

Nonclinical factors associated with premature termination of adjuvant chemotherapy for stage I-III breast cancer



Xiao-Cheng Wu, Trevor Thompson, Meichin Hsieh, Meijiao Zhou, Patricia Andrews, Michelle Loch, Timothy Styles, Vivien W. Chen

2015 NAACCR Annual Conference
Charlotte, North Carolina
June 18, 2015

Background



- Clinical trials and cohort studies have indicated that adjuvant chemotherapy decreases cancer recurrence and improves survival significantly for early stage breast cancer patients.
- Numerous studies examined disparities in dissemination of guidelines-recommended chemotherapy and factors associated with non-guidelines concordant care

Background

- It has been reported that early termination of adjuvant chemotherapy has an adverse impact on prognosis of breast cancer (Hershman D, 2005).
- Population-based patterns of care studies have not examined early termination of chemotherapy due to difficulties in collecting such data.
- CDC-funded Comparative Effectiveness of Research (CER) project collected detailed information on chemotherapy including completion status.

Objectives

- Examine the association of non-clinical factors with early termination of adjuvant chemotherapy among stage I-III breast cancer patients.

Methods

- Data sources:
 - CDC-funded Comparative Effectiveness Research (CER) project including data from seven state cancer registries (CO, FL, ID, LA, NC, NH, and RI).
 - 3 CER registries were excluded due to high proportion of missing information on chemo completion status.

Methods

- Medical record re-abstraction for information available up to 12 months after diagnosis:
 - hospitals
 - non-hospital settings, including
 - free-standing ambulatory centers
 - radiation facilities
 - physician practice groups
 - medical oncologists

Methods

- Eligibility criteria
 - Women at all ages
 - Residents in the 7 states at diagnosis
 - Stage I-III breast cancer (C50.0-50.9, excluded 9050-9055, 9140, 9590-9992) diagnosed in 2011.
 - Microscopically confirmed
 - No autopsy or death-certificate-only cases
 - Received chemotherapy
 - Have information on chemo completion status

Methods

- Non-clinical (socio-demographic) variables
 - Age: <40, 40-49, 50-64, 65-69, 70-79, 80/+
 - Race/ethnicity: NHW, NHB, API, Hispanics, Others, Unk
 - Insurance: Private, Medicare/other public, Medicaid, None, Unknown
 - Census-tract level poverty: low <20%, high \geq 20% of people under federal poverty level.
 - Census-tract level education: low <25%, high \geq 25% of people 25 years and older with at least a high school education.

Methods

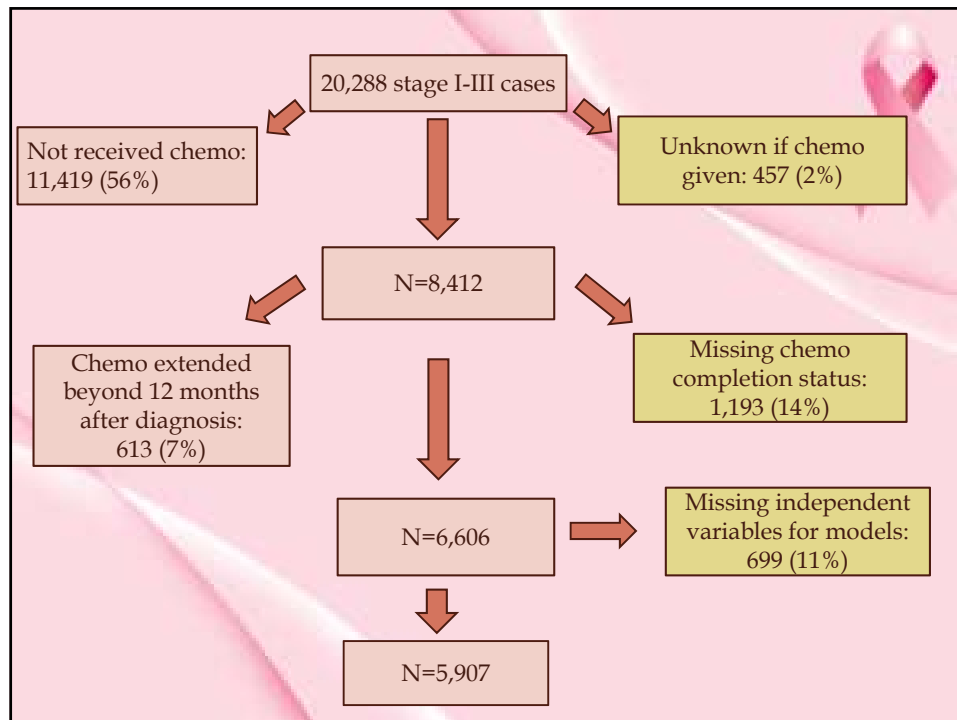
- Clinical variables:

- **Regional lymph node:** no, micro-metastasis (<2 mm), N1/N2/N3
- **Tumor size (cm):** ≤ 0.5 , 0.6-<1.0, 1.0-2.9, ≥ 3.0 , unknown
- **Histology:** Ductal/lobular/mixed, Tubular/Colloid, others
- **Grade:** well, moderate, poorly/undifferentiated, unknown
- **Hormone receptor:** ER+ or PR+, ER- & PR-, unknown
- **Comorbidity:** none, mild, moderate/severe
- **Primary treatment:** no surgery, mastectomy, lumpectomy + radiation, lumpectomy only, unknown

Methods

- Comorbid conditions:

- **None:** No documentation of Charlson condition
- **Mild:** one or more Charlson conditions with a weight of 1 and no condition with a weight ≥ 2
- **Moderate/Severe:** One or more Charlson conditions with a weight ≥ 2
 - Diabetes with sequelae (weight=2)
 - Hemiplegia/Paraplegia (weight=2)
 - Renal disease (weight=2)
 - Moderate/severe liver disease (weight=3)
 - AIDS (weight=6)



Methods

- Univariate analysis
- Multivariate logistic regression
Outcome: Early termination of Chemo (Yes, No)
- Imputation: Data were imputed using predictive mean matching with the `argImpute` function in R.

Using age, race/ethnicity, education, poverty, insurance, residence (urban, rural, mixed), state, 1st primary (yes/no), grade, nodes, histology type, tumor size, ER/PR, hormones, surgery type, the individual comorbid conditions*, weight, height, smoking status, and chemo completion status to predict missing value.

- SAS programs.

Results

- Overall, 23% of the patients terminated chemo early.

Reason chemo not completed	
Health issues/complications	63.3%
Deceased	1.7%
Patient/family choice	21.7%
Cytopenia	2.3%
Other reasons	11.0%
Total	100%

Results

	All cases (N=6,606)	Early chemo termination (N=1,543)
Age at diagnosis		P<0.0001
<40	8.7%	21.0%
40-49	24.0%	18.3%
50-64	45.4%	22.4%
65-69	11.1%	25.7%
70-79	9.3%	37.1%
80/+	1.5%	45.9%

Results

	All cases (N=6,606)	Early chemo termination (N=1,543)
Race/ethnicity		P=0.4409
White	69.5%	22.7%
Black	18.3%	24.4%
API	1.6%	25.2%
Hispanic	9.7%	25.6%
Other	0.9%	22.8%
Unknown	0.2%	33.3%

Results

	All cases (N=6,606)	Early chemo termination (N=1,543)
Insurance		P<0.0001
Private	63.7%	20.0%
Medicare/Other Public	17.1%	31.6%
Medicaid	12.8%	28.6%
None	4.5%	26.4%
Unknown	2.0%	18.5%

Results

	All cases (N=6,606)	Early chemo termination (N=1,543)
Census tract poverty		P=0.2160
Low (<20%)	86.7%	23.1%
High (>20%)	12.6%	25.0%
Unknown	0.7%	26.5%
Census tract education		P=0.0184
High (<25%)	84.0%	22.7%
Low (\geq 25%)	15.3%	26.6%
Unknown	0.7%	26.7%

Multivariate Logistic Regression Model

Outcome: Early chemo termination (Yes vs. No)

	Model 1	Model 2	Model 3
Race			
White	1.00	1.00	1.00
Black	1.21 (1.03-1.42)	1.12 (0.96-1.32)	1.06 (0.89-1.28)
API	1.29 (0.79-2.09)	1.30 (0.80-2.12)	1.24 (0.74-2.03)
Hispanic	1.21 (0.98-1.49)	1.18 (0.96-1.46)	0.76 (0.60-0.97)
Other	1.16 (0.60-2.24)	1.13 (0.58-2.20)	0.85 (0.43-1.69)

Model 1: adjusted for age only

Model 2: adjusted for age and clinical factors (comorbidity, lymph node, tumor size, histology type, grade, surgery and radiation).

Model 3: adjusted for age, clinical factors, and demographic factors (race/ethnicity, insurance, poverty, education, urban/rural, and registry).

Multivariate Logistic Regression Model
Outcome: Early chemo termination (Yes vs. No)

	Model 1	Model 2	Model 3
Insurance			
Private	1.00	1.00	1.00
Medicare/ Other public	1.40 (1.16-1.70)	1.38 (1.14-1.67)	1.44 (1.18-1.75)
Medicaid	1.62 (1.35-1.93)	1.52 (1.27-1.82)	1.54 (1.27-1.86)
None	1.60 (1.21-2.12)	1.49 (1.12-1.98)	1.48 (1.10-1.98)

Model 1: adjusted for age only
 Model 2: adjusted for age and clinical factors (comorbidity, lymph node, tumor size, histology type, grade, surgery and radiation).
 Model 3: adjusted for age, clinical factors, and demographic factors (race/ethnicity, insurance, poverty, education, urban/rural, and registry).

Multivariate Logistic Regression Model
Outcome: Early chemo termination (Yes vs. No)

	Model 1	Model 2	Model 3
Poverty			
Low (<20%)	1.00	1.00	1.00
High (>20%)	1.09 (0.91-1.31)	1.05 (0.87-1.26)	0.97 (0.78-1.20)
Education			
High (<25%)	1.00	1.00	1.00
Low (≥25%)	1.22 (1.04-1.44)	1.18 (1.00-1.39)	1.13 (0.93-1.37)

Model 1: adjusted for age only
 Model 2: adjusted for age and clinical factors (comorbidity, lymph node, tumor size, histology type, grade, surgery and radiation).
 Model 3: adjusted for age, clinical factors, and demographic factors (race/ethnicity, insurance, poverty, education, urban/rural, and registry).

Multivariate Logistic Regression Models

Outcome: Early chemo termination (Yes vs. No)

	Model 1	Model 2	Model 3
Comorbidities			
None	1.00	1.00	1.00
Mild	1.08 (0.91-1.27)	1.07 (0.91-1.27)	1.11 (0.93-1.33)
Moderate/ severe	2.27 (1.25-4.11)	2.14 (1.17-3.91)	1.90 (1.02-3.54)

Model 1: adjusted for age only
 Model 2: adjusted for age and clinical factors (comorbidity, lymph node, tumor size, histology type, grade, surgery and radiation).
 Model 3: adjusted for age, clinical factors, and demographic factors (race/ethnicity, insurance, poverty, education, urban/rural, and registry).

Multivariate Logistic Regression Model

Outcome: Early chemo termination (Yes vs. No)

	Model 1	Model 2	Model 3
Primary treatment			
Mastectomy	1.00	1.00	1.00
Lumpectomy + radiation	0.99 (0.86-1.12)	1.05 (0.91-1.21)	1.02 (0.89-1.18)
Lumpectomy wo radiation	1.62 (1.26-2.07)	1.73 (1.34-2.22)	1.85 (1.43-2.40)
No surgery	3.07 (2.12-4.44)	2.81 (1.94-4.08)	2.77 (1.88-4.07)

Model 1: adjusted for age only
 Model 2: adjusted for age and clinical factors (comorbidity, lymph node, tumor size, histology type, grade).
 Model 3: adjusted for age, clinical factors, and demographic factors (race/ethnicity, insurance, poverty, education, urban/rural, and registry).

Conclusions/Discussions

- Medicaid or Medicare/other public insurance is a significant predictor for early termination of chemo after adjusting for age, clinical, and other socio-demographic factors.
 - Wells JS, et al (2015) reported patients not covered by private insurance were more likely to complete less than 100% of chemotherapy.
- Consistent with recent studies (Andic F 2010, Lipscomb J, 2012, Wells JS, 2015), race/ethnicity is a not significant predictor for early termination of chemo after the adjustment.
- Poverty and education are not significant predictors for early termination of chemo after the adjustment.

Conclusions

- Moderate/severe comorbidity is a significant predictor for early termination of chemo.
- No guideline primary treatment (lumpectomy without radiation therapy or no surgery) significantly predicts early termination of chemo.

Strength:

- The first population-based study on early chemo termination
- Large sample size
- Include all major race/ethnicity categories
- Data are relatively current (2011 diagnosis)

Limitation:

- 15% of cases unknown chemo completion status
- Comorbidity collection was not standardized
- Only examined early termination (yes, no). Not examined adherence, which includes
 - Delayed chemo, missed and cancelled appointments
 - Reduced dose
- Underlying cause for the association of insurance with early chemo termination is unknown.

Acknowledgement

- CDC-funded CER Project
- CDC-NPCR specialized cancer registries
- NCI-SEER Program
- All from CDC and participating registries who were involved in this study.

