

Development and Validation of a Chemotherapy Toxicity Risk Score for Older Patients with Breast Cancer Receiving Adjuvant/Neoadjuvant Treatment

A R01 and BCRF Funded Prospective Multicenter Study
On Behalf of the Cancer and Aging Research Group

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Disclosures

Hurria:

- Research Funding:
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Magnuson:

- None

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Background

- Breast cancer is a disease of older adults
- Older adults are underrepresented in clinical trials
- Older adults are at increased risk for treatment toxicity
- Few tools available to help weigh the risk and benefits of adjuvant therapy in older adults
 - CARG toxicity tool developed and validated in older adults with all solid tumor malignancies

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Development of a Predictive Model for Tolerance to Therapy in Older Patients with Breast Cancer



Same Chronological Age; Different Functional Age

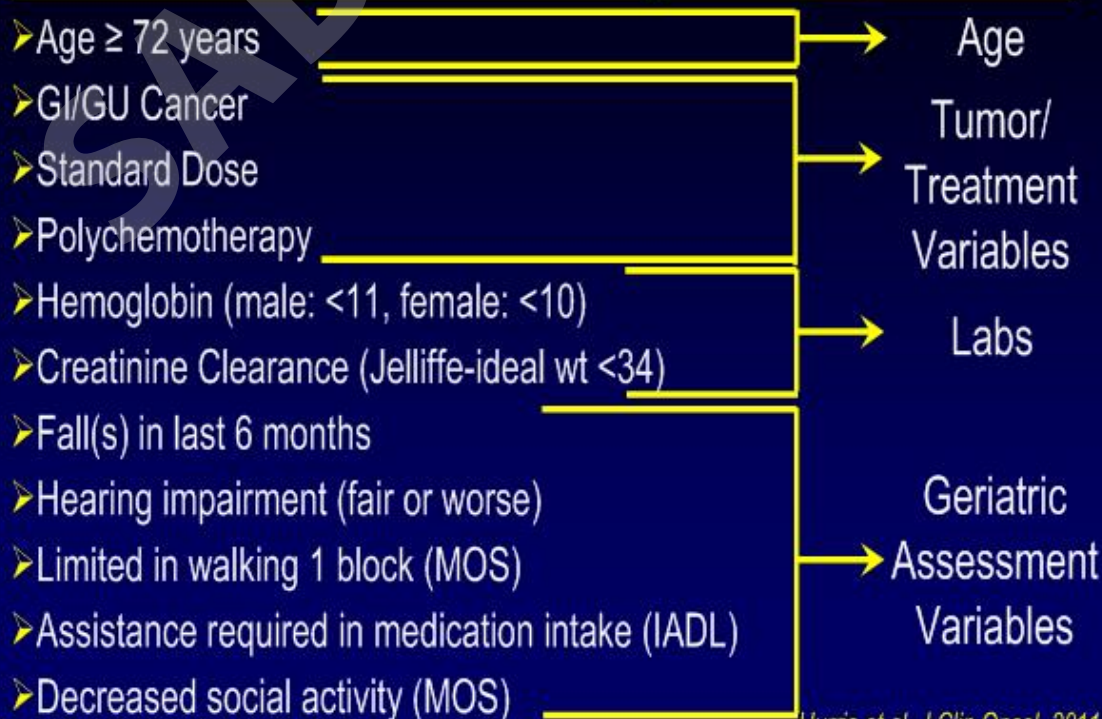
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Geriatric Assessment

Functional Status	Activities of Daily Living; Instrumental Activities of Daily Living; Karnofsky Performance Rating Scale; Timed Up & Go; Number of Falls in Last 6 Months
Comorbidity	Physical Health Section
Cognition	Blessed Orientation-Memory-Concentration Test
Psychological Status	Mental Health Index-17
Social Functioning	MOS Social Activity Limitations Measure
Social Support	MOS Social Support Survey: Emotional & Tangible Subscales
Nutrition	Body Mass Index; % Unintentional Weight Loss in the Last 6 Months

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CARG Toxicity Tool



Hurria et al, *J Clin Oncol*, 2011

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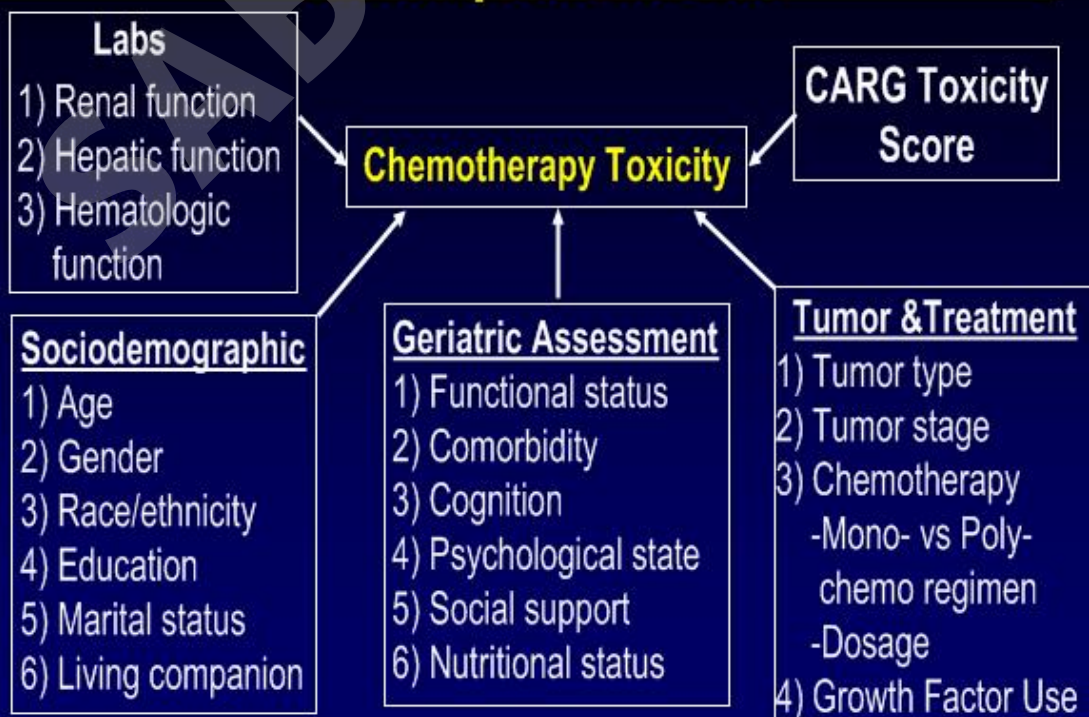
Objective

- To build upon the CARG score by developing and validating a breast cancer specific adjuvant chemotherapy toxicity score for older patients (CARG-BC)

- To evaluate the CARG-BC's association with:
 - dose modifications
 - reduced relative dose intensity
 - hospitalizations

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Conceptual Model



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Study Schema

Eligibility Criteria

- Age \geq 65
- Stage I-III BC
- To receive adjuvant or neoadjuvant chemotherapy

Timepoint 1:

Pre-chemo
Geriatric
Assessment

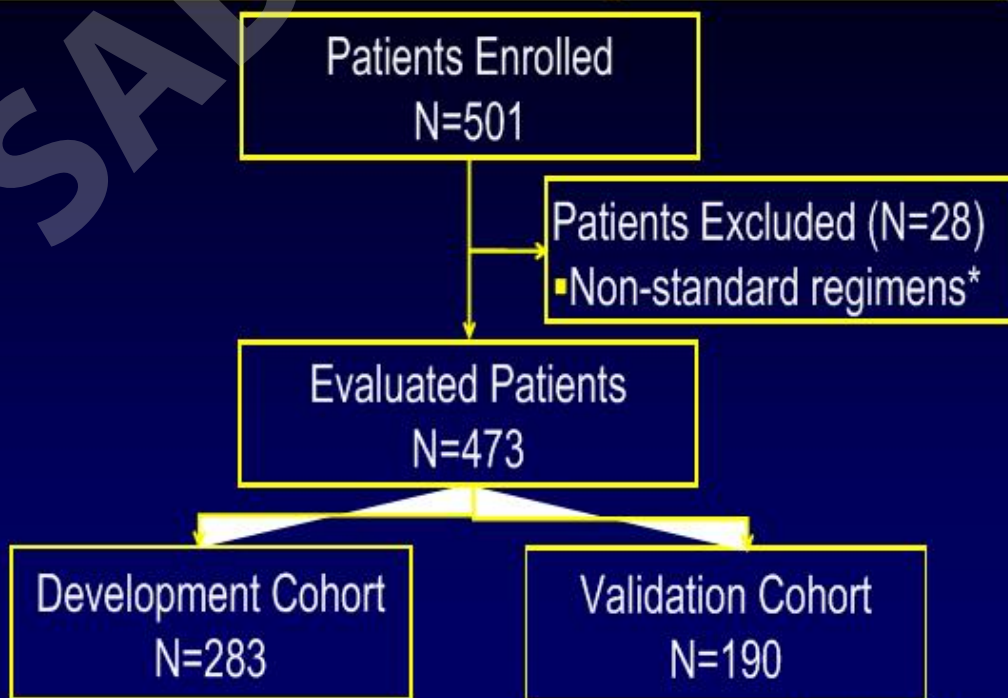


Timepoint 2:

Post-chemo
Geriatric
Assessment

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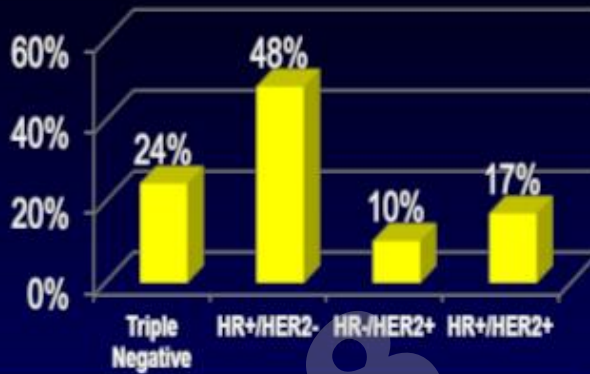
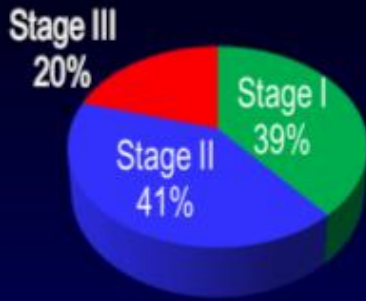
CONSORT Diagram



*per NCCN Guidelines

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Disease and Treatment Characteristics

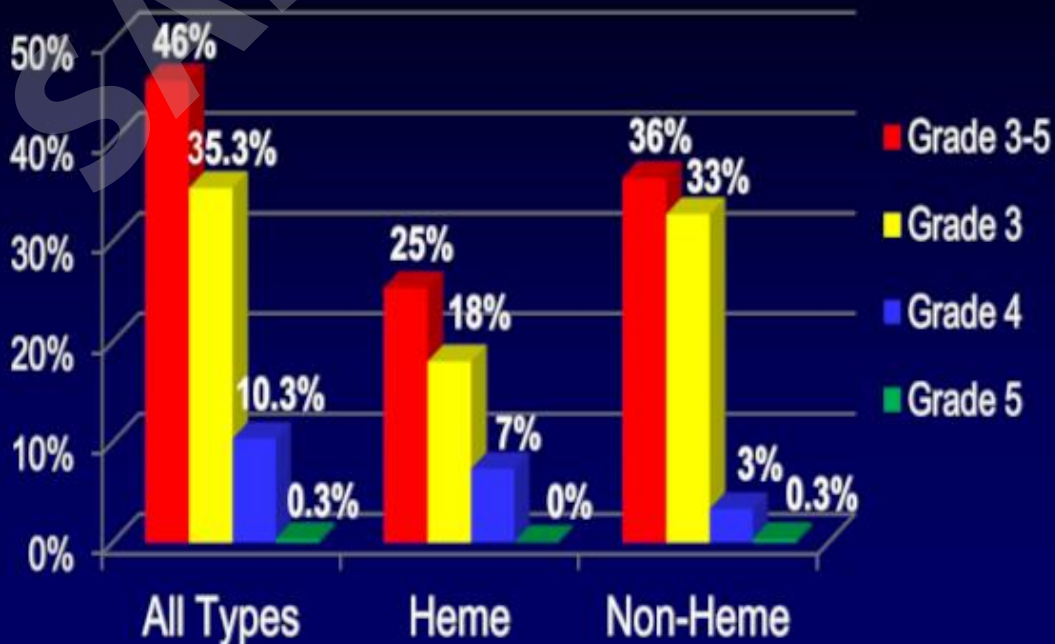


Median Age
(Range):
70 (65-85)

Adjuvant Treatment	82.3%
Poly Chemotherapy	90.1%
Anthracycline-Based Regimen	38.1%
Standard Dose	97.5%

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Toxicity Summary



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Treatment Related Outcomes

- 24% required a dose reduction during therapy
- 26% had a dose delay
- 24% discontinued therapy
- 25% received a relative dose intensity < 85%
- 23% had a hospitalization during treatment

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Statistical Analysis

- CARG score
- Selection of additional variables
 - Disease, tx, labs, GA variables: $p < 0.1$ in bivariate analysis or clinically relevant
- Predictive model development
 - Best-subsets selection method
 - Goodness of fit & AUC
- Internal validation (10-fold cross-validation)
- External validation
- Other outcomes (Chi-square test)

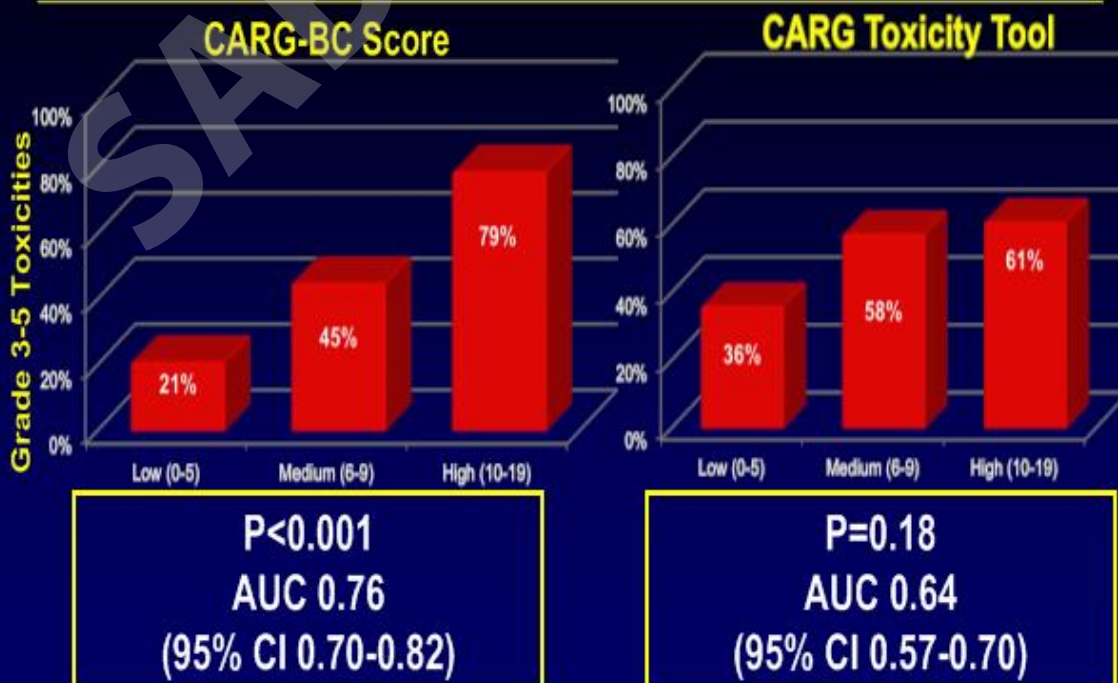
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CARG-BC Risk Score

Risk factors for Gr. 3-5 Toxicity	OR (95% CI)	Score
CARG Score: Medium Risk	2.47 (1.35-4.51)	3
High Risk	2.26 (0.70-7.35)	
Anthracycline	1.37 (0.65-2.85)	1
Stage II/III	1.79 (1.00-3.23)	2
Duration of tx > 3 months	2.98 (1.46-6.09)	4
Abnormal liver function	2.21 (0.90-5.47)	3
Limited in walking a mile	2.22 (1.21-4.05)	3
Lack of someone to provide advice	2.34 (0.99-5.58)	3

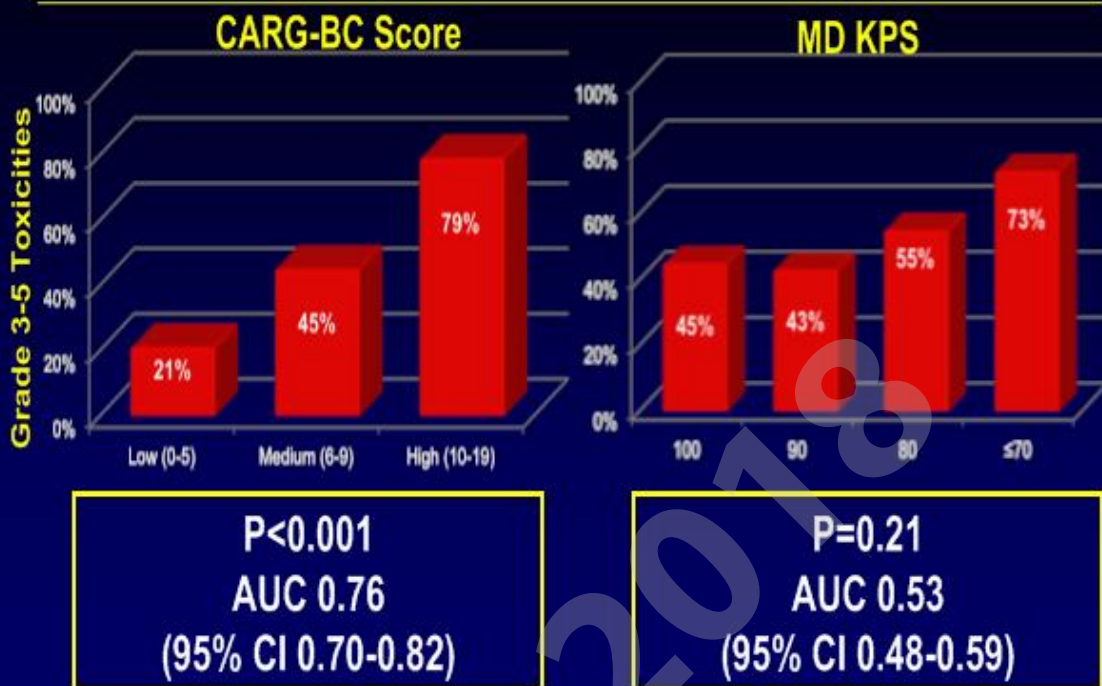
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CARG-BC Model Performance



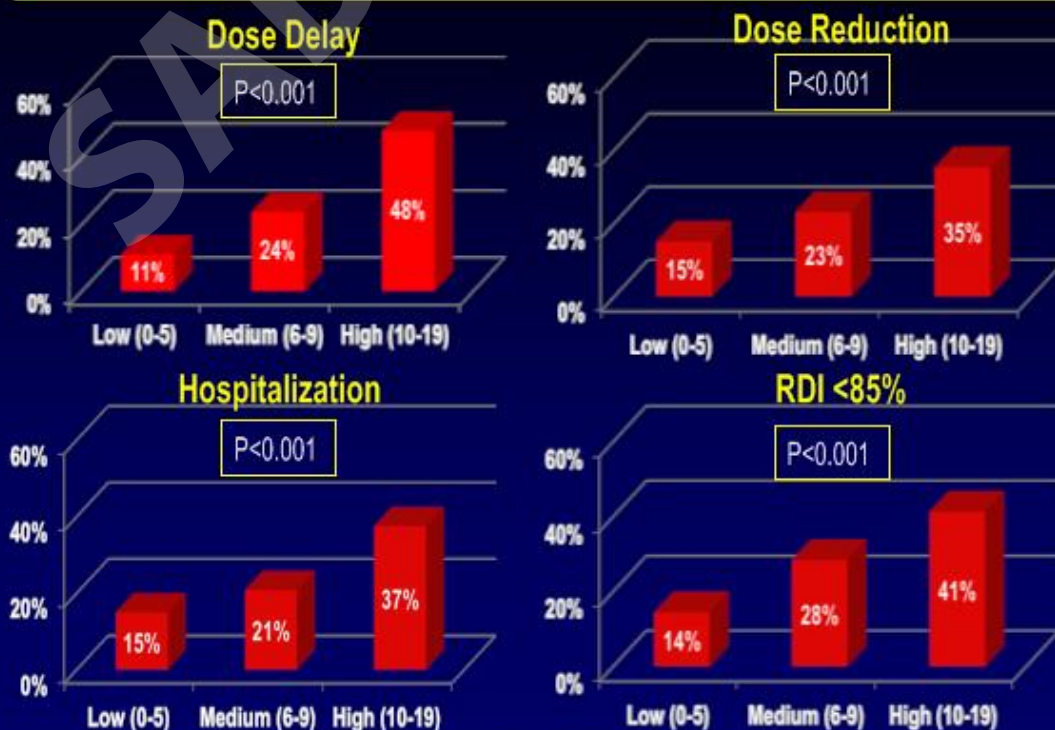
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CARG-BC Model Performance



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CARG-BC For Other Outcomes



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Conclusions

- Developed and validated a chemotherapy toxicity risk score (CARG-BC) that predicts toxicity for older patients with stage I-III BC
- The CARG-BC score is also associated with dose reduction, delay, reduced RDI, and hospitalizations
- This tool could be considered as part of adjuvant treatment decision-making

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Acknowledgements

The Patients Who Participated and Their Families
Their Doctors

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Arti Hurria, M.D.

“Historically, research left out people who were older and more experienced, which doesn’t make much sense. We’re changing that. Older people have much to teach us.” — Arti Hurria, MD, FASCO

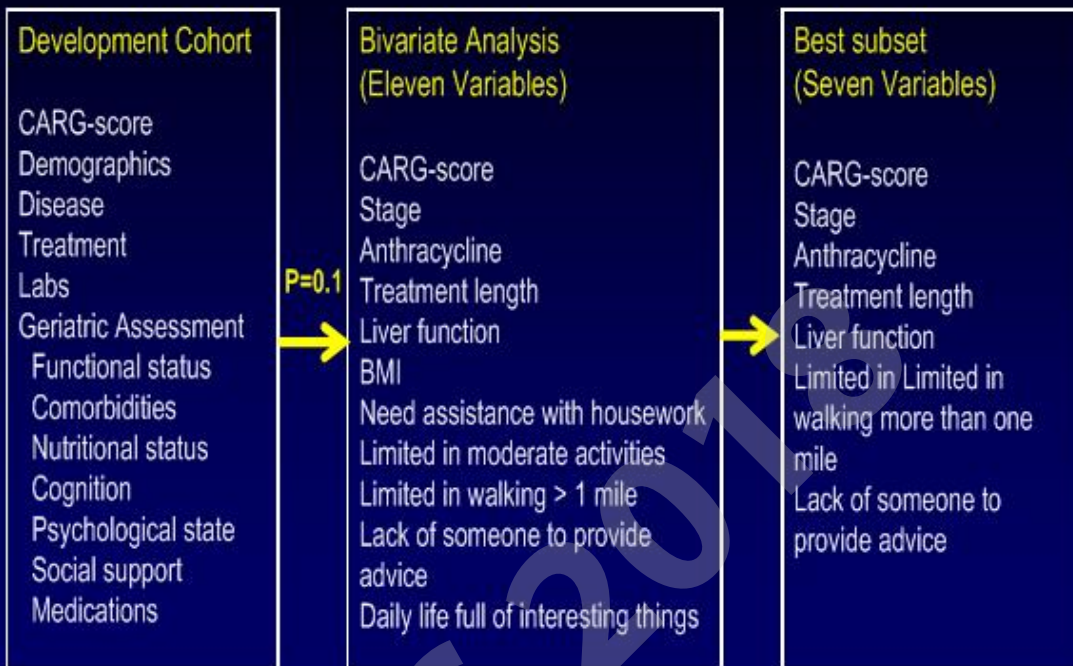
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Thank you!



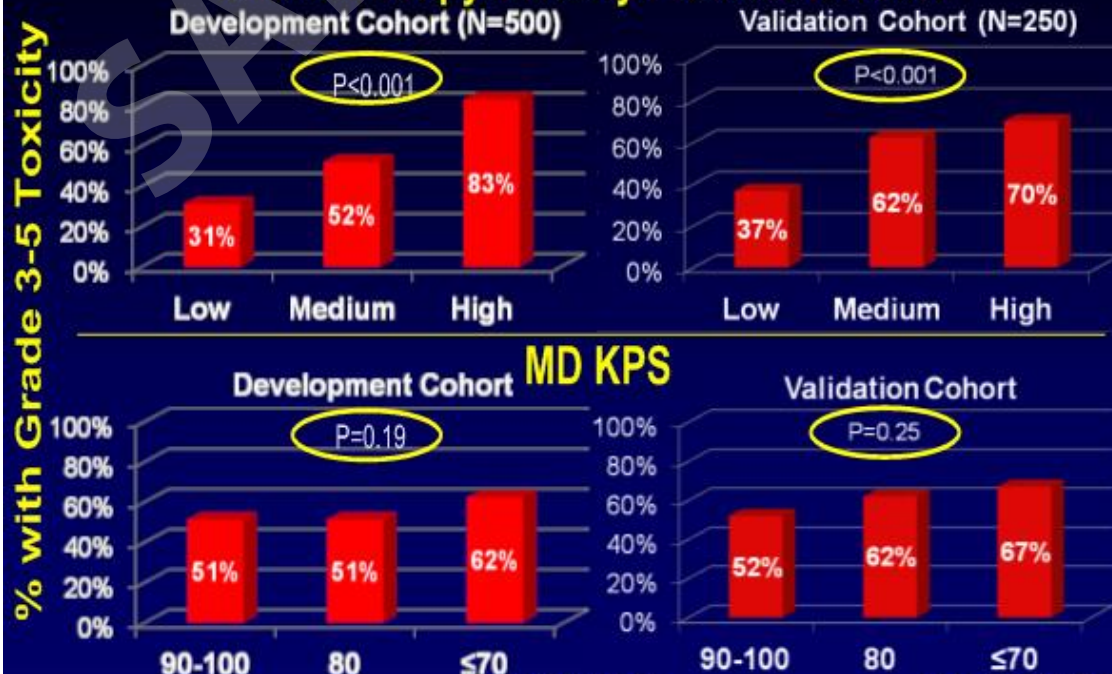
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Statistical Analysis



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MD-rated KPS vs. CARG Score Chemotherapy Toxicity Predictive Model



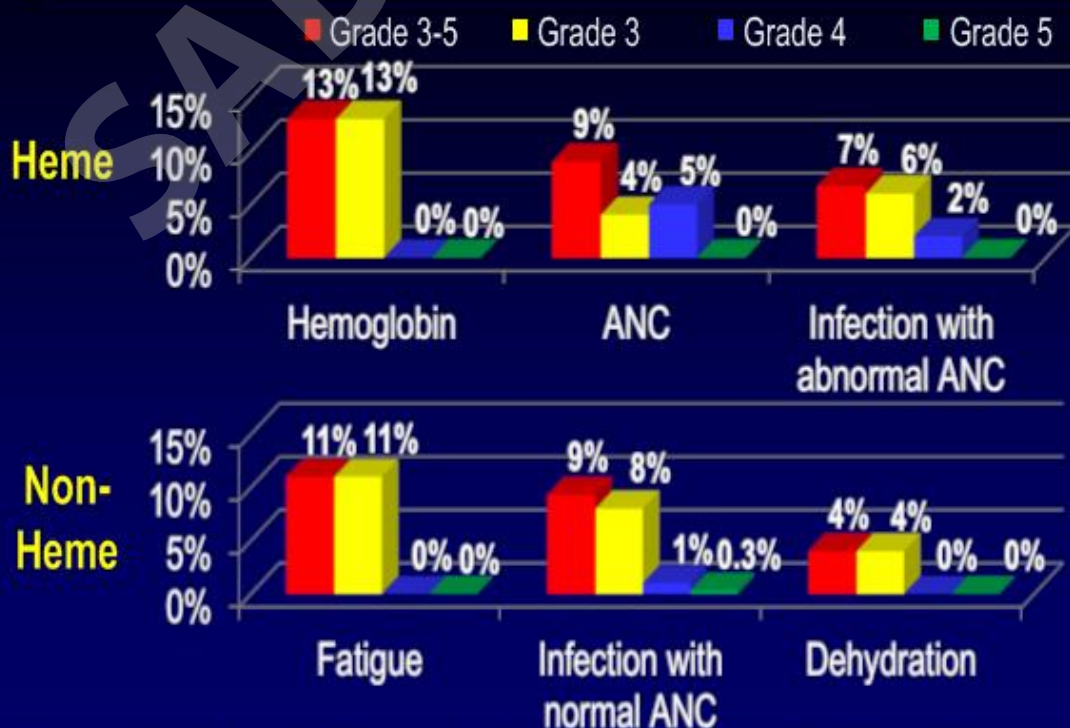
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Geriatric Assessment Results

- 19% required assistance with IADLs
- 94% reported a KPS \geq 70%
- 9% reported a fall in the last 6 months
- 85% had at least 1 comorbidity
- 6% reported weight loss of \geq 5% in the last 6 mo.
- 42% had a BMI \geq 30

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Most Common Grade 3-5 Toxicities



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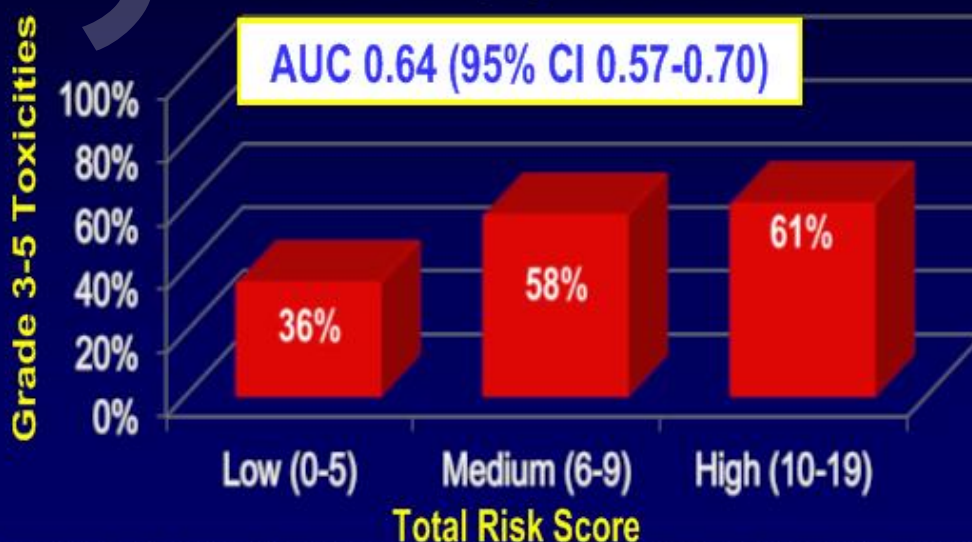
Bivariate Analysis (p<0.1)

- Disease/Tx Characteristics
 - Stage II/III
 - Anthracycline-based regimens
 - Duration of treatment > 3 months
- Labs
 - Abnormal liver function
- Geriatric Assessment Variables
 - Functional Status: IADL (1 item); ADL (2 items)
 - Nutrition: BMI ≥ 30
 - Social Support (1 item)
 - Psychological State (1 item)

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CARG Score Applied to the Development Cohort

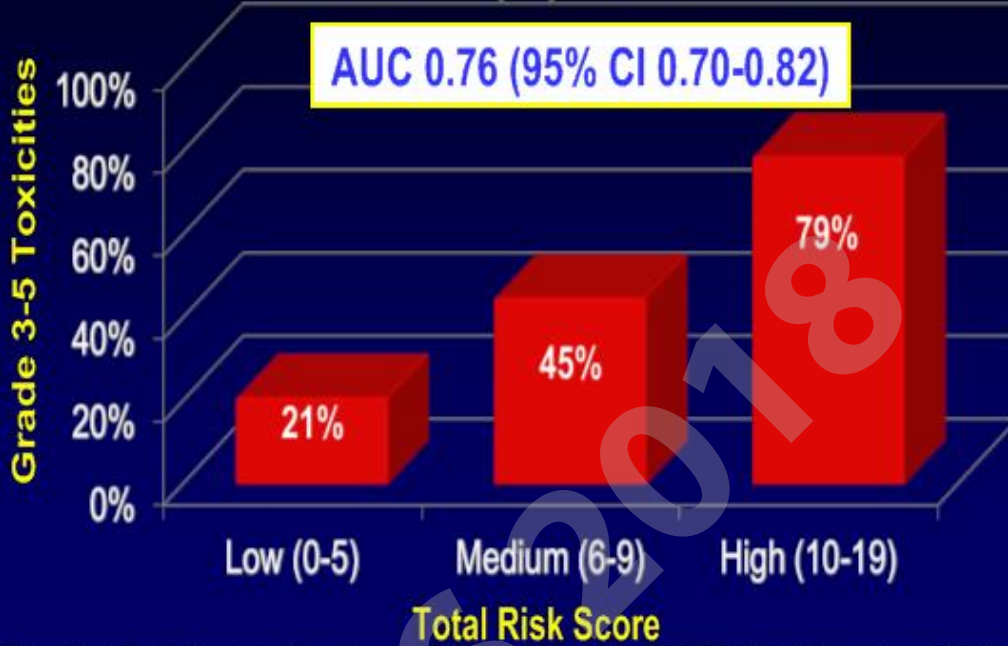
Risk of Toxicity by CARG Score



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CARG-BC Model Performance

Risk of Toxicity by CARG-BC Score



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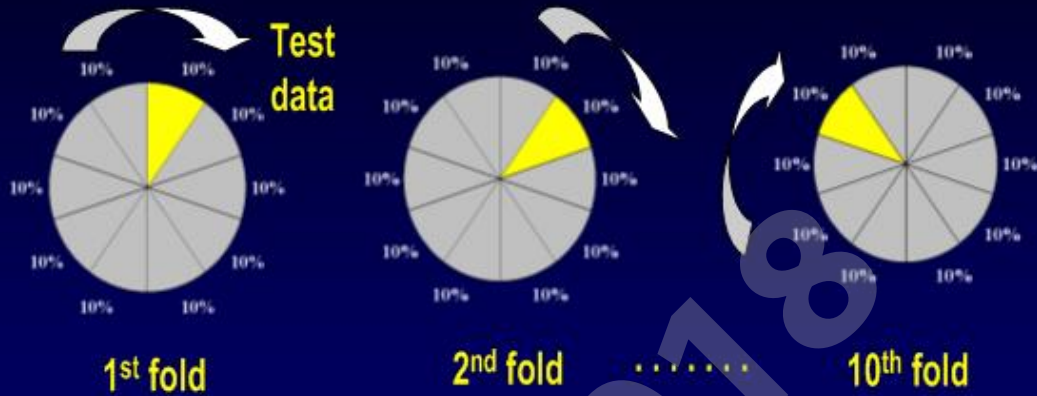
Model Performance: Goodness of Fit

Median score (Range): 7 (0-19)



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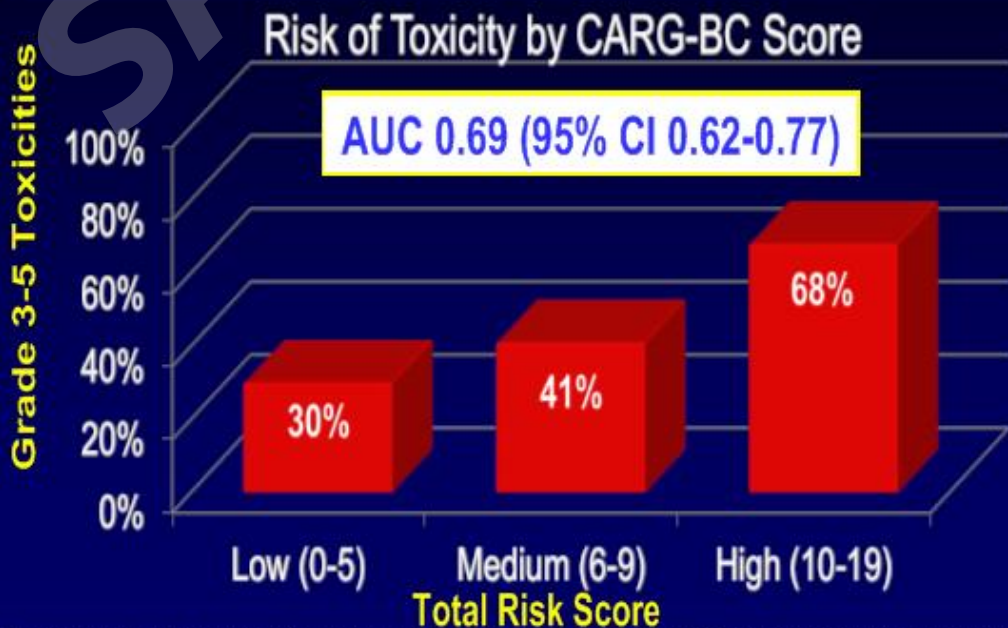
Internal Validation: The 10-fold Cross Validation



Original AUC = 0.76
10-fold cross validation AUC = 0.78

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External Validation: CARG-BC Performance



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