unresectable Stage III NSCLC Who Received Durvalumab After Chemoradiotherapy: Findings From the PACIFIC-R Study

- Retrospective study of patients who started durvalumab within an **early access program** between September 2017 and December 2018
- N=1399 from 11 countries, median f/u 23.5mo
- **European Medicines Agency allows** use of either cCRT or sCRT

Prior CRT type

Median (95% CI), months

Concurrent	23.7 (20.1–25.8)
Sequential	19.3 (13.9–25.3)



No. at risk	1071	843	672	549	245	41	0
	201	152	112	91	45	2	0

Supplementary Table 6. Patient Demographics and Disease Characteristics by Prior CRT Type

Characteristic	Concurrent CRT (N = 1,071)	Sequential CRT (N = 201)
Median age at EAP inclusion, years (range)	65.0 (26–88)	67.0 (35–86)
Age category at EAP inclusion, n (%)		
<70 years	760 (71.0)	119 (59.2)
70–75 years	218 (20.4)	50 (24.9)
>75 years	93 (8.7)	32 (15.9)

Supplementary Table 8. Real-world PFS in Subgroups of Interest

		Median RwPFS		RwPFS rate, %		
		Months	95% CI	12 Months	18 Months	24 Months
Full analysis set	N = 1,399	21.7	19.1–24.5	62.2	54.1	48.2
Age (at EAP inclusion)						
<70 years	n = 958	22.8	19.4–25.7	62.1	54.6	49.2
70–75 years	n = 296	22.4	16.3–28.4	63.3	53.0	49.0
>75 years	n = 145	19.2	13.3–24.0	60.4	52.7	40.5
Prior CRT type						
Concurrent	n = 1,071	23.7	20.1–25.8	63.4	55.3	49.7
Sequential	n = 201	19.3	13.9–25.3	58.6	51.0	45.0

rwPFS, real-world progression-free survival

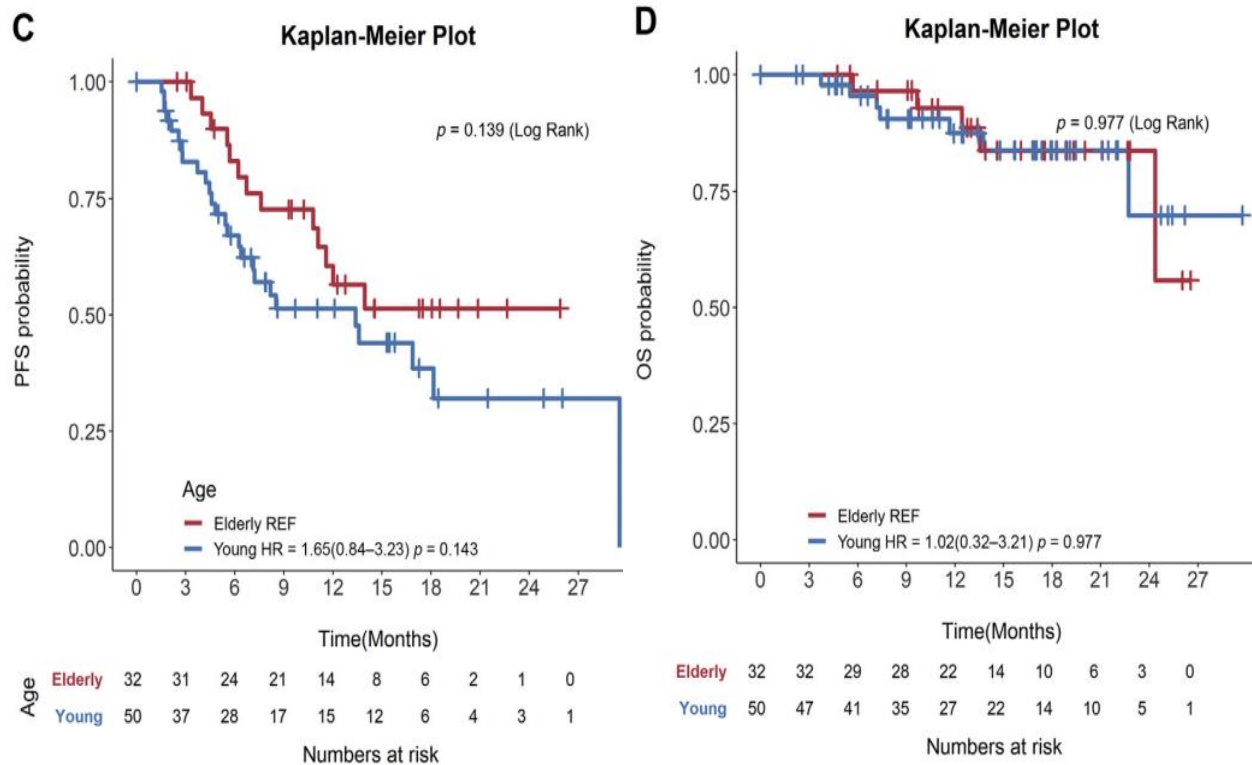
Real world data of I/O consolidation after CRT in elderly patient

BRIEF REPORT

Concurrent Chemoradiation With or Without Durvalumab in Elderly Patients With Unresectable Stage III NSCLC: Safety and Efficacy

Sally C. M. Lau, MD, MPH,^a Malcolm Ryan, BSc,^a Jessica Weiss, PhD,^b

- Retrospective study of patients treated with curative intent CRT at single cancer center at Toronto from 2018 to 2020, N=115 (N=82 received durvalumab), analyzed to age: 70 years old



CRT-Associated Adverse Events	All Patients N = 115, n (%)		Elderly Patients n = 44, n (%)		Young Patients n = 71, n (%)		p Value ^a
	All Grades	Grade ≥3	All Grades	Grade ≥3	All Grades	Grade ≥3	
Esophagitis	89 (77)	8 (7)	34 (77)	4 (9)	55 (77)	4 (6)	0.48
Neutropenia	62 (54)	39 (34)	25 (57)	13 (30)	37 (52)	26 (37)	0.54
Infections							
All causes	25 (22)	15 (13)	14 (32)	8 (18)	11 (15)	7 (10)	0.26
Hospitalizations							
All causes	NA	21 (18)	NA	12 (27)	NA	9 (13)	0.08
Febrile neutropenia	NA	11 (10)	NA	6 (14)	NA	5 (7)	0.33
Nonneutropenic infections	NA	4 (3)	NA	3 (7)	NA	1 (1)	0.16
Esophagitis	NA	3 (3)	NA	1 (2)	NA	2 (3)	1.0
Other	NA	3 (3)	NA	2 (5)	NA	1 (1)	0.56

Immune-Related Adverse Events	All Patients N = 82, n (%)		Elderly Patients N = 32, n (%)		Young Patients N = 50, n (%)		p Value
	All Grades	Grade ≥3	All Grades	Grade ≥3	All Grades	Grade ≥3	
Any irAE	51 (62)	6 (7)	22 (69)	3 (9)	29 (58)	3 (6)	0.67
All-cause pneumonitis	30 (37)	4 (5)	13 (41)	1 (3)	17 (34)	3 (6)	1.0
Immune-related pneumonitis ^c	11 (13)	2 (2)	7 (22)	1 (3)	4 (8)	1 (2)	1.0
Endocrinopathies							
Thyroid abnormalities	15 (18)	0 (0)	6 (19)	0 (0)	9 (18)	0 (0)	NA
Adrenal insufficiency	4 (5)	1 (1)	2 (6)	1 (3)	2 (4)	0 (0)	0.39
Diabetic Ketoacidosis	2 (2)	2 (2)	2 (6)	2 (6)	0 (0)	0 (0)	0.15
Colitis	7 (9)	1 (1)	1 (3)	0 (0)	6 (12)	1 (2)	1.0
Hepatitis	4 (5)	1 (1)	2 (6)	0 (0)	2 (4)	1 (2)	1.0
Dermatitis ^d	4 (5)	0 (0)	3 (9)	0 (0)	1 (2)	0 (0)	NA
Rheumatologic events ^e	4 (5)	0 (0)	1 (3)	0 (0)	3 (6)	0 (0)	NA

I/O consolidation after sCRT

ORIGINAL ARTICLE



Durvalumab After Sequential Chemoradiotherapy in Stage III, Unresectable NSCLC: The Phase 2 PACIFIC-6 Trial



- Stage III, unresectable NSCLC, no progression after platinum-based sCRT Durvalumab (1500 mg intravenously) **every 4 weeks for up to 24 months**

Table 3. Safety Summary

AE Category, n (%)	ECOG PS 0 or 1 (n = 114)		ECOG PS 2 (n = 3)		All Patients (N = 117)	
	Any Cause	PRAE ^a	Any Cause	PRAE ^a	Any Cause	PRAE ^a
Any	108 (94.7)	87 (76.3)	3 (100)	3 (100)	111 (94.9)	90 (76.9)
Grade 3 or 4	22 (19.3)	5 (4.4)	0	0	22 (18.8)	5 (4.3)
Serious	23 (20.2)	6 (5.3)	0	0	23 (19.7)	6 (5.1)
Fatal	2 (1.8)	1 (0.9)	0	0	2 (1.7)	1 (0.9)
Leading to discontinuation of durvalumab	25 (21.9)	19 (16.7)	0	0	25 (21.4)	19 (16.2)
Immune mediated	46 (40.4)	42 (36.8)	2 (66.7)	2 (66.7)	48 (41.0)	44 (37.6)

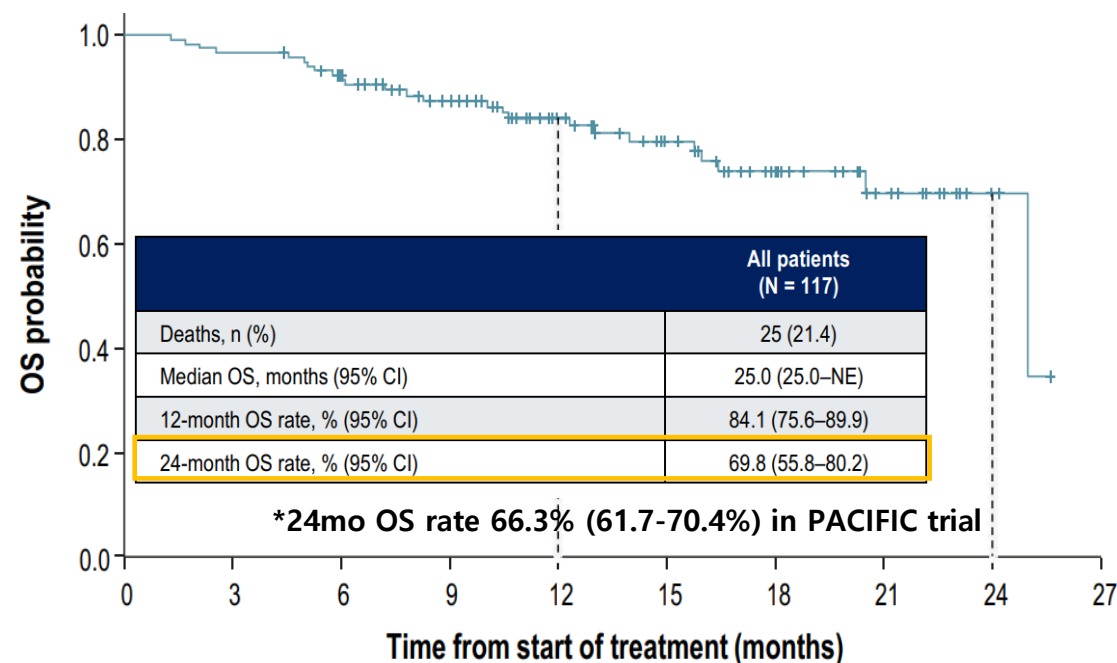
Table 5. Summary of Pneumonitis, Interstitial Lung Disease, and Radiation Pneumonitis Events by Severity

AE Preferred Term, n (%)	Max. CTCAE Grade (N = 117)					Action Taken With Durvalumab (N = 117)	
	Any AE	Grade 1	Grade 2	Grade 3 or 4	Grade 5	Interrupted	Discontinued
Pneumonitis	22 (18.8)	2 (1.7)	17 (14.5)	2 (1.7)	1 (0.9)	8 (6.8)	12 (10.3)
Interstitial lung disease	3 (2.6)	1 (0.9)	2 (1.7)	0	0	0	3 (2.6)
Radiation pneumonitis	4 (3.4)	1 (0.9)	1 (0.9)	2 (1.7)	0	0	3 (2.6)

Table 1. Baseline Patient and Disease Characteristics

Characteristic	ECOG PS 0 or 1 (n = 114)	ECOG PS 2 (n = 3)	All Patients (N = 117)
Median age (range), y	68.0 (39-85)	65.0 (53-77)	68.0 (39-85)
Age group, n (%)			
<65 y	39 (34.2)	1 (33.3)	40 (34.2)
>65 y	75 (65.8)	2 (66.7)	77 (65.8)
≥75 y	20 (17.5)	1 (33.3)	21 (17.9)

*>75yrs old patients 8.7% in cCRT, 15.9% in sCRT in PACIFIC-R study



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 - ✓ **Tyrosine kinase inhibitor**
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Targeted therapy in older patients with NSCLC

Systematic Review

Targeted Therapy for Older Patients with Non-Small Cell Lung Cancer: Systematic Review and Guidelines from the French Society of Geriatric Oncology (SoFOG) and the French-Language Society of Pulmonology (SPLF)/French-Language Oncology Group (GOLF)

Laurent Greillier^{1,2,3,†}, Manon Gauvrit^{4,†}, Elena Paillaud^{5,6,7}, Nicolas Girard^{2,3,8,9}, Coline Montégut^{7,10}

➤ Efficacy of EGFR TKI

- The efficacy of anti-EGFR TKI in terms of ORR, PFS, and OS seems **similar in patients** aged ≥ 65 years (**even over 75 years**) and younger patients
- PFS and OS were in **favor of osimertinib** as a first-line treatment in older subjects (as young patients) compared to 1st generation TKI (erlotinib and gefitinib)

Table 1. Efficacy results in older patients in retrospective and prospective cohorts (≥ 65 years).

Publication/ Country	Targeted Therapy	Patient Number	ECOG-PS ≥ 2 (%)	Median Age, Years	Objective Tumor Response (95% CI)	Median PFS, Months (95% CI)	Median OS, Months (95% CI)
Furuta 2018 [37]/Japan	Osimertinib	18	0	80	61	17.7 (8.4-NR)	38.6 (14.3–52.8)
Nakao 2020 [38]/Japan	Osimertinib 80 mg/day	36	0	80	58.3 (42.2–72.9)	11.9 (7.9–17.5)	22.0 (16.0-NR) at 1 year: 77.8%, at 2 years: 49.5%
Auliac 2019 [39]/France	Osimertinib 80 mg/day	43	42.4	84.6		17.5 (12.2–19.0)	22.8 (15.7-NR)

Table 2. Targeted therapy efficacy results in older patients in randomized or non-randomized trials (subgroup post-hoc analysis).

Publication/ Country	Targeted Therapy	Patients Number	Age Group	ECOG-PS ≥ 2 (%)	PFS (Months) (95% CI)	OS (Months) (95% CI)
Soria 2018 [49]/International	Osimertinib 80 mg/day or gefitinib 250 mg/day or erlotinib 150 mg/day	556		0		
		298	<65		HR 0.44 (0.33–0.58)	
		258	≥ 65		HR 0.49 (0.35–0.67)	
Ramalingam 2020 [50]/International	Osimertinib 80 mg/day or gefitinib 250 mg/day or erlotinib 150 mg/day	556		0		
		298	<65			HR 0.72 (0.54–0.97)
		258	≥ 65			HR 0.87 (0.63–1.22)
Mok 2017 [51]/ International	Osimertinib 80 mg/day	279				
		242	<65		HR 0.38 (0.28–0.54)	
		177	≥ 65		HR 0.34 (0.23–0.50)	
Douillard 2014 [52]/International	Gefitinib 250 mg/day	106		6.6		
		55	≤ 65		65.5 (52.3–76.6)	
		51	> 65		74.5 (61.1–84.5)	

Target therapy in older patients with NSCLC

Systematic Review

Targeted Therapy for Older Patients with Non-Small Cell Lung Cancer: Systematic Review and Guidelines from the French Society of Geriatric Oncology (SoFOG) and the French-Language Society of Pulmonology (SPLF)/French-Language Oncology Group (GOLF)

Laurent Greillier^{1,2,3,†}, Manon Gauvrit^{4,†}, Elena Paillaud^{5,6,7}, Nicolas Girard^{2,3,8,9}, Coline Montégut^{7,10},

➤ Toxicity of EGFR-TKI

	M/C Gr 3-4 A/E in elderly patient	Common A/E
Afatinib	Hematologic toxicity (~33%)	mucositis (3% to 50%), diarrhea (8% to 33%), skin rash (5% to 33%), paronychia (5% to 28%), and asthenia (1% to 33%).
Erlotinib	Diarrhea (3-17%)	diarrhea (3% to 17%) and skin rashes (4% to 14%)
Gefitinib	Increase AST/ALT(7-50%)	anorexia (5% to 20%), diarrhea (1% to 17), and skin rash (2% to 16)
Osimertinib	Anemia (~43%)	paronychia(~42%), anorexia (11%), QT prolongation

- The probability of **Grade 3-4 Toxicity** and **interstitial pneumonitis**(5-10%) is more common in older patients

Target therapy in older patients with NSCLC

Systematic Review

Targeted Therapy for Older Patients with Non-Small Cell Lung Cancer: Systematic Review and Guidelines from the French Society of Geriatric Oncology (SoFOG) and the French-Language Society of Pulmonology (SPLF)/French-Language Oncology Group (GOLF)

Laurent Greillier^{1,2,3,†}, Manon Gauvrit^{4,†}, Elena Paillaud^{5,6,7}, Nicolas Girard^{2,3,8,9}, Coline Montégut^{7,10}

➤ Feasibility of EGFR-TKI

Table 6. Targeted therapy feasibility results in older patients in non-randomized trials.

Molecules	Afatinib	Gefitinib	Osimertinib	Erlotinib
Median duration of treatment (months)	4.0 (1-69)	1.6-8.0	15.0 ± 9	1-39 1-9 1.7-6.2
Dose reduction (%)	47.5-89	20-45	19-39	7-56
Treatment discontinuation due to toxicity (%)	5-21	3-52	9-28	4-45
Dose reduction due to toxicity (%)		17	9-28	7-56

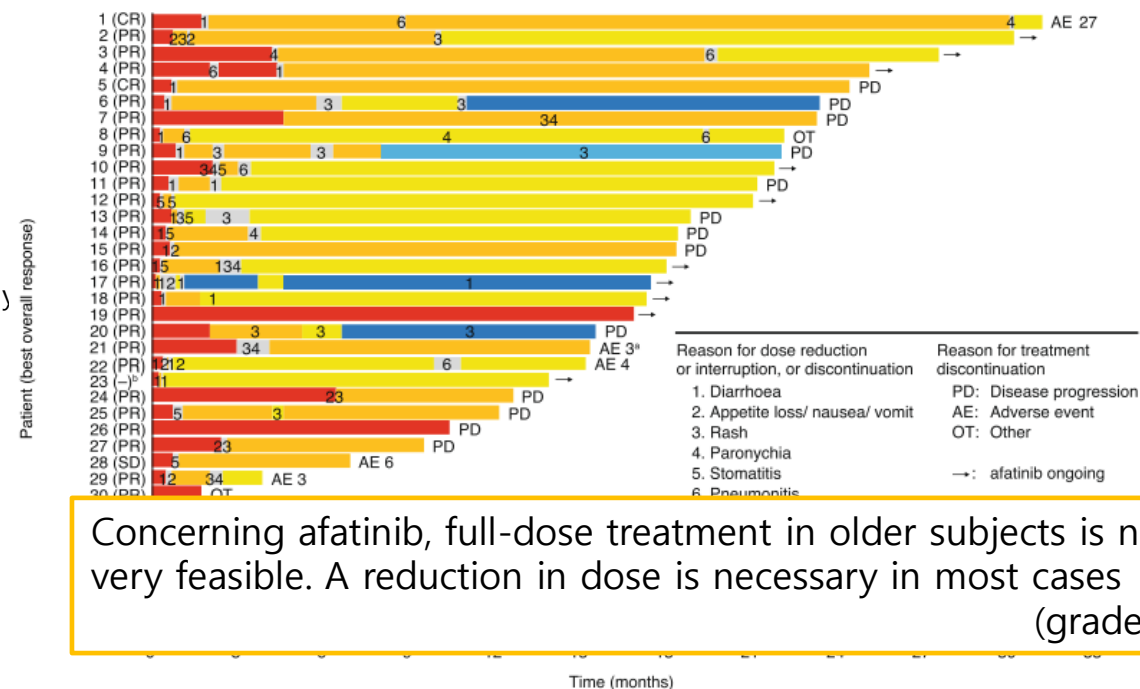
Table 1. Targeted therapy efficacy in older patients in retrospective and prospective cohorts (≥65 y)

Publication/Country	Targeted Therapy	Patient Number	ECOG-PS ≥ 2 (%)	Median Age, Years	Objective Tumor Response (95% CI)	Median PFS, Months (95% CI)	Median OS, Months (95% CI)
Imai 2018 [27]/Japan	Afatinib 30 mg/day	40	2.5	77	72.5 (58.6-86.3)	12.9 (8.8-19.3)	NR At 1 year: 87.4%, 2 years: 60.6%
Minegishi 2021 [28]/Japan	Afatinib 40 mg/day	37	0	77.5	75.7 (58.8-88.2)	14.2 (9.5-19.0)	35.2 (35.2-NR) At 1 year: 83.8%, 2 years: 78.3%

➤ A phase II study of first-line afatinib for patients aged ≥75 years with EGFR(+) NSCLC

Table 3 Afatinib exposure and treatment adjustment due to treatment-related adverse events

Category	Safety analysis set N = 38
Afatinib exposure	
Median treatment duration ^a , days (range)	494 (8-950)
Median treatment days ^b , n (range)	492 (8-932)
Mean afatinib dose ^c , mg	29.7 (10.6-40.0)
Median relative dose intensity ^d , % (range)	74.2 (26.4-100)
Treatment adjustments, n (%)	
Initial treatment dose 40 mg	38 (100)
Dose reduction	30 (78.9)
Final treatment dose	
40 mg	8 (21.1)
30 mg	12 (31.6)
20 mg	14 (36.8)
30 mg QOD	1 (2.6)
20 mg QOD	3 (7.9)
Treatment interruption	28 (73.7)
Treatment discontinuation	8 (21.1)



Concerning afatinib, full-dose treatment in older subjects is not very feasible. A reduction in dose is necessary in most cases (grade A).

Immunotherapy in older patients with NSCLC

REVIEW ARTICLE

Immunotherapy in older patients with non-small cell lung cancer: Young International Society of Geriatric Oncology position paper

Fabio Gomes¹, Melisa Wong², Nicolò Matteo Luca Battisti³, Tiana Kordbacheh⁴, Mandy Kiderlen⁵, Alastair Greystoke⁶ and

➤ Efficacy of I/O as monotherapy or combination with Ctx

Table 1. Summary of data from immunotherapy single-agent trials for NSCLC.

Study	Design and setting	Trial arms	N and age (years)	Key findings in older adults
<i>Pembrolizumab</i>				
KEYNOTE-024 NCT02142738	Phase 3 First line Squamous and non-squamous PD-L1 > 50%	Pembrolizumab versus platinum-based chemotherapy	n = 305 (1:1) Median age 65 (range 33–90) Age ≥65: 54%	OS ≥ 65y: HR 0.64 (95% CI 0.42–0.98) OS < 65y: HR 0.60 (95% CI 0.38–0.96)
KEYNOTE-042 NCT02220894	Phase 3 First line Squamous and non-squamous PD-L1 > 1%	Pembrolizumab versus platinum-based chemotherapy	n = 1274 (1:1) Median age 63 (range 25–90) Age ≥65: 45%	OS ≥ 65y: HR 0.82 (95% CI 0.66–1.01) OS < 65y: HR 0.81 (95% CI 0.67–0.98)
KEYNOTE-010 NCT01905657	Phase 3 Second line and subsequent Squamous and non-squamous PD-L1 > 1%	Pembrolizumab versus Docetaxel	n = 1034 (1:2) Median age 63 (range 54–70) Age ≥65: 41%	OS ≥ 65y: HR 0.76 (95% CI 0.57–1.02) OS < 65y: HR 0.63 (95% CI 0.50–0.79)
<i>Atezolizumab</i>				
OAK NCT02008227	Phase 3 Second line and subsequent Squamous and non-squamous	Atezolizumab versus Docetaxel	n = 850 (1:1) Median age 64 (range 33–85) Age ≥65: 47%	OS ≥ 65y: HR 0.66 (95% CI 0.52–0.83) OS < 65y: HR 0.80 (95% CI 0.64–1.00)

Table 2. Summary of data from combination trials of systemic treatments for NSCLC.

Study	Design and setting	Trial arms	N and age (years)	Key findings in older adults
<i>Pembrolizumab plus chemotherapy</i>				
KEYNOTE-189 NCT02578680	Phase 3 First line non-squamous PD-L1 (any)	Cisplatin or carboplatin, pemetrexed (maintenance pemetrexed) versus Cisplatin or carboplatin, pemetrexed + pembrolizumab (maintenance pemetrexed + pembrolizumab)	n = 616 (1:2) Median age 64 (range 34–84) Age ≥65: 49%	OS > 65y: HR 0.64 (95% CI 0.43–0.95) OS < 65y: HR 0.43 (95% CI 0.31–0.61)
KEYNOTE-407 NCT02775435	Phase 3 First line squamous PD-L1 (any)	Carboplatin, (nab)-paclitaxel (maintenance pemetrexed) versus Carboplatin, (nab)-paclitaxel + pembrolizumab (maintenance pemetrexed + pembrolizumab)	n = 559 (1:1) Median age 65 (range 29–88) Age ≥65: 55%	OS > 65y: HR 0.74 (95% CI 0.51–1.07) OS < 65y: HR 0.52 (95% CI 0.34–0.80) PFS > 65y: HR 0.63 (95% CI 0.47–0.84) PFS < 65y: HR 0.50 (95% CI 0.37–0.69)

Safety and feasibility of Immunotherapy in older patients

ORIGINAL ARTICLE

A Real-World Study on the Effectiveness and Safety of Pembrolizumab Plus Chemotherapy for Nonsquamous NSCLC

Daichi Fujimoto, MD,^{a,b} Satoru Miura, MD, PhD,^{c,*} Kenichi Yoshimura, MD, PhD

- In **treatment naïve** patients in JAPAN, multicenter data
N=299; median age was 68 years; 43 were aged >75 years (14.4%)

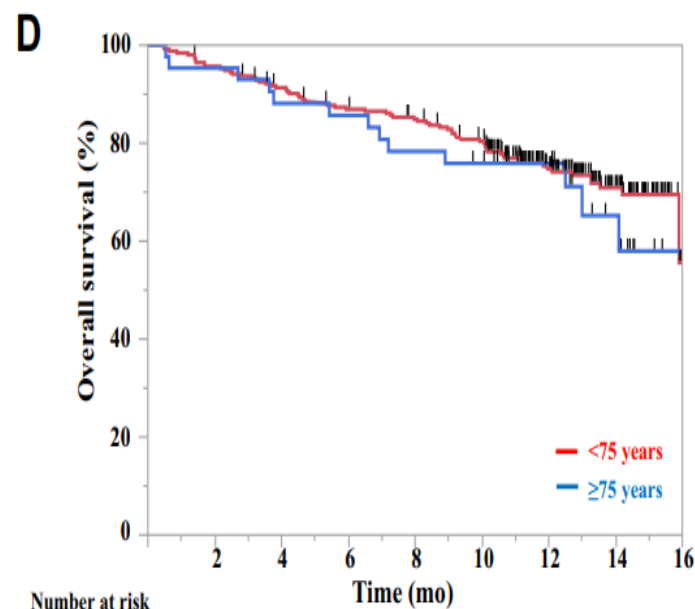
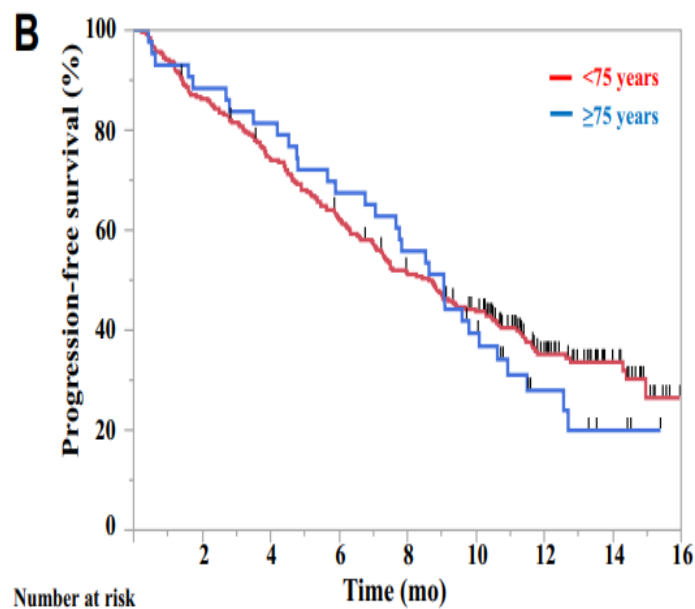


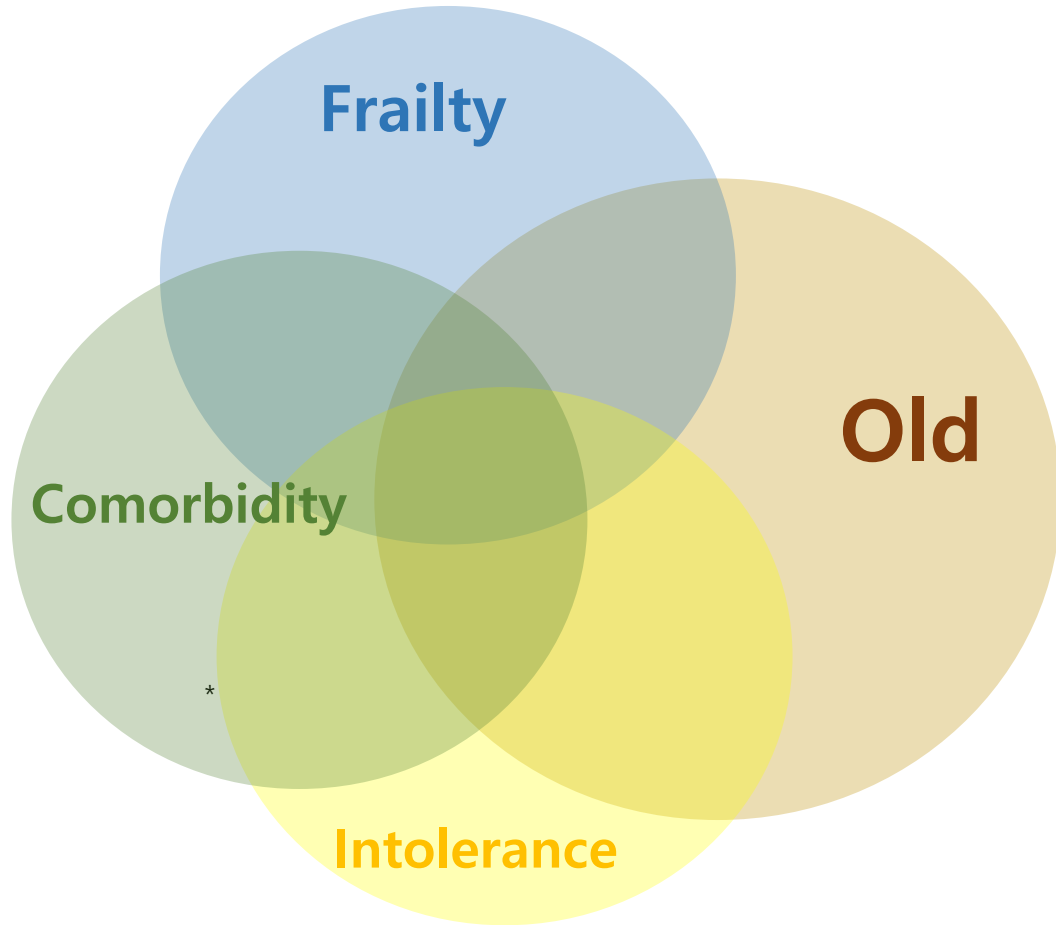
Table 4. Comparison of Patients With and Without Toxicity-Related Discontinuation of All-Treatment Components

Characteristics	Patients With Discontinuation (n = 71)	Patients Without Discontinuation (n = 228)	p Value
Age (y)			<0.001
Median (range)	70 (46-82)	68 (31-84)	
ECOG PS, n (%)			0.83 ^a
0	21 (30)	74 (32)	
1	47 (66)	143 (63)	
2	1 (1)	10 (4)	
3	2 (3)	1 (1)	

Supplemental Data 5. Patient characteristics and safety profiles stratified by age

Characteristic	<65 years (n=110)	65–74 years (n=146)	≥75 years (n=43)	p-value*
AEs leading to discontinuation	15 (14)	39 (27)	17 (40)	0.01
Severe AEs	18 (16)	31 (21)	11 (26)	0.57

Summary



- To provide the best prognosis to elderly patients,
 - Find a high risk patients using geriatric assessment
 - Provided an intervention for impaired problems
 - Modification or choice alternative treatment modality, based on the clinical evidence

THANKS
for your
ATTENTION

*