

Geriatric screening tools in older patients with cancer

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CONFLICT OF INTEREST DISCLOSURE

I have the following potential conflicts of interest to report

- Sanofi
- Nutricia
- Amgen
- Roche

Introduction

- Age is the most important risk factor for cancer
- 60% of cancers are diagnosed in patients ≥ 65 years
- Senior adults have been underrepresented in clinical trials, leading to a limited existence of evidence-based guidelines for treatment
- Standard evaluation of older cancer patients may lead to:
 - overtreatment and toxicity
 - undertreatment, loss of efficacy, and poorer outcomes

Therapeutic challenges in older patients with cancer

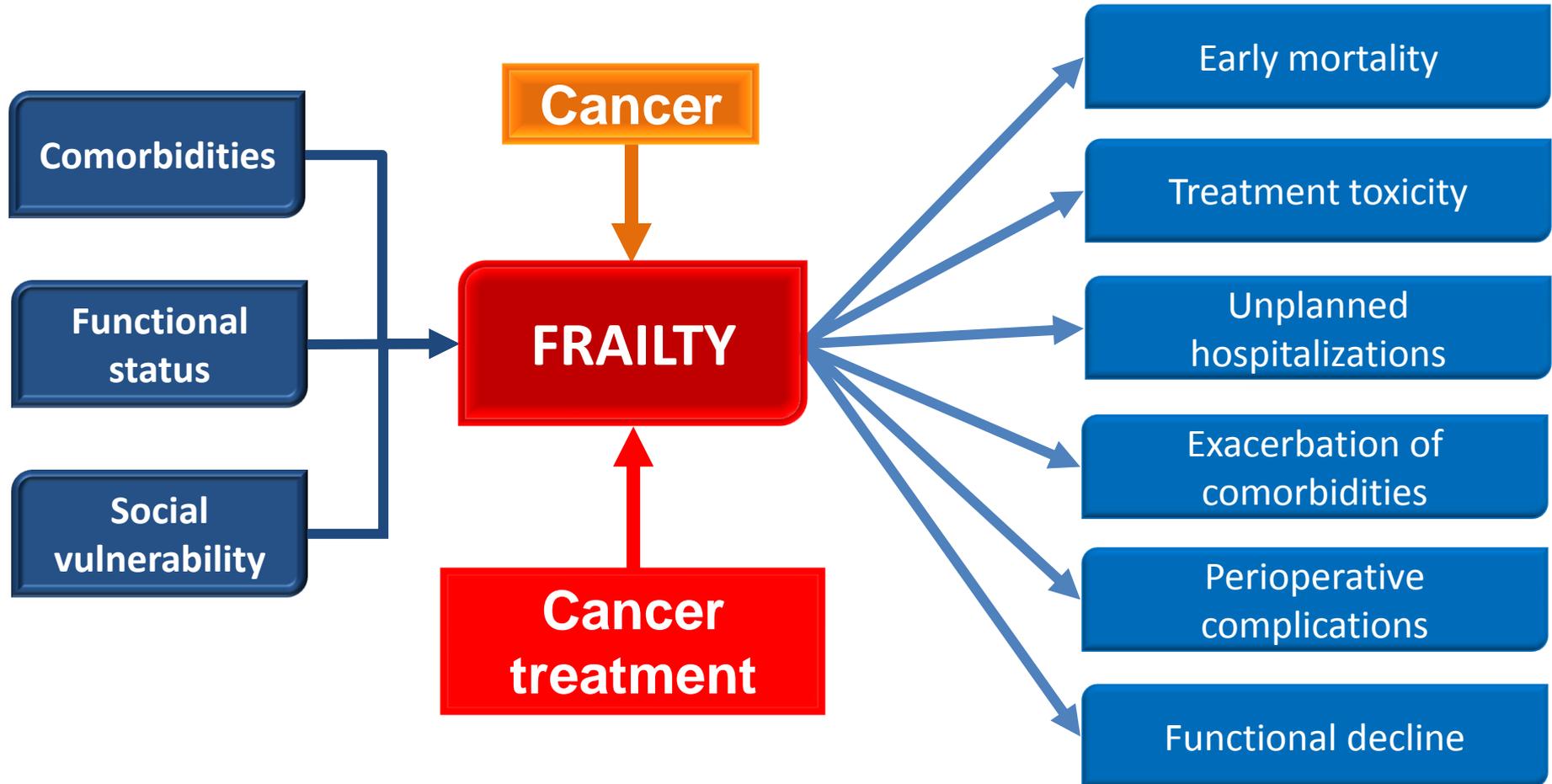
- Older cancer patients represent therapeutic challenges because they are an **heterogeneous population** with various combinations of comorbidities, physiological reserves, disabilities and geriatric syndromes.
- The way to approach this heterogeneity is the geriatric assessment
- Geriatric evaluation gives an opportunity to better:
 - evaluate risks of adverse events
 - appreciate treatment benefits
 - define an adequate treatment strategy



Comprehensive **G**eriatric **A**ssessment



Why identifying aging-related vulnerabilities ?



Geriatric Assessment (GA)

- GA takes more than one hour
- We are few geriatricians, and less trained to oncology
- GA is not necessary for all elderly cancer patients



**A screening strategy
 appears necessary**

Domains	Tools	References
Dependency	Activities of daily living (ADL) Instrumental activities of daily living (IADL)	Katz et al, 1963 Lawton et al, 1969
Mobility Fall risk	Falls within 6 or 12 last months Short Physical Performance Battery Gait speed, appui monopodal Timed Get Up and Go Test	Lamb et al, 2005 Vellas et al, 1997 Podsiadlo et al, 1991
Nutrition	Mini nutritional assessment (MNA) Weigh loss within 3 and 6 last months Body Mass Index	Guigoz et al, 1997
Cognition	Mini Mental State Examination (MMSE) Short Portable Mental Status Questionnaire Clock Drawing Test, Trail-making Test a/b	Folstein et al, 1975
Mood	Geriatric Depression Scale (GDS)	Yesavage et al, 1983
Comorbidities Medication	Cumulative Illness Rating Scale – Geriatrics Number of medications a day	Linn et al, 1968

A set of screening tools has been developed to guide the therapeutic decision



And to respond at the following questions:

- How to identify older cancer patients who may benefit from a CGA?
- How to identify older cancer patients who are at risk of chemotoxicity?
- How to identify older cancer patients who are at risk of early death?

How to identify older cancer patients who may benefit from a GA ?

- **17 screening tools have been reported to identify frail patients who need a GA**
(Decoster et al* in a recent review)
 - a-CGA (*abbreviated CGA*)
 - ECOG-PS (*Eastern Cooperative Oncology Group - Performance Status*)
 - Fried frailty phenotype
 - GFI (*Groningen Frailty Indicator*),
 - F-TRST (*Flemish version of Triage Risk Screening Tool*),
 - **G8** (*Geriatric 8*)
 - **VES-13** (*Vulnerable Elders Survey-13*)
- In daily geriatric oncology practice, frailty has been defined as an impairment of one or more domains of the GA
- **Only two screening tests have been specifically developed in older cancer patients: aCGA and G8**
- **The most studied tools in older cancer patients are G8 and VES-13**

* Decoster L et al. *Annals of Oncology* 2015; 26: 288–300

Screening for vulnerability in older cancer patients: Vulnerable Elders Survey-13 screening tool

- A **13-item self-administered tool*** that asks to report:
 - age
 - physical status
 - functional capacity
 - self-reported health

• Time to perform: **5 to 10 min**

• **Abnormal if $\geq 3 \rightarrow$ CGA**

• Se ranged from 39% to 88%**

Sp ranged from 62% to 100%**

VES-13

1. Age _____
2. In general, compared to other people your age, would you say that your health is:
3. How much difficulty, on average, do you have with the following physical activities:
 - a. stooping, crouching or kneeling?
 - b. lifting, or carrying objects as heavy as 10 pounds?
 - c. reaching or extending arms above shoulder level?
 - d. writing, or handling and grasping small objects?
 - e. walking a quarter of a mile?.....
 - f. heavy housework such as scrubbing floors or washing windows?.....
4. Because of your health or a physical condition, do you have any difficulty:
 - g. shopping for personal items (like toilet items or medicines)?.....
 - h. managing money (like keeping track of expenses or paying bills)?
 - i. walking across the room?
 - j. doing light housework (like washing dishes, straightening up, or light cleaning)? ...
 - k. bathing or showering?.....

* Saliba D et al. J Am Geriatr Soc 2001; 49(12): 1691-9

** Decoster L et al. Annals of Oncology 2015; 26: 288-300

Screening for vulnerability in older cancer patients: G8 screening tool*/**

G8

- **8 questions, by a trained nurse:**
 - appetite, weight loss, BMI
 - mobility
 - mood and cognition
 - number medications
 - patient self-reported health
 - age categories
- Time to perform: **4.4 ± 2.9 min**
- **Abnormal if ≤14/17 → CGA**
- Se from 65% to 92%***
 Sp from 3% to 75%***

	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
		3 : no weight loss
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 < 18,5
		1 : BMI = 18,5 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
		2 : better
	Age	0 : >85
		1 : 80-85
		2 : <80
TOTAL SCORE		0 - 17

* Bellera CA et al. *Ann Oncol* 2012; 23(8): 2166-72
 ** Soubeyran P et al. *PLoS One* 2014; 9(12): e115060
 *** Decoster L et al *Annals of Oncology* 2015; 26: 288–300

Modified-G8 screening tool

- G8 lacks sensitivity and specificity.
- We have developed and validated an optimized version of G8
- **6 questions, by a trained nurse:**
 - weight loss
 - cognition and mood
 - performance status
 - self-reported health status
 - polypharmacy
 - history of heart failure/coronary disease
- Time to perform: **3.8 ± 1.5 min**
- **Abnormal if $\geq 6/35$ → CGA**
- Se: 89% (86.5-91.5) vs. 87.2% (84.3-89.7)
Sp: 79% (69.4-86.6) vs. 57.7% (47.3-67.7)

Martinez-Tapia C et al. *The Oncologist* 2016; 21(2): 188-95

Modified-G8

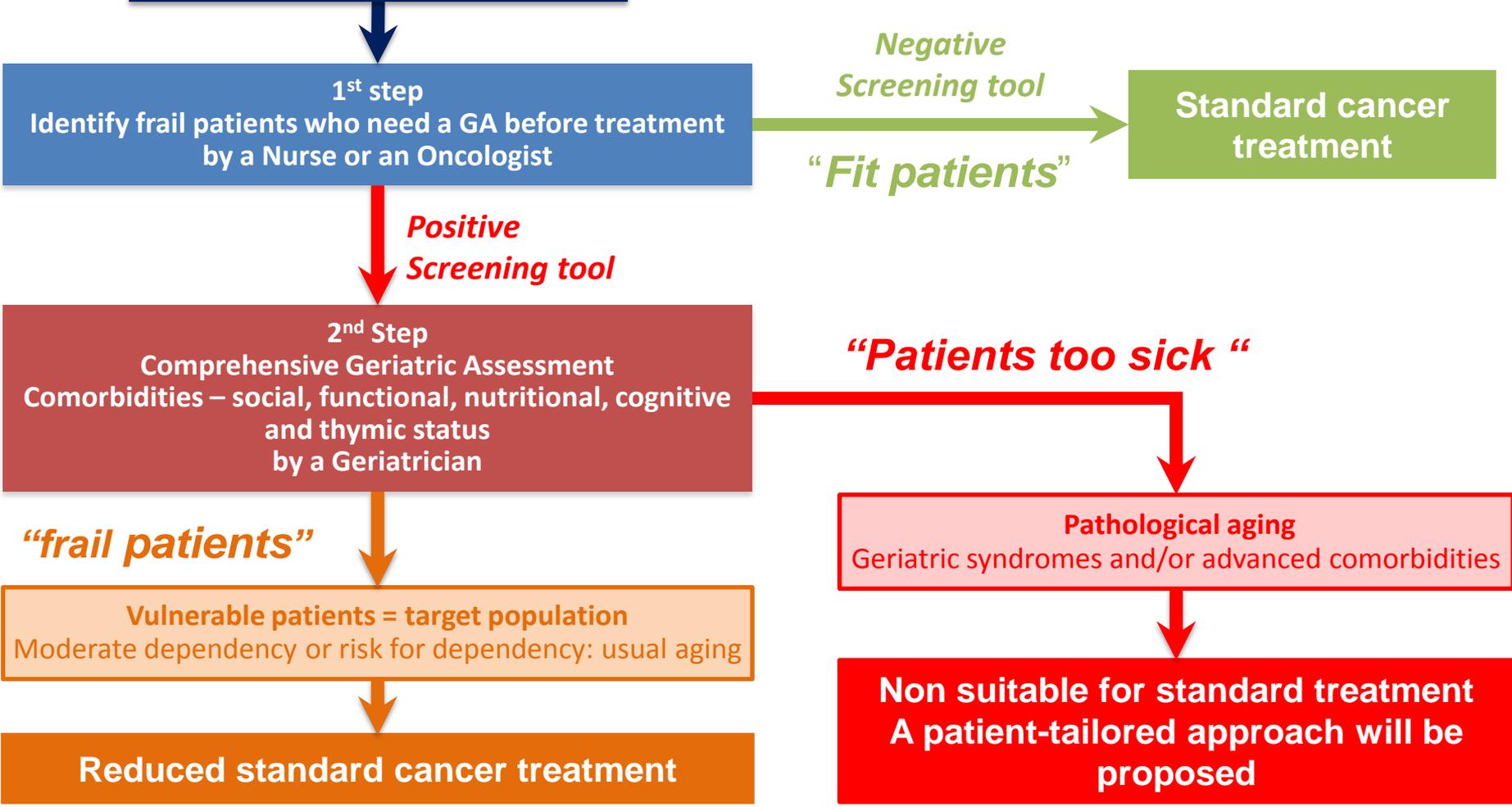
6 items

+ if ≥ 6

Items	Score
1 Weight loss during the past 3 months	
>3 kg / patient does not know	10
1-3 kg	2
No weight loss	0
2 Neuropsychological problems	
Mild / severe dementia or depression	3
No neuropsychological problems	0
3 Takes at least six drugs per day	
Yes	2
No	0
4 Compared to other people of the same age, how does the patient rate his or her health status?	
Not as good / patient does not know	3
As good or better	0
5 Performance Status (PS)	
PS 2, 3, or 4: Ambulatory but unable to carry out any work activities / Confined to bed >50% / Disabled	12
PS 1: Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature	4
PS 0: Fully active	0
6 Past history of heart failure or coronary artery disease	
Yes	5
No	0
Total	/ 35

A screening strategy

Older cancer patients



How to identify older cancer patients who are at risk of chemotoxicity ?

- Older adults are vulnerable to chemotherapy toxicity
- There are limited data to identify patients at risk
- **Two screening tools have been developed to identify vulnerable older patients at risk for chemotherapy toxicity**

Hurria A. et al. J Clin Oncol 2011; 29(25): 3457-65

Predicting chemotherapy toxicity in older adults with cancer:
 a prospective multicenter study

The Cancer and Aging Research Group (CARG) toxicity tool

- 500 out-patients 73 ± 6.2 y. (65-91)

➤ 65-69	175 (35%)	}	60%
➤ 70-74	127 (25%)		
➤ 75-79	105 (21%)		
➤ 80-84	73 (15%)	}	40%
➤ 85-91	20 (4%)		

- **Cancers**

➤ lung	143 (29%)
➤ GI	135 (27%)
➤ GYN	87 (17%)
➤ breast	57 (11%)
➤ GU	50 (10%)
➤ others	28 (6%)

- 281 females (56%)
- 106 (21%) live alone

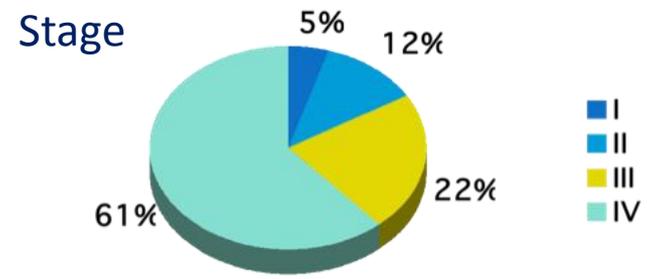
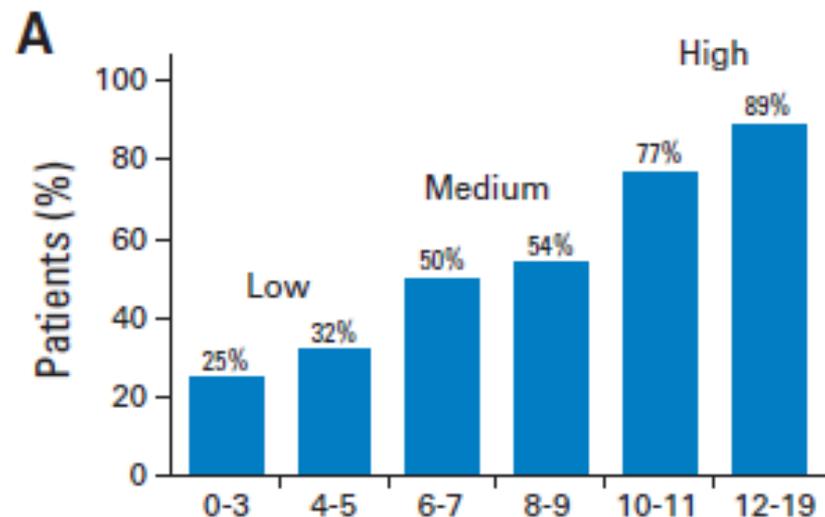


Table 5. Predictive Model

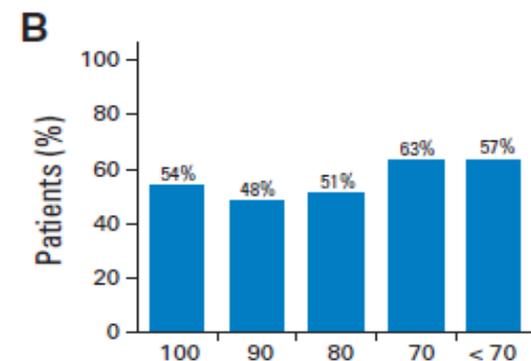
Risk Factor	Prevalence		Grades 3 to 5 Toxicity		OR	95% CI	Score
	No.	%	No.	%			
Age ≥ 72 years	270	54	163	60	1.85	1.22 to 2.82	2
Cancer type GI or GU	185	37	120	65	2.13	1.39 to 3.24	2
Chemotherapy dosing, standard dose	380	76	204	54	2.13	1.29 to 3.52	2
No. of chemotherapy drugs, polychemotherapy	351	70	192	55	1.69	1.08 to 2.65	2
Hemoglobin < 11 g/dL (male), < 10 g/dL (female)	62	12	46	74	2.31	1.15 to 4.64	3
Creatinine clearance (Jelliffe, ideal weight) < 34 mL/min	44	9	34	77	2.46	1.11 to 5.44	3
Hearing, fair or worse	123	25	76	62	1.67	1.04 to 2.69	2
No. of falls in last 6 months, 1 or more	91	18	61	67	2.47	1.43 to 4.27	3
IADL: Taking medications, with some help/unable	39	8	28	72	1.50	0.66 to 3.38	1
MOS: Walking 1 block, somewhat limited/limited a lot	109	22	69	63	1.71	1.02 to 2.86	2
MOS: Decreased social activity because of physical/emotional health, limited at least sometimes	218	44	126	58	1.36	0.90 to 2.06	1

Abbreviations: GU, genitourinary; IADL, instrumental activities of daily living; MOS, Medical Outcomes Study; OR, odds ratio.

The Cancer and Aging Research Group (CARG) toxicity tool



Ability of risk score to predict grade 3 to 5 chemotherapy toxicity



Ability of Karnofsky Index to predict grade 3 to 5 chemotherapy toxicity

Extermann M et al. Cancer 2012; 118(13): 3377-86

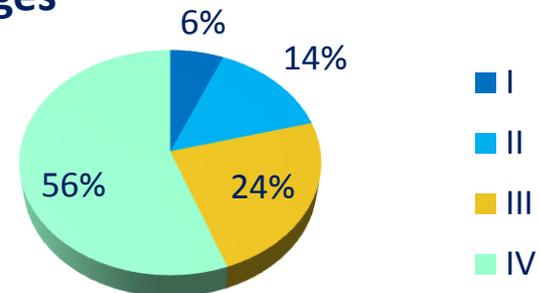
Predicting the risk of chemotherapy toxicity in older patients:
 The Chemotherapy Risk Assessment Scale for High-age patients
 score: **CRASH Score**

- 331 out-patients 76 y. (70-92)
- 166 females (50%)
- No. of medications 6/d (0-20)

• Cancers :

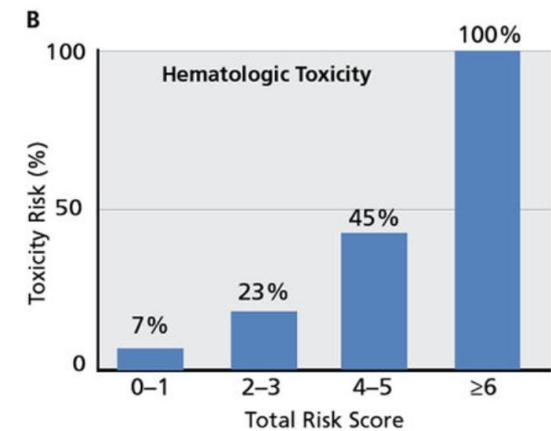
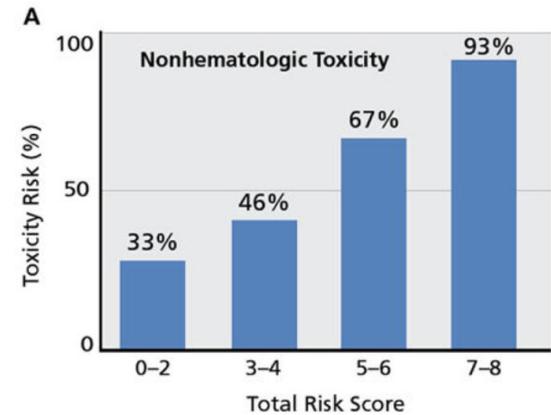
➤ lung	71	(21.5%)
➤ GI	41	(12.4%)
➤ NHL	47	(14.2%)
➤ breast	71	(21.5%)
➤ bladder	23	(6.9%)
➤ other	93	(24.4%)

Stages



Risk Assessment Scale for High-age patients score: CRASH Score

Predictors	Points		
	0	1	2
Hematologic score^a			
Diastolic BP	≤72	>72	
IADL	26-29	10-25	
LDH (if ULN 618 U/L; otherwise, 0.74 /L*ULN)	0-459		>459
Chemotox ^b	0-0.44	0.45- 0.57	>0.57
Nonhematologic score^a			
ECOG PS	0	1-2	3-4
MMS	30		<30
MNA	28-30		<28
Chemotox ^b	0-0.44	0.45-0.57	>0.57



CRASH Points^b

0	1	2
Capecitabine 2g	Capecitabine 2.5 g	5-FU/LV (Roswell-Park)
Cisplatin/pemetrexed	Carboplatin/gemcitabine AUC 4-6/1 g d1,d8	5-FU/LV (Mayo)
Dacarbazine	Carboplatin/pemetrexed	5-FU/LV and bevacizumab
Docetaxel weekly	Carboplatin/paclitaxel q3w	CAF
FOLFIRI	Cisplatin/gemcitabine d1,d8	Carboplatin/docetaxel q3w
Gemcitabine 1 g 3/4 wk	ECF	CHOP
Gemcitabine 1.25 g 3/4 wk	Fludarabine	Cisplatin/docetaxel 75/75
Paclitaxel weekly	FOLFOLX 85 mg	Cisplatin/etoposide
Pemetrexed	Gemcitabine 7/8 wk then 3/4 wk	Cisplatin/gemcitabine d1,d8,d15
	Gemcitabine/irinotecan	Cisplatin/paclitaxel 135-24 h q3w
	PEG doxorubicin 50 mg q4w	CMF classic
	Topotecan weekly	Doxorubicin q3w
	XELOX	FOLFOLX 100-130 mg
		Gemcitabine/pemetrexed d8
		Irinotecan q3w
		Paclitaxel q3w
		Docetaxel q3w
		Topotecan monthly

How to identify older cancer patients who are at risk of death?

- Failure to consider prognosis in the context of clinical decision-making can lead to poor care
- Some studies have reported the ability of GA domains to predict mortality*
- Prognostic models based on GA parameters have been developed in the general geriatric population (**e-prognosis Website**)
- But they have not yet been studied specifically within the oncology population
- Prognostic tools specifically focusing on older patients with cancer are needed

* Soubeyran P et al. *J Clin Oncol* 2012; 30(15): 1829e34

Ferrat E et al *J Gerontol Ser A Biol Sci Med Sci* 2015; 70(9): 1148e55

Aaldriks AA et al. *Crit Rev Oncol Hematol* 2011; 79(2): 205e12

Kristjansson SR et al. *Crit Rev Oncol Hematol* 2010; 76(3): 208e17

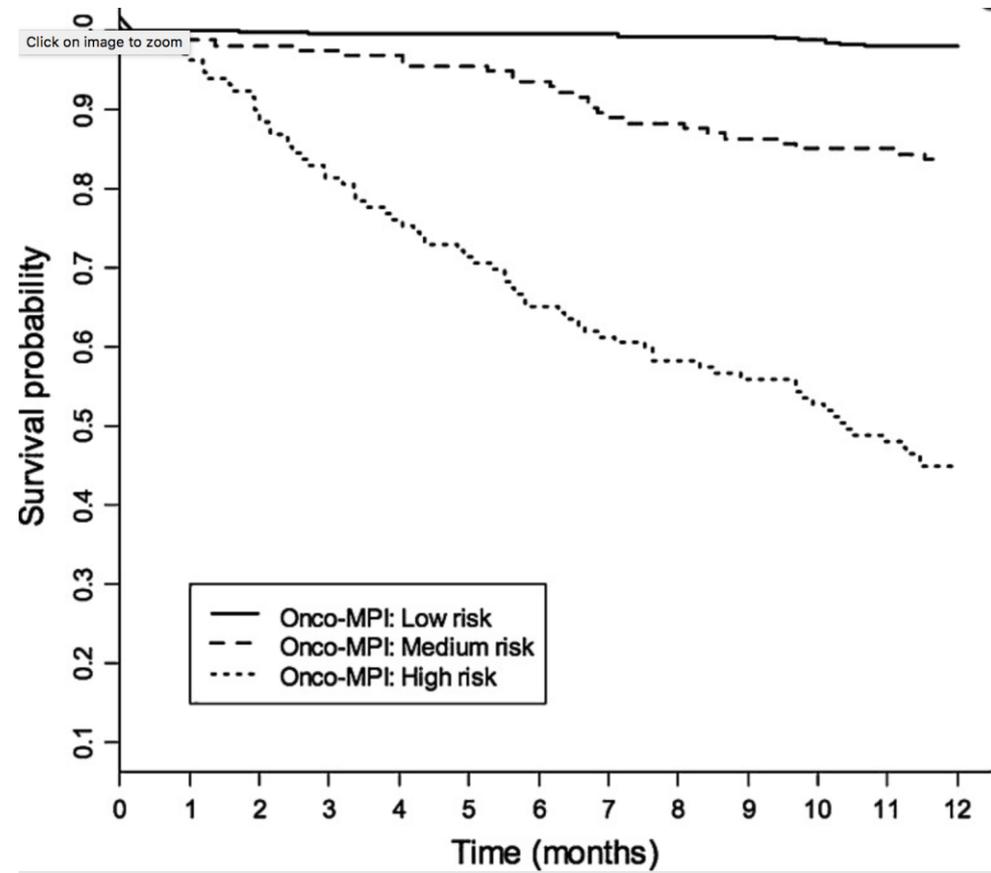
Wildiers H et al. *J Clin Oncol* 2014; 32(24): 2595–2603

How to identify older cancer patients who are at risk of death?

- 5 indices that estimate mortality risk for community-dwelling older adults have been developed:
 - **Gagne (2011)**: mortality risk score to predict 1-year mortality
 - **Mazzaglia (2007)**: 7-items questionnaire for primary care to predict 15-month mortality
 - **Carey (2004)**: 2-year mortality index for community-dwelling elders
 - **Lee (2006)**: 4-year mortality index in community-dwelling adults age >50 y.
 - **Schonberg (2009)**: 5-year mortality index in a sample of adults >65 y.
- 8 indices estimate mortality risk for hospitalized older adults:
 - **Pilotto (2008)**: 1-year prognostic index for hospitalized elders age ≥65 y.
 - **Di Bari (2010)**: 1-year mortality index for emergency triage of elders age >75 y.
 - **Fischer (2006)**: 1-year mortality index for hospitalized elders
 - **Inouye (2003)**: Burden of Illness Score for Elderly Persons to estimate 1-year mortality
 - **Teno (2000)**: 1 and 2-year mortality based on medicine and ICU patients >80 y.
 - **Levine (2007)**: 1-year prognostic model for hospitalized elders following discharge
 - **Walter (2001)**: 1-year mortality index for elders following hospital discharge
 - **Drame (2008)**: 2-year mortality index in hospitalized adults age >75 y. (emergency)

The oncological-multidimensional prognostic index (Onco-MPI)

- One of these tools, the **MPI***, has been recently adapted to elderly cancer patients**
- Onco-MPI risk score defined three categories: low risk, medium risk and high risk
- Kaplan-Meier survival curves, within 1 year of follow-up



* Pilotto A, Panza F, Ferrucci L. *Arch Intern Med.* 2012;172(7):594-5

** Brunello A et al. *Cancer Res Clin Oncol* 2016; 142: 1069-77

Multidimensional Frailty Score in surgery

- Kim SW et al. has developed a scoring model to predict unfavorable outcomes after surgery in older patients
- High-risk patients (**multidimensional frailty score >5**) showed an increasing **1-year postoperative mortality risk** (HR=9.01; 95%CI(2.15-37.78); $p=.003$)

Frailty Score and Postoperative Mortality Risk

Table 2. Composition of Multidimensional Frailty Score

Item	Score		
	0	1	2
Malignant disease	Benign disease	Malignant disease	NA
Charlson Comorbidity Index	0	1-2	>2
Albumin, g/dL	>3.9	3.5-3.9	<3.5
ADLs (modified Barthel Index)	Independent	Partially dependent	Fully dependent
IADLs (Lawton and Brody Index)	Independent	Dependent	NA
Dementia (MMSE-KC)	Normal	Mild cognitive impairment	Dementia
Risk of delirium (Nu-DESC)	0-1	≥2	NA
MNA	Normal	Risk of malnutrition	Malnutrition
Midarm circumference, cm	>27.0	24.6-27.0	<24.6

NCAS – Nice Cancer Aging Survival score

Presented at ASCO 2016, this predictive tool has been developed to predict early mortality specifically in geriatric population with cancer

Bouhassass et al. *A clinical score to predict the early death at 100 days in older metastatic cancers (in press)*

- 312 patients, median age 82 y.
- The independent predictors of death at 100 days were:
 - age >85y. OR = 2.1; p=.03
 - 2 metastatic localizations (ML) OR=2.4; p=.004
 - >2 ML OR=6.3; p=.001
 - MNA <17 OR=8.7 p<.0001
 - ≤23.5 and ≥17 OR=5.4; p=.002
 - home confinement OR=1.8; p=.047
 - ADL <5,5 OR=2.1; p=.017
 - cancers with global risk of death at 100 days >30% OR=2.05; p=.016

✓ MNA ≤ 23.5	3 pts
✓ ML >2	3 pts
✓ ML =2	1 pt
✓ Home confinement	1 pt
✓ ADL <5.5	1pt
✓ Age >85y.	1 pt
✓ Cancers at risk for 100-d mortality >30%	1pt

Score ranged from 0 to 10

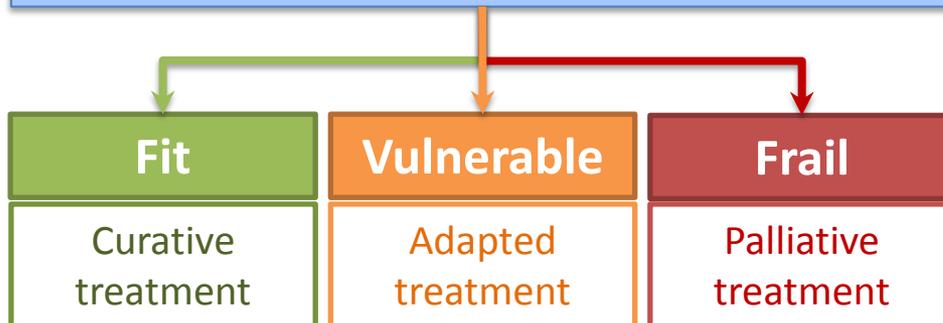
Bouhassass R et al. A clinical score to predict the early death at 100 days after a comprehensive geriatric assessment (CGA) in elderly metastatic cancers, analysis from a prospective cohort study with 1048 patients. JCO 2016: e21532-e21532

Frailty classifications and mortality

Ferrat E et al. Performance of Four Frailty Classifications in Older Patients With Cancer: Prospective Elderly Cancer Patients Cohort Study. *J Clin Oncol*, 2017; 35(7): 766-77

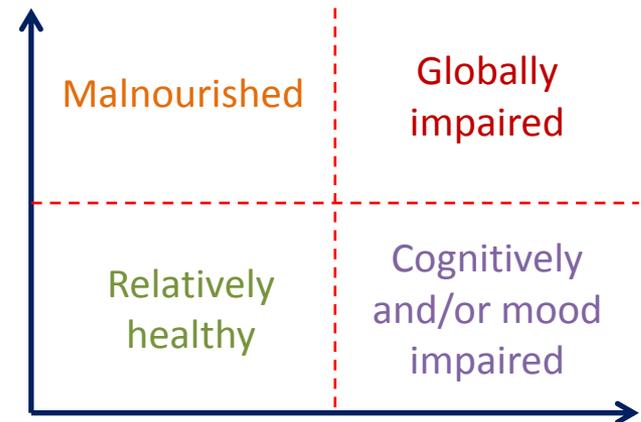
Based on clinical expertise and consensus

- 2000 – Balducci’s classification¹
- 2010 – SIOG classification (prostate cancer)²
- 2014 – Updated SIOG classification³



Based on statistical approach

- 2016 – Latent class classification⁴



⇒ **These four frailty classifications have good prognostic performance for predicting 1-year mortality in older patients with various cancers⁵**

1. Balducci L et al. *Crit Rev Oncol Hematol*, 2000; 35: 147-54

2. Droz JP et al. *BJU Int*, 2010; 106: 462-9

3. Droz JP et al. *Lancet Oncol*, 2014; 15:e404-e414

4. Ferrat E et al. *J Gerontol A Biol Sci Med Sci*, 2016; 71:1653-60

5. Ferrat E et al. *J Clin Oncol* 2017;35:766-777

Take home messages

- Several screening tools exist to identify patients who may benefit from a CGA, but **G8**, **modified-G8** and **VES-13** are the most studied and used tools in geriatric oncology
- Two scores have specifically been developed to assess the risk of chemotoxicity: **CARG** and **CRASH** scores
- Even if many mortality scores have been developed in geriatric setting, only few have been now studied in geriatric oncology setting: **oncology-MPI**, **multidimensional frailty score**, and **Nice Cancer Aging Survival score for older patients**



