Addressing the Needs of an Aging Nation: Merging Geriatricians and Oncology

Arti Hurria, MD
Director, Cancer and Aging Research Program
Associate Professor
City of Hope
Outline

- Geriatric Oncology: Rationale

- Research Directions
  - Predicting Chemotherapy Toxicity
  - Developing a Geriatric Assessment Tool for Oncologists
  - Cognitive Effects of Cancer Therapy

- Mentoring and Education
  - Mentoring the Next Generation of Geriatric Oncologists
  - Educating a Multidisciplinary Team
Cancer is a Disease Associated with Aging

60% of cancer occurs in people ≥ age 65

CDC, Morbidity and Mortality Weekly Report 2013
US Population Age ≥ 65 (millions)

2010
Largest growth in
Year

Shift in 2030:
Largest growth in the 80+ age groups

U.S Census Bureau 2010
Projected Rise in Cancer Incidence from 2010 to 2030

Year

Cancer Incidence (million)

2010

2030

Projected increase in cancer incidence from 2010 to 2030:
- 67% in patients 65+
- 11% in patients <65

Smith et al, J Clin Oncol 2009
Why Geriatric Oncology?
What’s Different About Older Patients?

- **Heterogeneity of Health Status**
  - Physiologic changes with aging
  - Increased prevalence of comorbid diseases

- **Side Effects and Symptoms**
  - Increased rates of adverse effects to medications
  - Atypical presentation of common illnesses

- Increased importance of social support
- Different goals of therapy
Clinical Trials Often Do Not Measure These Endpoints

Do We Address the Questions that Patients Want to Know?

Doctor, if I take the therapy…

- what is the quality of my survival?
- will I be functionally impaired?
- will I be cognitively impaired?
- what does my family need to prepare for?
The Mission ("the Dream")

One day, all older adults with cancer will receive personalized tailored care, utilizing evidence-based medicine with a multidisciplinary approach.

Cancer and Aging Research Program formed in November 2006
Efforts to Achieve the Mission – Grounded in Research and Education

Since Nov 2006:

➢ 24 geriatric oncology protocols
  ▪ Over 3200 patients accrued to cancer & aging studies

➢ Expanded peer-reviewed funding
  ▪ K award to 12 NIH grants

➢ Disseminate our findings
  ▪ Over 120 publications
  ▪ Development of the *Journal of Geriatric Oncology*
Identifying Older Adults at Increased Risk of Chemotherapy Toxicity
Aging is a Heterogeneous Process

Same Chronological Age; Different Functional Age
Geriatric Assessment

Factors other than chronological age that predict morbidity & mortality in older adults

- Functional status
- Comorbid medical conditions
- Cognition
- Nutritional status
- Psychological state
- Social support
- Medications (polypharmacy)
Can a Geriatric Assessment Predict Severe Chemotherapy Side Effects?
(K23, PI: Hurria)

- Primary Objective:
  - To determine the ability to identify patients at risk for severe chemotherapy-related side effects

- 10 participating institutions:
  - Cancer and Aging Research Group

- Published in the *Journal of Clinical Oncology*

  - Acknowledged as one of their top 50 cited articles
Eligibility criteria
- Age 65 or older
- Diagnosis of cancer
- To start a new chemotherapy regimen

Timepoint 1:
Pre-chemo Geriatric Assessment

Timepoint 2:
Post-chemo Geriatric Assessment
Chemotherapy: toxicity grading at each visit

Sample size: 750 patients
(500 Development Cohort; 250 Validation Cohort)

Hurria et al, JCO 2011
Predictors of Toxicity

- Age ≥ 72 years
- GI/GU Cancer
- Standard Dose
- Polychemotherapy
- Hemoglobin (male: <11, female: <10)
- Creatinine Clearance (Jelliffe-ideal wt <34)
- Fall(s) in last 6 months
- Hearing impairment (fair or worse)
- Limited in walking 1 block (MOS)
- Assistance required in medication intake (IADL)
- Decreased social activity (MOS)

Hurria et al, JCO 2011
MD-rated KPS vs. Predictive Model

Chemotherapy Toxicity Predictive Model

Development Cohort (N=500)

- Low: 31%
- Medium: 52%
- High: 83%

Validation Cohort (N=250)

- Low: 37%
- Medium: 62%
- High: 70%

P<0.001

% with Grade 3-5 Toxicity

MD KPS

Development Cohort

- 90-100: 51%
- 80: 51%
- ≤70: 62%

Validation Cohort

- 90-100: 52%
- 80: 62%
- ≤70: 67%

P=0.19

P=0.25

Hurria et al. JCO 2011
Current/Future Directions
**Objective:** To identify clinical and biological predictors of severe chemotherapy side effects in older patients with breast cancer

<table>
<thead>
<tr>
<th>Breast Cancer Cases (starting chemo)</th>
<th>Breast Cancer Control (no chemo)</th>
<th>Healthy Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>353 enrolled</td>
<td>90 enrolled</td>
<td>100 enrolled</td>
</tr>
</tbody>
</table>

**Timepoint 1:**
- Geriatric Assessment
- Blood Draw (biomarkers of aging)
- Upward arrows indicate multiple blood draws and geriatric assessments
- Chemotherapy: toxicity grading at each visit

**Timepoint 2:**
- Geriatric Assessment
- Blood Draw (biomarkers of aging)

**Timepoint 3:**
- Geriatric Assessment
- Blood Draw (biomarkers of aging)
- 2+ yrs

*Across 14 institutions*  
*COH Only*
Validation in Other Disease Types: Ongoing Cooperative Group Trials

- Ovarian: First Line Age $\geq$ 70 (Dr. VonGreunigan)
- Breast: Endocrine Therapy +/- Bevacuzimab (Dr. Dickler)
- Breast: Taxanes in Metastatic Breast Cancer (Dr. Rugo)
- AML: First Line Age $\geq$ 60 (Dr. Klepin/Dr. Ritchie)
- CLL: First Line Age $\geq$ 65 (Dr. Woyach)
- GI: First Line Age $\geq$ 75 (Dr. McCleary)
IRB#08147: Development of a Touchscreen Geriatric Assessment

- Computerized geriatric assessment
- Understand the needs of:
  - patients
  - their caregivers
- Collaborators:

Hsu et al. Cancer 2014
Objective: Evaluate the feasibility of capturing a geriatric assessment using an electronic geriatric assessment vs. paper-pencil

Arms:
- Paper-pencil and an electronic geriatric assessment (N=50)
- Electronic geriatric assessment at both timepoints (N=50)

Conclusions:
- Utilization of an electronic geriatric assessment is feasible
- Touchscreen methodology was preferred by patients
PREDICTION TOOL

Gender:

Select

Patient’s Age:

Patient’s Height
Select the Unit of Measure:

Select

Select the Height

Patient’s Weight:
Select the Unit of Measure:

Select

Select the Weight

Submit

Creatinine Clearance:
44 **

Toxicity Score:
10

Risk of Chemotherapy Toxicity:
72%

What does this mean?

* Dose delivered with first dose for chemotherapy
** Jelliffe formula

http://www.mycarg.org/mctc
Current/Future Directions
Objective: To determine whether the geriatric assessment driven interventions will lead to improvement patient outcomes

Pre-Chemotherapy (Baseline)
  • Geriatric Assessment
  • Calculation of Chemotherapy Toxicity Risk Score

RANDOMIZATION (2:1)

Usual Care

Usual Care + Geriatric Assessment Intervention
Facilitating Quality Cancer Care

Information Provided to the Healthcare Team

- Geriatric Assessment Results
- List of Potential Interventions
- Chemotherapy Toxicity Risk Score is Generated

<table>
<thead>
<tr>
<th>GA Results</th>
<th>Potential Interventions</th>
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<tbody>
<tr>
<td>Unintentional Weight Loss</td>
<td>- Nutritional Consult</td>
</tr>
<tr>
<td>Fall Risk</td>
<td>- Rehabilitation</td>
</tr>
<tr>
<td>Polypharmacy</td>
<td>- Pharmacy Consult</td>
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<tr>
<td>Limited Social Support</td>
<td>- Social Work</td>
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<tr>
<td></td>
<td>- Life Line</td>
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</table>
Facilitating Quality Cancer Care

Facilitates Communication and Decision-Making Between the Oncologist and Patient
Understanding the Cognitive Effects of Cancer Therapy in Older Adults
I would rather die than take a treatment that causes:

- functional impairment: 74%
- cognitive impairment: 88%

Fried et al. NEJM 2002: 346 (14): 1061
Worldwide Statistics: Cases of Dementia

Millions

Dementia in Older Adults

The Global Impact of Dementia 2013-2050
Few Cognitive Studies Focus on Older Adults

<table>
<thead>
<tr>
<th>Author</th>
<th>Design</th>
<th>Mean Age</th>
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<tr>
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<td>Ahles et al. 2002</td>
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<td>Tchen et al. 2003</td>
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<td>Bender et al. 2006</td>
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<td>Hurria et al. 2006</td>
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<td>Jenkins et al. 2006</td>
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<td>Hermelink et al. 2008</td>
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<td>Collins et al. 2009</td>
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<td>Jim et al. 2009</td>
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Longitudinal Cognitive Function of Older Women Receiving Adjuvant Chemotherapy

- Neuropsychological and functional testing performed:
  - Pre-chemotherapy
  - 6 months post-chemotherapy

25% with 1 SD decline in $\geq 2$ neuropsychological domains

Hurria et al. JAGS, 2006
N=35  
Age ≥ 65  
Breast Cancer  
Aromatase inhibitor

N=35  
Age ≥ 65  
Healthy Controls

Patients with Breast Cancer begin aromatase inhibitor

Timepoint 1:
- Memory Tests
- Geriatric Assessment
- Correlative Study:
  - PET scan
  - blood, urine

Timepoint 2:
- Memory Tests
- Geriatric Assessment
- Correlative Study:
  - PET scan
  - blood, urine

Results show no change in neuropsychological tests. Additional longitudinal follow-up is needed

Aromatase Inhibition & Cognitive Function

Cancer Time 2 > Cancer Time 1

Differences between Cancer Group (n=10) and Control Group (n=10)

Longitudinal changes in the right medial temporal lobe was found to be significant between the patient and control group

Pilot Studies – Interesting Observations

- Memory problems commonly reported prior to chemotherapy (2/3 age 65+)
- Patient perceived memory loss from pre- to post-chemo (50%)
- Neuropsychological test: 25% with 1SD decline
- Imaging may provide clues to underlying mechanisms
Current/Future Directions
Objective: Examining the effects of cancer treatment on memory in older women with breast cancer (age ≥ 60) and associations with quality of life.

Recruiting patients with breast cancer and healthy controls

Memory testing at 3 timepoints → 5 participating sites
  - Diagnosis
  - 12-months
  - 24-months

Optional saliva sample for APOE DNA testing

160 participants enrolled at COH
(68 cases & 92 controls)
Objective: Defining structural and functional changes of brain MRIs of older women (age ≥ 60) with breast cancer

3 arms: 1) Patients starting chemotherapy (N=25)
2) Patients starting on AI (not receiving chemo) (N=10)
3) Healthy women with no history of cancer (N=15)

Pre-Chemotherapy
- Memory Tests
- Geriatric Assessment
- Brain fMRI

Post-Chemotherapy
- Memory Tests
- Geriatric Assessment
- Brain fMRI

Toxicity Grading (NCI CTCAE v.4.0) for patients who receive chemotherapy

31 participants enrolled
Does Chemotherapy Accelerate Cognitive Aging?

Phase Shift Hypothesis:
The trajectory of cognitive dysfunction parallels normal aging

Accelerated Aging Hypothesis:
The trajectory of cognitive dysfunction is accelerated in comparison to normal aging

Hurria & Ahles 2012
IRB#14063: Cognitive Function of Older Breast Cancer Survivors (5-15 yrs post-dx) (R01, Multi PI: Hurria/Ahles [MSKCC]; BCRF, PI: Hurria)

**Breast Cancer Survivors**

Age ≥ 65
5-15 yrs post-diagnosis
- Prior exposure to chemo (N=160)
- No exposure to chemo (N=160)

**Healthy Controls** (N=160)

Age ≥ 65
No history of cancer and chemo

4 timepoints over 2 yrs
- Neuropsychological testing
- Geriatric assessment
- Frailty assessment
- Blood and saliva collection (APOE gene and allostatic load)

120 participants enrolled at COH
**Objective:** To correlate the fMRI parameters with findings in neurological functioning in older breast cancer survivors

**Breast Cancer Survivors**
- Prior exposure to chemo (N=20)
- No exposure to chemo (N=20)

**Healthy Controls** (N=20)
- Age ≥ 65
- No history of cancer and chemo

**One Timepoint**
- Brain fMRI
- NIH Toolbox Cognition Test
- Geriatric Assessment

**Enrollment onto IRB#14063**

**33 participants enrolled**
Education and Training
in Geriatric Oncology
Institute of Medicine:
“The healthcare workforce receives very little geriatric training and is not prepared to deliver the best possible care to older patients.”

<table>
<thead>
<tr>
<th>Healthcare Professionals</th>
<th>Geriatric Specialization or Certification</th>
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<tbody>
<tr>
<td>Physicians</td>
<td>1% - 2%</td>
</tr>
<tr>
<td>Nurses</td>
<td>&lt; 1%</td>
</tr>
<tr>
<td>Physician’s Assistant</td>
<td>&lt; 1%</td>
</tr>
<tr>
<td>Pharmacists</td>
<td>&lt; 1%</td>
</tr>
<tr>
<td>Social Workers</td>
<td>~4%</td>
</tr>
</tbody>
</table>

*IOM Report, Retooling for an Aging America: Building the Health Care Workforce 2008*
U13 AG038151 Grant
Collaboration with NIA, AGS, and Hartford

Goals:

- Support physician-scientists focused in aging research
  - GEMSSTAR awardees (R03 – RFA-AG-16-015)
- Accelerate the speed of discovery of geriatrics and gerontology research within the specialties

Three transdisciplinary meetings:

- Meeting #1: Frailty
- Meeting #2: Biology of aging
- Meeting #3: Cognition
R25 CA183723 Grant
Educating Nurses in Geriatric Oncology to Improve Quality Care

- Geriatric oncology curriculum for nurses
- Educate 400 nurses over 5 years
  - Team of 3 → Nurse manager, nurse educator, and RN/NP teams
- “Train the trainer”
  - Geriatric oncology initiatives at their own institution
  - Follow-up with participants 6, 12, and 18 months post-course
  - Monthly conference calls
Mentoring Junior Faculty in Geriatric Oncology: Report From the Cancer and Aging Research Group

Arti Hurria, City of Hope, Duarte, CA
Lodovico Balducci, H. Lee Moffitt Cancer and Research Institute, Tampa, FL
Arash Naeim, University of California, Los Angeles, Los Angeles, CA
Cary Gross, Yale University, New Haven, CT
Supriya Mohile, University of Rochester, Rochester, NY
Heidi Klepin, Wake Forest University, Winston-Salem, NC
William Tew, Memorial Sloan-Kettering Cancer Center, New York, NY
Leona Downey, University of Arizona, Tucson, AZ
Ajeet Gajra, University of New York Upstate Medical University, Syracuse, NY
Cynthia Owusu, Case Western Reserve University, Cleveland, OH
Homayoon Sanati, University of California at Irvine, Irvine, CA
Theodore Suh, The Cleveland Clinic, Cleveland, OH
Robert Figlin, City of Hope, Duarte, CA
Geriatric Assessment Development & Validation Cohort

Secondary Analyses as a Means of Mentoring
Polypharmacy in Older Adults with Cancer

Ronald Maggiore, MD

Use of Complementary Medications Among Older Adults With Cancer

Ronald J. Maggiore, MD1; Cary P. Gross, MD2; Kayo Togawa, MPH3; William P. Tew, MD4; Supriya G. Mohile, MD5; Cynthia Owusu, MD6; Heidi D. Klepin, MD7; Stuart M. Lichtman, MD8; Ajeet Gajra, MD9; Rupal Ramani, BS3; Vani Katheria, BSc3; Shira M. Klapper, BS10; Kurt Hansen, BS3; and Arti Hurria, MD3; on behalf of the Cancer and Aging Research Group

Polypharmacy and Potentially Inappropriate Medication Use in Older Adults with Cancer Undergoing Chemotherapy: Effect on Chemotherapy-Related Toxicity and Hospitalization During Treatment

Ronald J. Maggiore, MD, a William Dale, MD, PhD, b Cary P. Gross, MD, c,d Tao Feng, PhD, e William P. Tew, MD, f Supriya G. Mohile, MD, g Cynthia Owusu, MD, b Heidi D. Klepin, MD, i Stuart M. Lichtman, MD, f Ajeet Gajra, MD, j,k Rupal Ramani, BS, e Vani Katheria, BSc, e Laura Zavala, BS, e and Arti Hurria, MD, e on behalf of the Cancer and Aging Research Group

Maggiore et al, Cancer 2012

Maggiore et al, JAGS 2014
CA125 Level Association With Chemotherapy Toxicity and Functional Status in Older Women With Ovarian Cancer

Elizabeth Won, MD,* Arti Hurria, MD,† Tao Feng, MS,‡ Supriya Mohile, MD,§ Cynthia Owusu, MD,§ Heidi D. Klepin, MD,‖ Cary P. Gross, MD,¶ Stuart M. Lichtman, MD,* Ajeet Gajra, MD,# William P. Tew, MD,* and On behalf of the Cancer and Aging Research Group

Won et al, Int J Gynecol Cancer 2013

Psychological Status

Talia Weiss Wiesel, MA

The relationship between age, anxiety, and depression in older adults with cancer


Weiss Wiesel et al. Psycho-oncology 2014
Primary Dose Reductions

Ajeet Gajra, MD

Predictors of chemotherapy dose reduction at first cycle in patients age 65 years and older with solid tumors

Ajeet Gajra\textsuperscript{a,*}, Heidi D. Klepin\textsuperscript{b}, Tao Feng\textsuperscript{c}, William P. Tew\textsuperscript{d}, Supriya G. Mohile\textsuperscript{e}, Cynthia Owusu\textsuperscript{f}, Cary P. Gross\textsuperscript{g}, Stuart M. Lichtman\textsuperscript{d}, Tanya M. Wildes\textsuperscript{h}, Andrew E. Chapman\textsuperscript{i}, Efrat Dotan\textsuperscript{j}, Vani Katheria\textsuperscript{c}, Laura Zavala\textsuperscript{c}, Chie Akiba\textsuperscript{c}, Arti Hurria\textsuperscript{c,**}
on behalf of the Cancer and Aging Research Group (CARG)

Gajra et al, J Geriatr Oncol 2015

Targeted Therapy

Supriya Mohile, MD, MS

Toxicity of Bevacizumab in Combination with Chemotherapy in Older Patients

Supriya G. Mohile,\textsuperscript{a} Molly Hardt,\textsuperscript{b} William Tew,\textsuperscript{c} Cynthia Owusu,\textsuperscript{d} Heidi Klepin,\textsuperscript{e} Cary Gross,\textsuperscript{f} Ajeet Gajra,\textsuperscript{g} Stuart M. Lichtman,\textsuperscript{c} Tao Feng,\textsuperscript{h} Kayo Togawa,\textsuperscript{h} Rupal Ramani,\textsuperscript{h} Vani Katheria,\textsuperscript{h} Kurt Hansen,\textsuperscript{h} Arti Hurria,\textsuperscript{h}
on behalf of the Cancer and Aging Research Group

Mohile et al, Oncologist 2013
Outstanding Mentors are the Key to Success
Conceptual Model

**Researcher**
- Expert in the Field
- National Recognition
- Outstanding Training
- Academic Achievement

**Teacher**
- Relays Knowledge
- Instills Self-Confidence
- Realizes Potential
- Constructive Criticism

**Outstanding Mentor**

**Protector (Family)**
- Committed to Mentee
- Provide Shelter/Practical Necessities
- Selfless
- Creates Opportunities
- Fostering Independence
- Nurturing Environment

**Role Model**
- Respect
- Integrity
- Humility
- Perseverance
- Inspirational
Statistical Analysis

1. Bivariate analysis
2. Multivariate Logistic Regression
3. Developed a Predictive Model for the Perfect Mentor
4. Internal Validation
Perfect Mentor Model
Internal Validation: The 10-fold Cross Validation

The Perfect Mentor Does Exist
Conclusions

- The population is aging
- Cancer is a disease associated with aging

A melding of geriatric and oncology principles:
  - Understand the risks and benefits of treatment
  - Personalize cancer treatment decisions

- Mentors are needed ➔ A perfect mentor model does exist
The mission of the Cancer and Aging Research Group is to join geriatric oncology researchers across the nation in a collaborative effort of designing and implementing clinical trials to improve the care of older adults with cancer.
Acknowledgments

The Cancer and Aging Research Program
Acknowledgments

UNC Collaborators
City of Hope

Funders
The NIA and NCI
American Society of Clinical Oncology
The John A. Hartford Foundation
The Association of Specialty Professors
The American Federation for Aging Research
The Breast Cancer Research Foundation
Hearst Foundation
UniHealth Foundation
Thank you!