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APPROCCIO AL PAZIENTE ONCOLOGICO ANZIANO

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19/12/2023

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I numeri del cancro in Italia: AIOM 2020

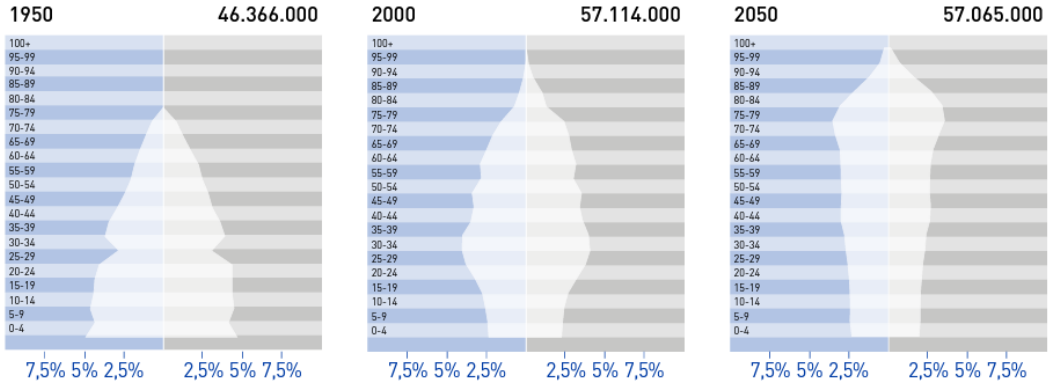


FIGURA 7. Struttura per età della popolazione italiana (http://populationpyramid.net/it)

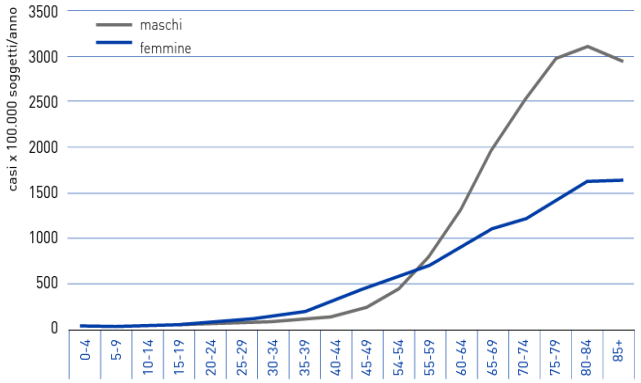


FIGURA 5. AIRTUM 2010-2015. Incidenza. Tassi età-specifici (x 100.000) per sesso. Tutti i tumori esclusi carcinomi della cute

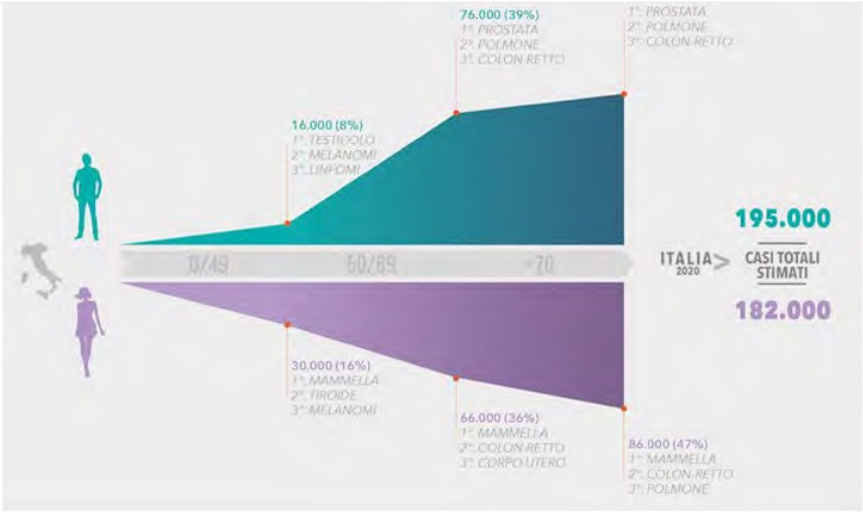
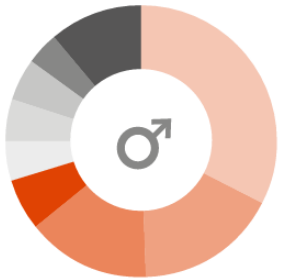
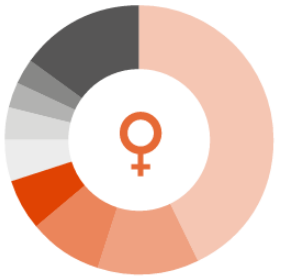


FIGURA 20. ***I Numeri del Cancro 2020*: neoplasie maligne incidenti nella popolazione italiana; le sedi più frequenti nei due sessi**

Nel corso del 2020, l'incidenza delle neoplasie maligne è stata stimata pari a 377.000 nuovi casi. In ambedue i sessi, l'incidenza cresce con l'età ed è maggiore negli uomini (uomini = 195.000; donne = 182.000). La figura mostra la progressiva incidenza delle neoplasie nelle 3 classi di età considerate (0-49; 50-69; >70 anni). I numeri assoluti e le percentuali si riferiscono ai tumori incidenti in ciascuna delle 3 fasce di età. Per ciascuna fascia di età, sono indicate le 3 sedi neoplastiche più frequenti.



Tumore	n.	%
Prostata	563.960	33
Colon-retto-ano	280.277	17
Vescica	255.015	15
Rene e vie urinarie	97.249	6
Linfomi non-Hodgkin	82.780	5
Melanomi, cute	80.069	5
Polmone	77.159	5
Testicolo	63.395	4
Altri	187.145	11



Tumore	n.	%
Mammella	834.154	43
Colon-retto-ano	233.245	12
Tiroide	166.914	9
Utero (corpo)	122.553	6
Melanomi, cute	89.831	5
Linfomi non-Hodgkin	73.584	4
Vescica	58.608	3
Utero cervice	51.136	3
Altri	292.061	15

FIGURA 7. Proporzione di persone che vivono dopo una diagnosi di tumore in Italia nel 2020, per i tipi di tumore più frequenti e sesso

- Rispetto alla media europea, pazienti anziani hanno una sopravvivenza peggiore
- Possibili cause:
- ritardo diagnostico, diversa biologia,
- ageismo, minor accesso ai trials, minor accesso alle terapie (under-treatment)
- Multimorbilità, fragilità

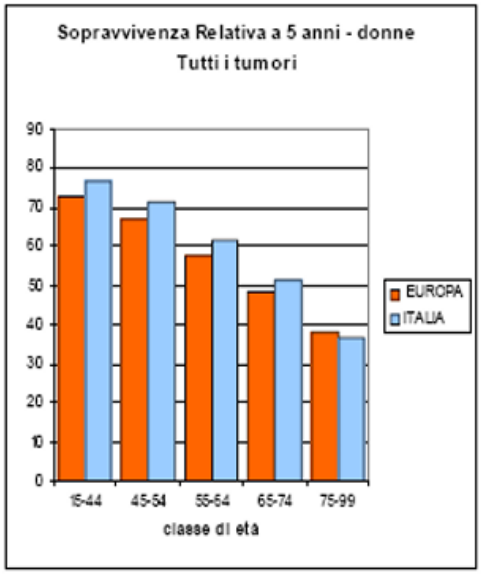
Is cancer biology different in older patients?

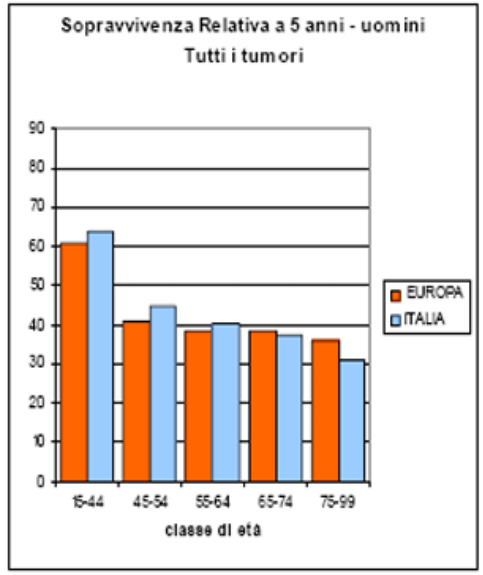
Yannick Van Herck*, Annelies Feyaerts*, Shabbir Alibhai, Demetris Papamichael, Lore Decoster, Yentl Lambrechts, Michael Pinchuk, Oliver Bechter, Jaime Herrera-Caceres, Frédéric Bibeau, Christine Desmedt, Sigrid Hatse, Hans Wildiers

Differenze biologiche in 5 tumori analizzati

- Mammella: più indolenti, grado inferiore, sottotipo luminale e HR+
- Polmone: più frequente SCC (prognosi peggiore)
- Prostata e Melanoma: più aggressivi
- CRC: aumenta incidenza del tumore del colon destro (prognosi peggiore)

Diverse alterazioni molecolari e mutazioni





AIOM LG anziano 2019

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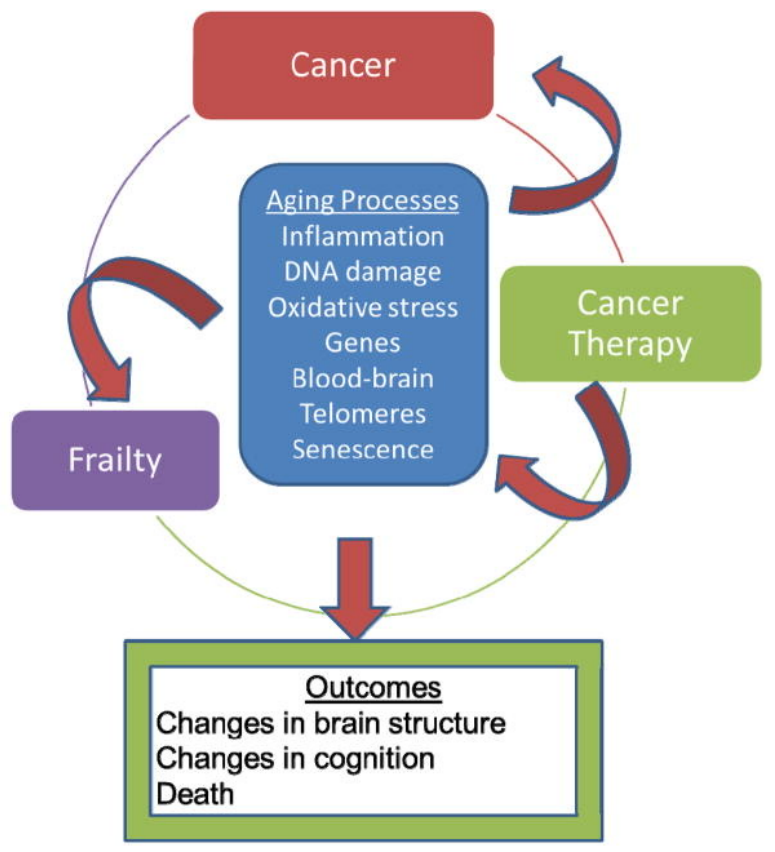
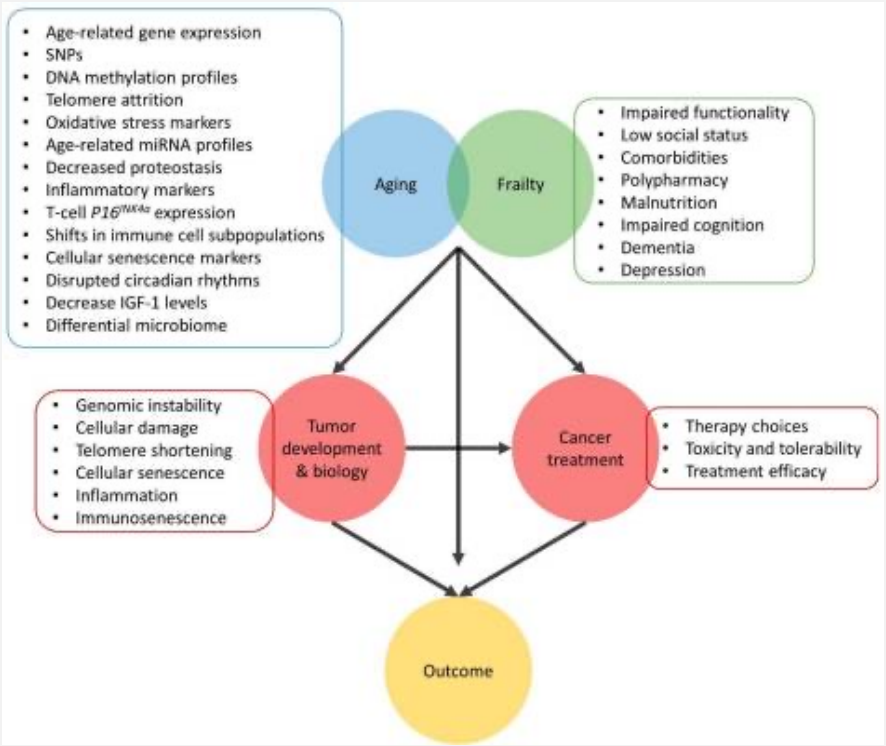


Mandelblatt JS, *Semin Oncol*. 2013; 40: 709-25.



Berben L, *Cancers. 2021*;13(6):1400.

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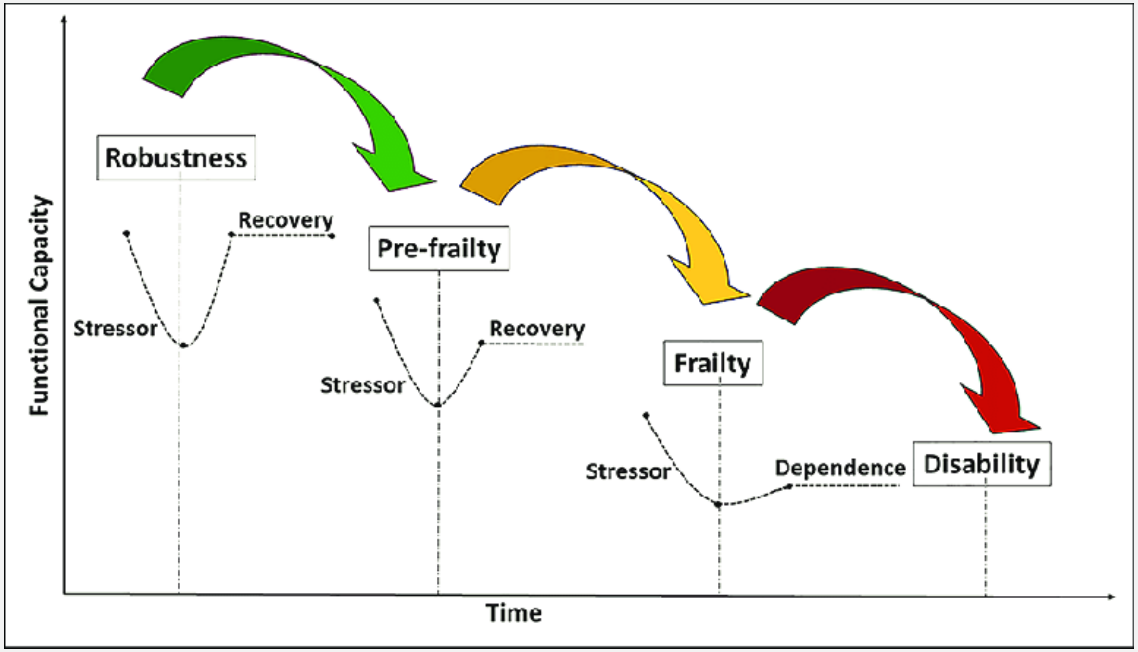
FRAGILITÀ

Sindrome geriatrica caratterizzata da ridotta riserva fisiologica e capacità di tollerare stressor ambientali

- rischio più elevato di esiti sfavorevoli legati alla salute
- aumento della morbilità, disabilità, mortalità e peggiore qualità di vita



Dent E. The journal of nutrition, health & aging. 2019; 23

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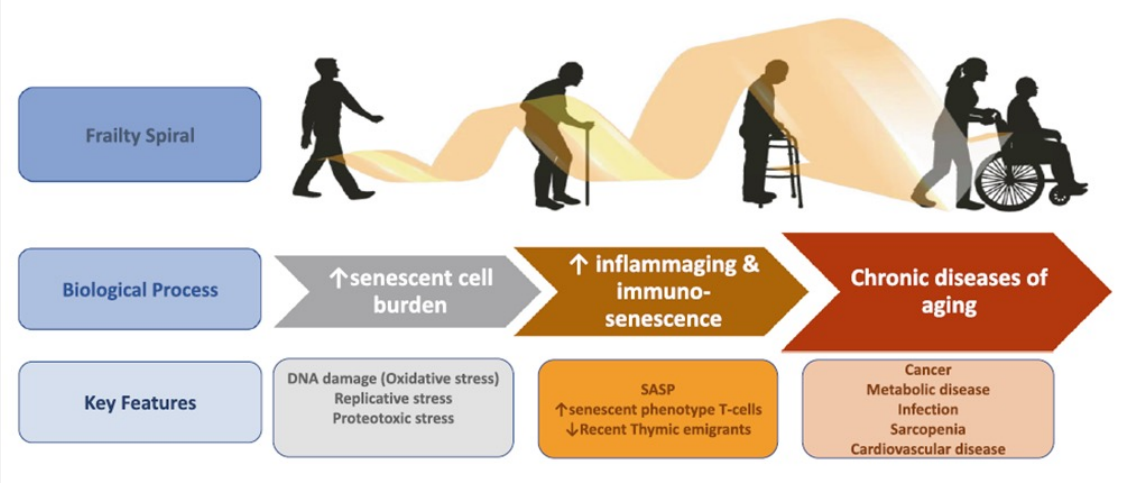
FRAGILITA’



Cancro e terapie anti-tumorali come stressore

→diminuzione delle riserve funzionali dell’individuo

→peggioramento traiettoria funzionale e sopravvivenza

Cook G, Leukemia. 2020; 34: 2285-94

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PERCHÉ VMD NEL PAZIENTE ONCOLOGICO?

- Personalizzazione del trattamento oncologico in base al profilo di vulnerabilità clinica
- Individuazione ed eventuale correzione dei problemi clinici non riscontrati durante le visite oncologiche
- Valutazione predittiva ed eventuale correzione dei fattori di rischio di possibile tossicità e complicanze peri- e post-trattamento antineoplastico
- Valutazione prognostica dell'aspettativa di vita

Wildiers, *Journal of Clinical Oncology*. 2014;32(24):2595-603.

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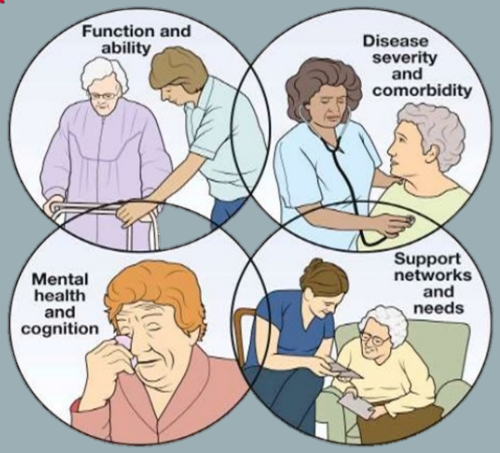

Valutazione geriatrica

Processo multidimensionale e multidisciplinare che identifica bisogni medici, sociali e funzionali e permette sviluppo di un progetto di cura integrato e coordinato per affrontare questi bisogni.

VOLUME 32 · NUMBER 24 · AUGUST 20 2014

JOURNAL OF CLINICAL ONCOLOGY

REVIEW ARTICLE

International Society of Geriatric Oncology Consensus on Geriatric Assessment in Older Patients With Cancer

Hans Wildiers, Pieter Heeren, Martine Puts, Eva Topinkova, Maryska L.G. Janssen-Heijnen, Martine Extermann, Claire Falandry, Andrew Artz, Etienne Brain, Giuseppe Colloca, Johan Flamaing, Theodora Karnakis, Cindy Kenis, Riccardo A. Audisio, Supriya Mohile, Lazzaro Repetto, Barbara Van Leeuwen, Koen Milisen, and Arti Hurria

Hans Wildiers, Pieter Heeren, Johan Flamaing, Cindy Kenis, and Koen Milisen, University Hospitals Leuven,

Updated recommendations regarding the management of older patients with breast cancer: a joint paper from the European Society of Breast Cancer Specialists (EUSOMA) and the International Society of Geriatric Oncology (SIOG)

Laura Biganzoli, Nicolò Matteo Luca Battisti, Hans Wildiers, Amelia McCartney, Giuseppe Colloca, Ian H Kunkler, Maria-João Cardoso, Kwok-Leung Cheung, Nienke Aafke de Glas, Rubina M Trimboli, Beatriz Korc-Grodzicki, Enrique Soto-Perez-de-Celis, Antonio Ponti, Janice Tsang, Lorenza Marotti, Karen Benn, Matti S Aapro, Etienne G C Brain

Breast cancer is increasingly prevalent in older adults and is a substantial part of routine oncology practice. However, *Lancet Oncol* 2021

VOLUME 36 · NUMBER 22 · AUGUST 1, 2018

JOURNAL OF CLINICAL ONCOLOGY

ASCO SPECIAL ARTICLE

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. Janelsins, Alok A. Khorana, Heidi D. Klepin, Stuart M. Lichtman, Karen M. Mustian, William P. Tew, and Arti Hurria

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Valutazione multidimensionale ed interventi di supporto

SPECIAL SERIES: CARING FOR OLDER ADULTS WITH CANCER

Geriatric Assessment and Management in Canc

Siri Rostoft, MD, PhD[1,2]; Anita O'Donovan, PhD[3]; Pierre Soubeyran, MD, PhD[4]; Shabbir M. H. Alibhai, MD, MSc[5,6]; and Marije E. Hamaker, MD, PhD[7]

CONTEXT

Key Objective

Why is geriatric assessment and management (GA&M) recommended for older patients with cancer pretreatment?

Knowledge Generated

Older patients are heterogeneous, and tailoring cancer treatment to the individual requires weighing risks against benefits in the context of frailty, which is best assessed through geriatric assessment. GA&M can improve prognostication and risk stratification and communication with patients and caregivers, guide treatment adaptations, and provide nononcologic interventions to increase resilience.

Relevance

As increasing evidence shows that GA&M can improve the course of treatment, with less chemotherapy-related toxicity, lower rates of complications after surgery, and improved functional status and quality of life, the challenge is now about implementation into clinical practice.

TABLE 1. Geriatric Assessment Domains, Tools, and Proposed Interventions

Domain	Assessment Tool Examples	Evidence	Intervention and Examples
Functional status	ADLs (ie, transferring and eating) IADLs (ie, managing finances, cooking, and driving)	Association with chemotherapy toxicity, hospital admissions, functional decline, and mortality[4,39,46,55]	Aids such as motorized wheelchair Meals on Wheels Physiotherapy Occupational therapy
Objective physical performance	4 m gait speed, TUG; SPPB; grip strength; sarcopenia	Prediction of mortality, treatment-related complications, and functional decline[56-58]	Structured exercise Assistive devices
Falls	No. falls in previous 6 months	Related to chemotherapy toxicity, postoperative complications, and functional decline[24,59]	Falls prevention program
Cognitive function	MMSE, MoCA, Mini-Cog, and BOMC	Assessment of capacity for consent or treatment adherence and cognitive decline associated with treatment. Association with poorer overall survival, chemotherapy toxicity, and delirium[22,43,60]	Support during treatment trajectory Delirium prevention program Treatment reminders, eg, text messages for daily radiation therapy appointments
Mood (depression)	GDS, HADS, and PHQ2/9	Assessment of psychologic adjustment to treatment. Association with postoperative complications, treatment tolerance, functional decline, and mortality[45,46,55,61]	Cognitive-behavioral therapy Medical therapy Counseling
Nutritional status	MNA, BMI, and weight loss combined	Association with mortality, likelihood of treatment completion, and healthcare consumption[62,63]	Dietary counseling
Comorbidity	CIRS-G, CCI, and OARS comorbidity	Assessment of competing causes of mortality, survival, treatment tolerance, and hospital admissions[61,64]	Referral to organ specialist
Polypharmacy	List of medications, STOPP-START, and Beers criteria	Postoperative complications, chemotherapy toxicity, functional decline, and mortality[65]	Geriatrician or clinical pharmacist review of medications
Social support	Focused questions regarding social support, MOS-SSS, and MPSSS	Association with cancer progression, chemotherapy toxicity, poorer survival, and treatment adherence[66]	Home nursing Transportation assistance Buddy support schemes Referral to community or cancer support groups

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INTERVENTI DI SUPPORTO GERIATRICO

TABLE 2. Design of Studies on Geriatric Assessment and Management

Reference	Location	Publication Type	Selection Criteria	Cancer Type	Type of Treatment	Study Design	Type of GA	GA Included in Oncologic Treatment Decision?	Management Strategy for Geriatric Impairments and Follow-Up
Abel et al[67]	United States	A	Age ≥ 75	Hematologic	CT	Random assignment	C	Unclear	Geriatric co-management
Corre et al[34]	France	F	Age ≥ 70, PS 0-2	NSCLC	CT	Random assignment	A	Yes	None
Derman et al[68]	United States	F	Age ≥ 60	Hematologic	CT	Historic controls	MDT	Yes	Predefined intervention protocol
Kalsi et al[35]	United Kingdom	F	Age ≥ 70	Various	CT	Historic controls	C	No	Geriatric co-management
Li et al[6]	United States	A	Age ≥ 65	Various	CT	Random assignment	MDT	No	Predefined intervention protocol
Mohile et al[5]	United States	A	Age ≥ 70, > 1 geriatric impairment	Various	CT	Random assignment	A	Yes	Predefined intervention protocol
Nadaraja et al[69]	Denmark	F	Age ≥ 70	Various	CT	Random assignment	C	Yes	Geriatric co-management
Puts et al,[49] Sattar et al[70]	Canada	F	Age ≥ 70	Various	CT	Random assignment	A	No	Predefined intervention protocol
Soo et al[7]	Australia	A	Age ≥ 70	Various	CT	Random assignment	C	Unclear	Not specified
Hempenius et al[50,71]	Netherlands	F	Age > 65, GFI > 3	Various	Surgery	Random assignment	C	No	Geriatric co-management
Ho et al[72]	Hong Kong	A	Age > 70, fit for resection	Colorectal	Surgery	Random assignment	C	No	Geriatric co-management
Mak et al[73]	Hong Kong	A	Age > 70	Colorectal	Surgery	Matched controls	C	No	Geriatric co-management
Odetto et al[74]	Argentina	A	Age ≥ 70	Colorectal	Surgery	Random assignment	MDT	Yes	Not specified
Ommundsen et al[75]	Norway	F	Age > 65, frailty criteria	Colorectal	Surgery	Random assignment	C	No	Geriatric co-management
Qian et al[76]	United States	A	Age ≥ 65	GI	Surgery	Random assignment	C	No	Management recommendations made to surgery or oncology team
Singh et al[77]	United Kingdom	A	Frailty or multimorbidity	GI	Surgery	Historic controls	C	No	Proactive postoperative multidisciplinary support
Fletcher et al[36]	Australia	A	Age ≥ 70	Various	Various	Matched controls	MDT	Yes	Not specified
Magnuson et al[78]	United States	F	Age ≥ 70, stage III/IV	Various	Various	Random assignment	A	No	Predefined intervention protocol
Pattinson et al[79]	United Kingdom	A	Age ≥ 70	Upper GI	Various	Historic controls	MDT	Yes	Follow-up by GA team
Rao et al[48]	United States	F	Age ≥ 65, hospitalized, frail	Various	Various	Random assignment	C	No	Geriatric co-management

Abbreviations: A (publication type), abstract; A (type of GA), geriatric assessment by oncology team; C, geriatric consultation; CT, chemotherapy; F, full text; GA, geriatric assessment; GFI, Groningen Frailty Indicator; MDT, geriatric assessment by multidisciplinary team; NSCLC, non–small-cell lung cancer; PS, performance status.

Rostoft et al. JCO 2021

ASCO Special Articles

Practical Assessment and Management of Vulnerabilities in Older Patients Receiving Systemic Cancer Therapy: ASCO Guideline Update

William Dale, MD, PhD[1]; Heidi D. Klepin, MD, MS[2]; Grant R. Williams, MD, MSPH[3]; Shabbir M.H. Alibhai, MD[4]; Cristiane Bergerot, PhD[5]; Karlynn Brintzenhofeszoc, PhD, MSW[6]; Judith O. Hopkins, MD[7]; Minaxi P. Jhawer, MD[8]; Vani Katheria, MS[9]; Kah Poh Loh, MBBCh BAO, MS[10]; Lisa M. Lowenstein, PhD[11]; June M. McKoy, MD, MPH, JD, MBA[12]; Vanita Noronha, MD[13]; Tanyanika Phillips, MD[14]; Ashley E. Rosko, MD[15]; Tracy Ruegg, PhD, ANP[16]; Melody K. Schiaffino, PhD[17]; John F. Simmons Jr, MD[18]; Ishwaria Subbiah, MD[19]; William P. Tew, MD[20]; Tracy L. Webb, PA-C[21]; Mary Whitehead, BFA[22]; Mark R. Somerfield, PhD[23]; and Supriya G. Mohile, MD, MS[10]

DOI https://doi.org/10.1200/JCO.23.00933

ABSTRACT

PURPOSE To update the ASCO guideline (2018) on the practical assessment and management of age-associated vulnerabilities in older patients undergoing systemic cancer therapy.

METHODS An Expert Panel conducted a systematic review to identify relevant randomized clinical trials (RCTs), systematic reviews, and meta-analyses from January 2016 to December 2022.

RESULTS A total of 26 publications met eligibility criteria and form the evidentiary basis for the update.

RECOMMENDATIONS The Expert Panel reiterates its overarching recommendation from the prior guideline that geriatric assessment (GA), including all essential domains, should be used to identify vulnerabilities or impairments that are not routinely captured in oncology assessments for all patients over 65 years old with cancer. Based on recently published RCTs demonstrating significantly improved clinical outcomes, all older adults with cancer (65+ years old) receiving systemic therapy with GA-identified deficits should have GA-guided management (GAM) included in their care plan. GAM includes using GA findings to inform cancer treatment decision-making as well as to address impairments through appropriate interventions, counseling, and/or referrals. A GA should include high priority aging-related domains known to be associated with outcomes in older adults with cancer: physical and cognitive function, emotional health, comorbid conditions, polypharmacy, nutrition, and social support. Clinical adaptation of the GA based on patient population, resources, and time is appropriate.

The Panel recommends the Practical Geriatric Assessment as one option for this purpose (https://old-prod.asco.org/sites/new-www.asco.org/files/content-files/practice-patients/documents/2023-PGA-Final.pdf; https://youtu.be/jnaQIjOz2Dw; https://youtu.be/nZXtwaGh0Z0).

Additional information is available at www.asco.org/supportive-care-guidelines.

ACCOMPANYING CONTENT

Appendix

Data Supplement

Accepted May 30, 2023
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Evidence Based Medicine Committee approval:
April 21, 2023

J Clin Oncol 00:1-20

View Online Article

Valutazione multidimensionale

-strumento di stratificazione di fenotipi clinici
- gestione clinica/terapia di supporto basata su VMD
- processo decisionale medico
- obiettivi centrati su VMD e priorità del paziente

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TABLE 2. Characteristics and Selected Results of RCTs Identified in the Literature Search Conducted for Clinical Question 1—The Role of GA in Adults With Cancer to Suggest Specific Interventions to Improve Clinical Outcomes

Trial/Authors/ Citation	Setting/Design	Patient Characteristics	GA-Guided Intervention	Primary Outcomes	Secondary Outcomes
GAIN study (Li et al[4])	Academic setting: NCI-designated cancer center Single-center RCT	N = 605 Age 65+ years (mean age: 72.2 years) Solid tumors All cancer stages All fitness levels Chemo-based treatments	Intervention arm: Intervention and referrals, based on predetermined thresholds. Geriatric nurse practitioner–guided referrals to a multidisciplinary team (oncologist, nurse practitioner, social worker, physical and occupation therapist, nutritionist, and pharmacist). Follow-up by the geriatric nurse practitioner Control arm: GA information is sent to the oncologist	Chemotoxicity: 50% toxicity in intervention arm *v* 60% toxicity in control arm (P = .02)	(+) Significant improvement in advance directive (AD) completion in the intervention arm No significant changes in ER visits, hospitalizations, dose modifications, early discontinuation of treatment No difference in overall survival
GAP70+ study (Mohile et al[3])	Community oncology practices, NCORP network Cluster-randomized trial	N = 718 Age 70+ years (mean age: 77.2 years) Solid tumors + lymphoma Advanced cancer Presence of at least 1 impaired GA domain Chemo-based treatment regimen with ≥50% risk of serious toxicity	Intervention arm: GA summary and management recommendations (including dose reduction) sent to the oncologist Control arm: Oncologists received alerts for impaired depression or cognitive score	Chemo-toxicity: 50% toxicity in intervention arm *v* 70% toxicity in control arm (RR, 0.74; 95% CI, 0.64 to 0.86; P = .0001)	(+) Significantly fewer falls in the intervention arm (+) More medications discontinued (reducing polypharmacy) in the intervention arm (+) More dose reductions due to toxicity seen in the control arm (+) Reduced treatment intensity in the intervention arm, but no significant differences in overall survival
GERICO trial (Lund et al[14])	Academic setting Single-center RCT	N = 142 Age 70+ years (median age: 75 years) Colorectal cancer Stage II-IV Adjuvant or first-line palliative chemo Vulnerable (G-8 ≤14 patients) Life expectancy ≥3 months ECOG PS 0-2	Intervention arm: Interventions, including referral to dietician and exercise program, offered to patients after completion of GA. GA-based interventions were followed up after 2 months or more frequently, if needed Control arm: Patients received standard treatment (with a possible 25% primary dose reduction if toxicity concerns were raised at first oncologic assessment). Coexisting health problems among controls were assessed by either an oncologist or general practitioner	Chemotherapy completion (without dose reductions or delays): 45% in intervention arm *v* 28% in control arm (P = .0366)	(+) Intervention arm has less severe toxicity compared to control arm (+) Quality of life (decreased burden of illness and improved mobility) was significantly improved in the intervention arm (+) Significantly less secondary dose reductions and more patients received the planned dose in the intervention arm No significant differences in overall dose reductions and/or delays No significant differences in overall survival
COACH (Mohile et al[15])	Community oncology practices, NCORP network Cluster-randomized trial	N = 541 Age 70+ years (mean age: 76.6 years) Solid tumors + lymphoma Advanced cancer Presence of at least one impaired GA domain Caregiver age 21+ (could enroll if no caregiver; n = 414) Receiving any systemic therapy	Intervention arm: Geriatric assessment summary and management recommendations sent to the oncologist Control arm: Oncologists received alerts for impaired depression or cognitive score	Patient satisfaction with communication about aging-related concerns: intervention arm was more satisfied after the visit with communication about aging-related concerns (P = .04)	(+) Significantly more aging-related conversations in the intervention group (+) Significantly increased caregiver satisfaction with communication about aging-related concerns No significant differences in quality of life (for patients and caregivers) outcomes

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TABLE 2. Characteristics and Selected Results of RCTs Identified in the Literature Search Conducted for Clinical Question 1—The Role of GA in Adults With Cancer to Suggest Specific Interventions to Improve Clinical Outcomes (continued)

Trial/Authors/ Citation	Setting/Design	Patient Characteristics	GA-Guided Intervention	Primary Outcomes	Secondary Outcomes
5C trial (Puts et al[17])	Academic setting, tertiary cancer centers Single-blind multicenter RCT	N = 350 Age 70+ years (mean age: 76 years) Solid cancer, lymphoma, or myeloma First- or second-line chemo, immunotherapy, or targeted therapy Treatment received before or status after one cycle of therapy ECOG PS 0-2	Intervention arm: Patients received GA (per patient request most received the GA on or after treatment initiation). Based on the GA results, predefined evidence-based interventions that were deemed relevant by the intervention team and patient were implemented. Summary of GA results and recommendations were provided to the treating oncologist and primary care team. A nurse from the intervention team continued to follow the patients with monthly phone calls for 6 months. Control arm: Patients received SOC per their oncology team and healthy aging pamphlets	Quality of life: No significant difference in QOL at 6 or 12 months between arms	(+) 72% adherence rate to the intervention No significant differences in functional status, patient satisfaction, treatment modifications, unplanned hospitalization and/or emergency department visits, toxicity, and overall survival
INTEGRATE (Soo et al[16])	Academic setting: 2 metropolitan teaching hospitals, 1 metropolitan hospital Multicenter RCT	N = 154 Age 70+ years (median age: 75.5 years) Solid cancer or diffuse large B-cell lymphoma Chemo, targeted therapy, or immunotherapy No receipt of systemic anticancer therapy in the last 3 months	Intervention arm: Patients completed the study GA followed by geriatrician consultation at baseline and follow-up visits, with additional reviews as needed. A personalized management plan was created based on the patient's assessment and managed either by a single clinician and/or the multidisciplinary team based on needs identified. Most patients received the GA after treatment initiation Control arm: All participants received a booklet about chemo and brief verbal encouragement about exercise and nutrition. Control arm patients received standard care (eg, supportive care screening) and could be referred to a geriatrician by their clinician, but did not receive the study-specific CGA	Longitudinal change in QOL: the intervention arm reported better QOL over 24 weeks *v* the control arm ($P = .039$)	(+) Significant deterioration in social functioning seen in control arm *v* intervention arm; clinically important benefits of GA were suggested for several other domains (+) Significantly lower health care utilization (emergency presentations, hospitalizations) in the intervention arm (+) Significantly lower frequency of early discontinuation due to toxicity in the intervention arm Significantly more patients in the intervention arm with a self-reported KPS of 70 or less at 12 weeks No differences in treatment modification No differences in survival
EGeSOR (Paillaud et al[18])	Academic setting: 10 teaching hospitals, 3 nonteaching hospitals Multi-center RCT	N = 499 Age 65+ years (median age: 75.3 years) Head and neck cancer (macroscopic diagnosis, awaiting histologic confirmation)	Intervention arm: Patients completed a pretreatment GA with a geriatrician. The geriatrician participated in determining the cancer treatment plan and in the multidisciplinary team meeting. GA-driven interventions were recommended by the geriatrician or directly referred to the primary team. Patients continued to have follow-up visits with the geriatrician Control arm: Patients received SOC	Composite criterion including 6 month mortality, functional impairment, and weight loss. No statistically significant differences between arms	Not reported

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TABLE 2. Characteristics and Selected Results of RCTs Identified in the Literature Search Conducted for Clinical Question 1—The Role of GA in Adults With Cancer to Suggest Specific Interventions to Improve Clinical Outcomes (continued)

Trial/Authors/ Citation	Setting/Design	Patient Characteristics	GA-Guided Intervention	Primary Outcomes	Secondary Outcomes
Tailored GA follow-up (Ørum et al[19])	Academic setting Single-center RCT	N = 301 Age 70+ years (median age: 75 years) Head and neck, lung, upper GI tract, or colorectal cancer All stages Medical or radiation treatment	Intervention arm: Based on GA results, interventions were initiated if deficits were identified. The primary groups were pharmacologic, nutritional, physical, or social interventions. The GA results and interventions initiated were accessible to the oncologists in the medical chart and were sent electronically to the patient's general practitioner. The intervention group also received an individually TFU by the gMDT (up to 90 days following inclusion) Control arm: Received recommendations based on the baseline GA. The interventions were initiated according to CGA results. No TFU on the initiated interventions was performed, and no additional interventions were initiated by the gMDT	Adherence to cancer treatment: 61% of patients in the intervention arm completed treatment *v* 52% in the control arm (*P* = NS)	(+) Higher rates of hospitalizations in control arm (55%) *v* intervention arm (47%), but not statistically significant No significant differences in physical performance or daily life activities
HEME RCT (DuMontier et al[20])	Academic setting: NCI-designated cancer center Single Center RCT	N = 160 Age 75+ years (median age: 80.4 years) Lymphoma, leukemia, or multiple myeloma	Intervention arm: Received embedded geriatric consultation in addition to their standard oncologic care managed by their hematologic oncologist. Patients met with a geriatrician and were provided further management and interventions individualized to the patient based on clinical judgment and best-available evidence (including GA); no prespecified interventions were required. If indicated, geriatricians communicated with the patient's primary care provider and provided referrals (eg, physical therapy, psychiatry). Follow-up appointments were encouraged, but not required Control arm: Received standard care	1-year overall survival: No significant difference between arms (*P* = .65)	(+) Increased end-of-life goals-of-care discussions in the intervention arm (+) A majority of hematology-oncology clinicians' rated the GA consultation as useful (62.9%-88.2%) No significant differences in emergency department visits and hospitalizations

NOTE. (+) indicates statistically significant outcomes.

Abbreviations: CGA, comprehensive geriatric assessment; COACH, Improving Communication in Older Cancer Patients and Their Caregivers; ECOG, Eastern Cooperative Oncology Group; EGeSOR, Effectiveness of Geriatric Assessment-Driven Interventions on Survival and Functional and Nutritional Status in Older Patients with Head and Neck Cancer; G-8, Geriatric-8; GA, geriatric assessment; GAIN, Geriatric Assessment-Driven Intervention; GAP70+, Geriatric Assessment for Patients 70 Years and Older; GERICO, geriatric intervention in frail older patients receiving chemotherapy for colorectal cancer; gMDT, geriatric multidisciplinary team; INTEGRATE, Integrated Geriatric Assessment and Treatment Effectiveness; N, sample size; NCORP, NCI, Community Oncology Research Program; QOL, quality of life; RCT, randomized controlled trial; RR, relative risk; SOC, standard of care; TFU, tailored follow-up; *v*, versus.

VALUTAZIONE MULTIDIMENSIONALE

TABLE 3. Practical Geriatric Assessment Proposed Scoring and Recommendations

Domain	Measure	Items	Definition of Impairments	Recommendation if Patient Meets Threshold for Impairment
Physical function/ performance	Falls Physical function 4-meter gait speed	Single item of falls in last 6 months Walking one block and climbing one flight of stairs Time in seconds	≥1 falls[44,45] Any limitation (a little or lot)[44] Time ≥4 seconds (or gait speed ≤1.0 m/s[46,47])	(For falls specifically)—check orthostatic blood pressure and adjust blood pressure medications if blood pressure is low or low normal. Offer falls prevention handout Weigh risks and benefits of cancer treatment options, incorporating information about physical performance Consider physical therapy (outpatient or home-based depending on eligibility for home care): request gait/assistive device evaluation, lower-extremity strength, and balance training Consider occupational therapy (if eligible for home care, referral for home safety evaluation): request evaluation and treatment
Functional status	OARS IADL OARS activities of daily living (IADL)	6 IADL items (walking, transportation, meals, housework, medicines, and money) 3 ADL items (in/out of bed, dressing, and bath/shower)	Any IADL items with some help or unable[44,48,49] Any ADL items with some help or unable	Consider the following potential cancer treatment modifications, particularly in the noncurative treatment setting: (1) consider single agent rather than doublet therapy; (2) modify dosage (eg, 20% dose reduction with escalation as tolerated); (3) modify treatment schedule if appropriate Consider more frequent toxicity checks (weekly or every other week) Consider physical therapy (outpatient or home-based depending on eligibility for home care): request gait/assistive device evaluation, strength, and balance training Consider occupational therapy (outpatient or home-based depending on eligibility for home care): request evaluation and treatment for functional impairment
Nutrition/weight loss	Single item from the G-8 and MNA	Weight loss during the past 3 months? 0 = weight loss >3 kg (6.6 lbs) 1 = does not know 2 = weight loss between 1 and 3 kg (2.2 and 6.6 lbs) 3 = no weight loss (range, 0-3)	Score of 0[50,51]	Discuss concerns related to nutrition and how potential treatment may impact nutrition Consider recommendations and/or handouts for nutritional supplements, liberalize calorie-restricted diets; small frequent meals, and/or high-protein/high-calorie snacks Consider referral to (1) nutritionist/dietician, (2) dentist if poor dentition or denture issues, (3) speech therapy if difficulty with swallowing; (4) meals-on-wheels Use caution with highly emetogenic regimens and use aggressive antiemetic therapy Refer to physical therapy/occupational therapy for functional impairments affecting food intake Consider medications for loss of appetite
Social support	MOS social support 8 item	Instrumental items 1-4 Emotional items 5-8	Any instrumental item with none, a little, or some of the time[52,53] Any emotional item with none, a little, or some of the time[50,53]	Discuss adequacy and availability of social support at home Discuss who the patient can contact in case of an emergency Confirm documented health care proxy is in the medical record Consider referral or information on (1) social worker or (2) visiting nurse service or home health aide (if meets criteria) Order on-person lifeline emergency service
Psychological	PROMIS Anxiety 4-item GDS 5	Summed 4-20 raw score Sum of 1 point for no answer to item 1 and 1 point for yes answers to items 2-5 (range 0-5)	Raw score: ≥11[54,55] Score: ≥2[56,57]	Discuss history of mood issues and treatment history Consider referral to (1) psycho-oncology (social work, clinical psychology) for counseling, (2) psychiatry if severe symptoms or if already on medications that are inadequate, (3) spiritual counseling or Chaplaincy services, (4) palliative care if other physical and/or cancer symptoms present Consider initiating pharmacologic therapy if appropriate in conjunction with PCP Provide linkage to community resources (such as support groups and local/national buddy or volunteer programs) Assess suicide risk and/or elder abuse if appropriate

(continued on following page)

VALUTAZIONE MULTIDIMENSIONALE

TABLE 3. Practical Geriatric Assessment Proposed Scoring and Recommendations (continued)

Domain	Measure	Items	Definition of Impairments	Recommendation if Patient Meets Threshold for Impairment
Comorbidity	OARS comorbidity Hearing Vision	No/yes summed (0-13) Interference for each Single item Single item	≥3 conditions[58,59] Or any condition with a great deal of interference Specific for any history of diabetes, heart disease, or liver/kidney disease Fair/poor/deaf Fair/poor/blind	Initiate direct communication (written, electronic, or phone) with patient's PCP about the plan for the patient's cancer Discuss how comorbidities affect risks and benefits of treatments choices Modify dosage or schedule if there is concern about treatment tolerability or if there is a concern about worsening of comorbidities If history of diabetes (of any level)—avoid neurotoxic agents if another option is equivalent If history of heart disease (of any level)—consider minimizing volume of agents and/or administer at slower infusion rate If history of chronic liver or kidney disease (of any level)—adjust medication dose as appropriate to avoid accumulation Ensure wearing hearing aids if indicated and consider hearing specialist referral Pocket talker available for office visits Ensure wearing glasses if indicated Test for glaucoma (especially with steroid use) Consider vision specialist referral
Cognitive function	Mini-Cog	1 point for each word recall 2 points for clock draw if normal, 0 if abnormal Total of 5 points (range 0-5)	Score: 0-2 high likelihood of cognitive impairment[60,61]	Provide explicit and written instruction for appointments, medications, and treatments Elicit input from trusted confidant or caregiver about patient's cognition Assess decision-making capacity and elicit health care proxy information and input if the patient lacks decision-making capacity Consider referral to cognitive specialist (eg, neurologist or geriatrician) Consider occupational therapy referral for cognitive rehabilitation If dementia is suspected, consider neuropsychological testing
Geriatric assessment screening tool[a]	G-8	8 items (food intake, weight loss, mobility, neuropsychological problem, body mass index, prescription drug, self-perception of health, and age)	Score: 0-14 recommend completing a full geriatric assessment evaluation[62,63]	Administer the full PGA and implement the recommendations noted above based on the patient-reported results
Risk of chemotherapy toxicity[b]	CARG toxicity tool	11 items (sociodemographics, tumor/treatment variables, laboratory test results [hemoglobin, creatinine clearance], and geriatric assessment variables)	Score: 0-5 low risk 6-9 intermediate risk 10-23 high risk[64,65]	For intermediate- and high-risk patients, consider administering the full PGA and implement the recommendations noted above based on the patient-reported results Consider the following potential cancer treatment modifications, particularly for intermediate- and high-risk patients and taking into consideration noncurative treatment settings: (1) consider single agent rather than doublet therapy; (2) modify dosage (eg, 20% dose reduction with escalation as tolerated); (3) modify treatment schedule if appropriate Consider more frequent toxicity checks (weekly or every other week)

Abbreviations: ADL, activities of daily living; CARG, Cancer and Aging Research Group; GDS, Geriatric Depression Scale; G-8, Geriatric-8; IADL, instrumental activities of daily living; MNA, Mini Nutritional Assessment; MOS, Medical Outcomes Survey; OARS, Older Americans Resources and Services; PGA, Practical Geriatric Assessment.

[a]The Vulnerable Elders Survey-13 (VES-13) is an alternative geriatric assessment screening tool.[66,67]

[b]Chemotherapy Risk Assessment Scale for High-Age Patients (CRASH) Score is an alternative tool that can be used to calculate risk of chemotherapy toxicity.[68]

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PROCESSO MULTIDIMENSIONALE

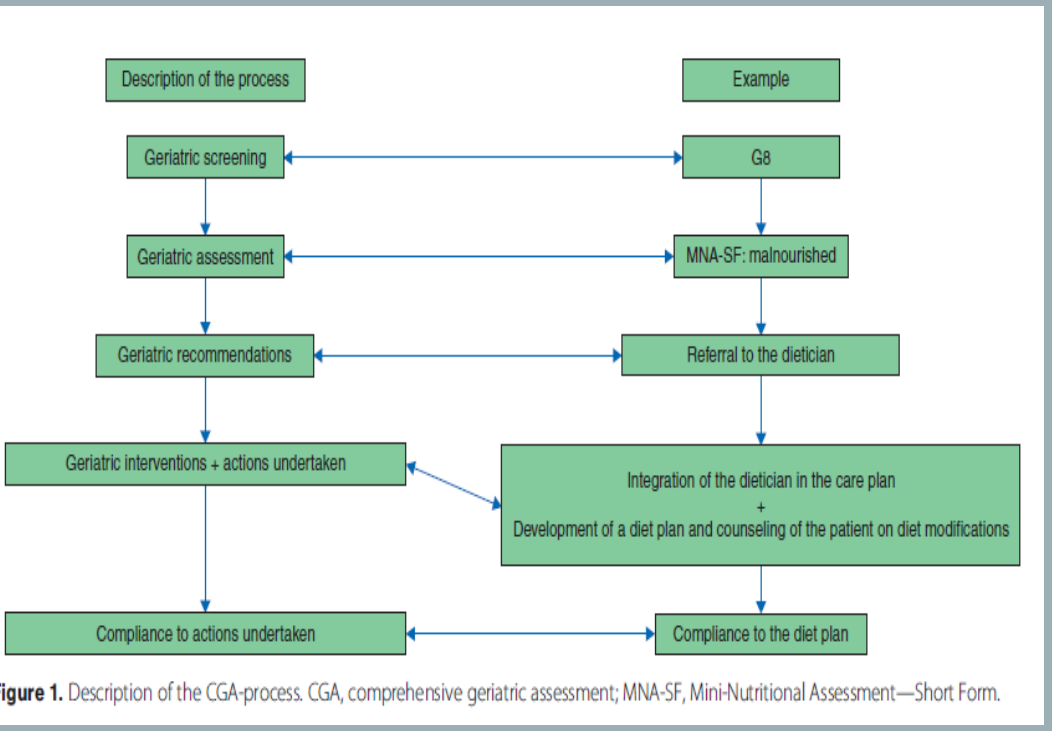
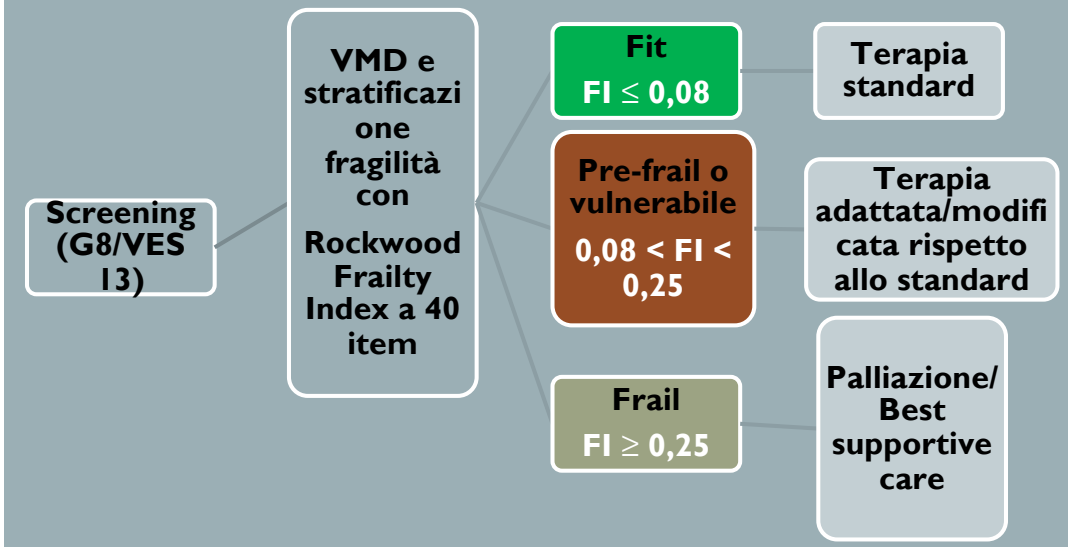


Figure 1. Description of the CGA-process. CGA, comprehensive geriatric assessment; MNA-SF, Mini-Nutritional Assessment—Short Form.



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Review

New Strategies for the Treatment of Older Myeloma Patients

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Simple Summary: While novel therapies have improved outcomes in multiple myeloma (MM), physicians are calling for greater caution when managing this hematologic malignancy in older patients due to their fragility, which increases their vulnerability to toxic events. Additionally, this patient population may be excluded from clinical trials due to comorbidities, whereby available data are not always applicable in real-word clinical practice. This review delves into available frailty assessment tools that can be used to identify patients who are unfit or frail and tailor therapy to achieve better outcomes while minimizing toxicity. Current therapeutic strategies for managing transplant-ineligible patients with newly diagnosed MM and relapsed or refractory MM are also described, with the aim of guiding physicians when selecting treatment options.

Abstract: Multiple myeloma (MM) mostly affects older patients, who represent a highly heterogeneous population. In the last few years, the introduction of novel agents led to a significant improvement in the outcome of MM patients. Nonetheless, this positive trend is less likely to occur in all older patients due to comorbidities/disabilities and major susceptibility to toxic events. Furthermore, older patients with major comorbidities are usually excluded or underrepresented in most registrational clinical trials. In this context, physicians have called for greater caution in the management of the disease. Several scores allow for the identification of frail and unfit patients and establish the possibility of tailoring therapy, reducing toxicity. This review explores the available tools for the assessment of frailty and what has been done to improve the discriminative power of the available scores. Thereafter, it describes the main therapeutic strategies for the management of transplant-ineligible (NTE) newly diagnosed (ND) MM patients and relapsed/refractory (RR) MM patients, in order to better guide physicians in choosing treatment options and to suggest possible strategies for more frail patients.

Keywords: multiple myeloma; elderly patients; frailty

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GERIATRIC ASSESSMENT

Demographic and social status, comorbidity, functional status, cognition, depression, nutrition, fatigue, polypharmacy, geriatric syndromes

SCORES	IMWG FRAILTY SCORE	SIMPLIFIED FRAILTY SCORE	R-MCI SCORE	REVISED FRAILTY INDEX (RFI)	MRP SCORE**	MAYO CLINIC SCORE
CRITERIA/ TOOLS	1. Age 2. CCI 3. ADL 4. IADL	1. Age 2. CCI 3. ECOG PS	1. Age 2. Renal function 3. Pulmonary function 4. Karnofsky PS 5. 5. Frailty status* 6. 6. Cytogenetics	1. Age 2. CCI 3. ADL 4. IADL CCI ≥3: - 1 point (RFI 1) - 2 points (RFI 2)	1. Age 2. WHO PS 3. ISS stage 4. CRP levels	1. Age 2. ECOG PS 3. NT-proBNP levels
CATEGORIES AND POINTS	FIT: 0 INTERMEDIATE FIT: 1 FRAIL: ≥2	NON-FRAIL: 0-1 FRAIL: ≥2	FIT: ≤3 INTERMEDIATE-FIT: 4-6 FRAIL: >6	FIT: 0 INTERMEDIATE-FIT: 1-2 FRAIL: ≥3	LOW RISK: < −0.256 MEDIUM RISK: −0.256 ≤ score ≤ −0.0283 HIGH RISK: > −0.0283	STAGE I: 0 STAGE II: 1 STAGE III: 2 STAGE IV: 3
SENESCENSE BIOMARKERS: DNA damage, telomere length, cell cycle arrest, etc.				SARCOPENIA: - Muscle mass: CT 3rd lumbar vertebra area - Muscle function: grips strength - Physical performance: gait speed, etc.		

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STRATIFICAZIONE DI FRAGILITÀ NEL MIELOMA MULTIPLO

PATIENT-RELATED FACTORS

- **Age**
- **Frailty**
- **Performance status**
- **Comorbidities**
- **Organ function**
- **Caregivers and social support**
- **Personal preference**
- **Quality of life**

DISEASE-RELATED FACTORS

- **Clinical MM presentation:**
  - renal failure
  - extramedullary disease
  - circulating plasma cells
  - rapid paraprotein increase
- **Cytogenetic risk**
- **Bone marrow reserve**

TREATMENT-RELATED FACTORS

- **Treatment goals** (survival prolongation vs. disease control)
- **Efficacy:**
  - degree of response
  - duration of response
  - treatment-free interval
- **Route of administration**
- **Potential adverse events**
- **Impact on quality of life and independence status**

Figure 2. Clinical considerations for treatment decision in transplant-ineligible patients. Abbreviations: MM, multiple myeloma.

Prognostic indicators of long-term mortality in older patients with multiple myeloma

Mariya Muzyka[1,2], Silvia Ottaviani[1], …, Irene Caffa[1,2], Tommaso Bonfiglio[1], Erica Parisi[2], Ana Guijarro[1,2], Alessio Signori, Marta Ponzano, Cristina Marulli, Luca Tagliafico[1], Roberto Lemoli[1,2], Alessio Nencioni[1,2#], Michele Cea[1,2#] and Fiammetta Monacelli[1,2#].

The primary aim of this study was to compare the prognostic accuracy of the gold standard IMWG FI with the geriatric based 40-item Rockwood Frailty Index (40-item Rockwood FI) on overall survival (OS) in older adults with a newly diagnosed MM.

Disease-related variables: SLiM-CRAB criteria present at diagnosis [20], histotype, MM staging according to Durie-Salmon (D-S) [21] and to the International Staging System (ISS) [22], cytogenetic risk with cytogenetic characterization ,presence of bone disease and number of lesions at diagnosis, presence of extramedullary disease at diagnosis, flow cytometric data if available.
Laboratory variables : blood count, creatinine, urea, coagulation profile (International normalized ratio (INR), prothrombin time (PT), partial thromboplastin time (PTT)), calcium, serum albumin, total serum proteins, total and direct bilirubin, Alanine transaminase (ALT), Aspartate transaminase (AST), beta2-microglobulin, Lactate dehydrogenase (LDH), serum free light chain (FLC) (ratio??), M component, 24-hour proteinuria and 24-hour Bence Jones proteinuria.
Frailty stratification: Full CGA assessment was performed and Frailty stratification

	Univariable		Multivariable		Multivariable stepwise	
	HR(95% CI)	p-value	HR(95% CI)	p-value	HR(95% CI)	p-value
Sex (female vs. male)	0.55 (0.15-1.96)	0.354	-	-	-	-
Age	1.10 (1.01-1.19)	0.022*	-	-	-	-
IMWG	1.67 (1.09-2.57)	0.019	1.54 (0.90-2.64)	0.112***	-	-
G8(≤14) (N=35)	0.76 (0.60-0.95)	0.016	0.92 (0.64-1.32)	0.640***	-	-
MMSE t0	0.90 (0.70-1.14)	0.368	-	-	-	-
Clock t0 (N=35)	1.43 (0.90-2.27)	0.127	-	-	-	-
MNA t0	0.81 (0.69-0.95)	0.008*	-	-	-	-
IADL t0	0.73 (0.56-0.96)	0.024*	-	-	-	-
Barthel/ADL t0	0.96 (0.91-1.01)	0.158	-	-	-	-
CIRS t0 (severity)	4.52 (1.05-19.36)	0.042	8.88 (1.03-76.47)	0.047	10.80 (1.67-69.72)	0.012
CIRS t0 (comorbidity)	1.21 (0.94-1.54)	0.137	-	-	-	-
GDS t0 (N=35)	1.27 (1.04-1.55)	0.021	0.96 (0.69-1.33)	0.805***	-	-
Tinetti t0 (N=34)	0.92 (0.81-1.04)	0.195	-	-	-	-
NRS RIPOSO t0	1.18 (0.95-1.48)	0.138	-	-	-	-
NRS DEAMB t0	1.25 (1.02-1.54)	0.034	1.27 (1.00-1.61)	0.051	1.30 (1.03-1.64)	0.026
Gjion t0	1.05 (0.86-1.29)	0.626	-	-	-	-
TUG (N=34)	1.07 (0.94-1.22)	0.311	-	-	-	-
HG	1.01 (0.96-1.06)	0.781	-	-	-	-
SARC F (N=20)	1.10 (0.80-1.51)	0.556	-	-	-	-
cut off CGA (≥3)	1.36 (1.03-1.79)	0.027*	-	-	-	-
num pharma	1.12 (0.96-1.31)	0.139	-	-	-	-
Rockwood t0 (0.1 increase)	1.57 (1.07-2.31)	0.021	1.58 (0.76-3.26)	0.221	2.12 (0.21-3.72)	0.009
SF36 t0/EurpQoL (0.1 increase) (N=35)	0.75 (0.55-1.02)	0.066	-	-	-	-

Submitted

SUGGESTIONE CLINICA MULTIDISCIPLINARE

Gloria Mangini

ASSESSMENT GERIATRICO NELLA GESTIONE DEL PAZIENTE ANZIANO AFFETTO DA SINDROME MIELODISPLASTICA: IL RUOLO DELLA STRATIFICAZIONE PER FRAGILITA' E DEI PROMS

INTRODUZIONE

Le **Sindromi Mielodisplastiche (MSD)** sono **malattie neoplastiche clonali** caratterizzate da **ematopoiesi inefficace** che si manifesta con displasia morfologica e **citopenia/e periferica/che**, è possibile la trasformazione in leucemia acuta mieloide (LAM). Colpiscono la popolazione anziana **(età media alla diagnosi 68-75 anni)**. Il trattamento dipende da fattori di rischio individuali che giocano un ruolo essenziale nel predire la sopravvivenza e la tolleranza alla terapia. I trattamenti al momento disponibili sono agenti stimolanti l'eritropoiesi (ESAs), agenti immunomodulanti, agenti ipometilanti (azacitidina), trapianto di cellule staminali e terapie di supporto (best supportive care e cure palliative). Nell'anziano costituiscono endpoints rilevanti, oltre alla risposta clinica, il mantenimento dell'assetto funzionale e di una buona qualità di vita [1]. Il Revised International Prognostic Scoring System (IPSS-R) e il WHO Classification-based PSS (WPSS) identificano cinque gruppi di rischio caratterizzati da diversa sopravvivenza (da 12 a 103 mesi) e diverso rischio di trasformazione in LAM (da 6 a 100%). L'IPSS-R include tra i fattori di rischio l'età e il Performance Status (Eastern Coopertive Oncology Group Performace Status) [2]. Tuttavia nei gruppi IPSS-R a rischio intermedio gli outcomes appaiono estremamente variabili [3]. La valutazione multidimensionale, la stratificazione per fragilità e l'inclusione di misure che valutino le aspettative e le priorità del paziente può orientare verso la pianificazioni di trattamenti personalizzati [4].

MATERIALI E METODI

Vengono valutati gli approcci volti al perfezionamento degli strumenti prognostici classici attraverso l'integrazione con i diversi domini della Valutazione Multidimensionale.

Keywords: Comprehensive Geriatric Assessment (CGA), Myelodysplastic syndromes, Myelodisplastic neoplasms, Elderly, Risk assessment, Frailty Index, Quality of Life, PROMs, Decision-making for older.

RISULTATI

Per indirizzare al trattamento ottimale i pazienti anziani alcuni modelli propongono di utilizzare l'IPSS e a seguire la Valutazione Multidimensionale (VMD) per suddividere i pazienti in categorie di rischio (go-go/fit, slow-go/vulnerable, no-go/frail) [5]. In altri modelli viene proposto di effettuare come screening iniziale un test di performance fisica Test Time Up and Go (TUGT) per identificare i pazienti Fit e poi completare la VMD per i restanti pazienti Pre-Frail e Frail [6]. **Sono fattori prognostici indipendenti di sopravvivenza la Fragilità, stimata tramite Clinical Frailty Scale (CFS) e le Comorbilità, quantificate con il Charlson Comorbility Index (CCI)** [7][8]. Altri fattori indipendentemente associati alla prognosi sono la presenza di deficit nelle attività base della vita quotidiana (ADL) e la malnutrizione (MNA) [9]. Fattori predittivi di ridotta sopravvivenza e di tossicità al trattamento sono la presenza di deficit nelle attività strumentali della vita quotidiana (IADL), la fatigue e la riduzione della qualità della vita (EQ-5D) [10]. Per tale valutazione è stata validata la Quality of Life in Myelodysplasia Scale (QUALMS) [11]. **Recentemente Starkman e Coll. hanno proposto un Frailty Index specifico per le MDS (MDS-FI) costituito da 42 deficits. Tale indice include BMI, Comorbilità, Clinical Frailty Scale (CSF), Scala delle IADL di Lawton-Brody (LB), Test di laboratorio e Test di performance fisica**; non include la percentuale di blasti e dati citogenetici poichè l'intento non è sostituire ma integrare il IPSS: **insieme all'età (>70 anni) e alla trasfusione-dipendenza MDS-FI aumenta il valore prognostico di IPSS del 53%** [12].

CONCLUSIONI

Il processo decisionale clinico (decision making) per i pazienti affetti da MDS è impegnativo: sia gli effetti della malattia che quelli del trattamento influiscono pesantemente sulla qualità della vita correlata alla salute (HRQoL). MDS-FI potrebbe orientare nella scelta del trattamento nei gruppi IPSS-R a rischio intermedio, prevedere la tossicità da chemioterapia, essere utilizzato per la rivalutazione periodica degli effetti ematologici, cognitivi e sociali dei trattamenti. Ridefinire il IPSS-R con il MDS-FI porta ad una stima migliore della sopravvivenza dei pazienti neodiagnosticati. **MDS-FI, incluso nei protocolli di cura insieme a misure di esito riferite dal paziente specifiche per le sindromi mielodisplastiche (MDS-specific Patient-Reported Outcome Measures) come il QUALMS (Quality of Life in Myelodysplasia Scale) [13] e a strumenti di shared decision-making come l'Outcome Prioritization Tool (OPT) [14], potrebbe contribuire alla definizione di un modello di cura dinamico centrato sulla persona.**
Tale modello faciliterebbe l'individuazione della terapia più appropriata e la definizione di obiettivi condivisi secondo i desideri e i bisogni emersi del malato [15].

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