Identifying patients at higher risk of toxicity after breast radiotherapy: analysis of patient-reported outcomes in the Michigan Radiation Oncology Quality Consortium cohort

R Jagsi[1], K Griffith[1], F Vicini[2], J Burmeister[3], M Dominello[3], I Grills[4], J Hayman[1], J Moran[1], P Paximadis[5], J Radawski[6], E Walker[7], L Pierce[1]

[1]University of Michigan, Ann Arbor; [2]MHP Radiation Oncology, Pontiac; [3]Karmanos Cancer Center, Detroit; [4]Beaumont, Royal Oak; [5]Spectrum Health, Lakeland; [6]West Michigan Cancer Center, Kalamazoo; [7]Henry Ford Health System, Detroit

MROQC
Michigan Radiation Oncology Quality Consortium

OBJECTIVE

- Patient-reported toxicities after breast radiotherapy merit understanding in order to inform decisions and target supportive care interventions.

METHODS

- As part of a collaborative quality improvement initiative, the Michigan Radiation Oncology Quality Consortium prospectively collects patient-reported outcomes data from women treated for breast cancer at 26 practices across the state.
- Of all 11,107 patients treated with lumpectomy and whole breast radiation therapy between 1/1/2012 and 12/31/2018, 2817 refused patient surveys.
- We describe here the maximal toxicity reported by the 7689 patients who provided survey responses within 7 days of end of treatment and for whom we had sufficient data to determine dose-fractionation and treatment fields.
- Multivariable logistic regression models separately identified the individual and treatment characteristics associated with 1. breast pain, 2. a bother scale (related to itching, stinging/burning, swelling, or hurting of the treated breast), 3. fatigue.
- Breast pain was considered moderate or severe when score ≥4 on modified 10-point Brief Pain Inventory measure.
- Bother from multiple breast symptoms was considered frequent when score ≥3 on a scaled measure (range 0-4) averaging responses on four items derived from the Skindex.
- Fatigue was considered severe when rated as present "always" or "most of the time" over past four weeks.

RESULTS

- Moderate or severe breast pain was reported by 2882 (37.5%) overall: 1022 (28.3%) of those receiving hypofractionation (HF) and 1860 (45.7%) of those receiving conventional fractionation (CF).
- Frequent bother from multiple breast symptoms was reported by 1029 (13.4%) overall: 288 (8.0%) after HF and 741 (18.2%) after CF.
- Severe fatigue was reported by 1795 (23.4%) overall: 681 (18.8%) after HF and 1114 (27.4%) after CF.
- In addition to treatment fractionation ($p<0.001$), younger age, higher BMI, and smoking were highly significant ($p<0.001$) predictors of all three forms of toxicity, as detailed in the Table.
- Black race ($p<0.001$) independently predicted greater breast pain (OR 1.9) and breast symptom bother (OR 1.6).
- Receipt of boost treatment also predicted greater breast pain ($p=0.0006$) and bother ($p=0.04$).

CONCLUSIONS

- In this large observational dataset of patient-reported toxicities after whole breast radiotherapy, substantial differences existed by radiotherapy dose-fractionation.
- Race differences in breast pain and bother existed despite controlling for multiple other factors, including age, body habitus, comorbidities, and treatment characteristics; further research is needed to understand what drives these differences in order to target potentially modifiable factors.
- Intensification of supportive care may be appropriate for subgroups identified as being vulnerable to greater toxicity.

RESULTS

Multivariable models of patient-reported toxicity outcomes

Independent variable	Odds ratio (CI) *p-Value*, in model with dependent variable=moderate or severe breast pain	Odds ratio (CI) *p-Value*, in model with dependent variable=frequent bother from breast symptoms	Odds ratio (CI) *p-Value*, in model with dependent variable=severe fatigue
Age: 70+ *vs.* 60–69	0.77 (0.67–0.89) *p<0.001*	0.63 (0.48–0.81) *p<0.001*	0.99 (0.84–1.16) *p<0.001*
Age: 50-59 *vs.* 60–69	1.49 (1.32–1.69)	1.82 (1.52–2.17)	1.34 (1.17–1.54)
Age: <50 *vs.* 60–69	1.90 (1.63–2.21)	2.66 (2.17–3.25)	1.44 (1.21–1.71)
BMI: Normal 18.5–<25 *vs.* overweight 25–<30	0.78 (0.68–0.90) *p<0.0001*	0.89 (0.72–1.09) *p<0.0001*	0.74 (0.63–0.87) *p<0.0001*
BMI: Obesity I 30–<35 *vs.* overweight 25–<30	1.32 (1.15–1.51)	1.15 (0.94–1.40)	1.22 (1.04–1.41)
BMI: Obesity II 35–<40 *vs.* overweight 25–<30	1.50 (1.28–1.77)	1.61 (1.29–2.01)	1.34 (1.12–1.61)
BMI: Obesity III ≥40 *vs.* overweight 25–<30	2.14 (1.79–2.57)	1.86 (1.47–2.36)	1.59 (1.31–1.94)
BMI: Underweight <18.5 *vs.* overweight 25–<30	0.98 (0.68–1.42)	0.82 (0.46–1.46)	1.08 (0.72–1.62)
Race: Black *vs.* white	1.94 (1.70–2.21) *p<0.0001*	1.58 (1.33–1.87) *p<0.0001*	0.96 (0.83–1.12) *p=0.88*
Race: Asian *vs.* white	1.32 (0.89–1.96)	0.84 (0.46–1.52)	1.15 (0.74–1.80)
Race: Other *vs.* white	1.74 (1.24–2.45)	1.94 (1.31–2.90)	1.01 (0.68–1.51)
Hypertension: Yes *vs.* no	0.95 (0.84–1.06) *p=0.33*	0.92 (0.78–1.08) *p=0.28*	1.09 (0.96–1.24) *p=0.17*
Diabetes: Yes *vs.* no	1.25 (1.08–1.44) *p=0.003*	1.22 (1.00–1.49) *p=0.05*	1.29 (1.10–1.51) *p=0.0015*
Smoking status: Former smoker *vs.* never smoker	1.25 (1.12–1.39) *p<0.0001*	1.33 (1.14–1.55) *p<0.0001*	1.12 (0.99–1.27) *p<0.0001*
Smoking status: Current smoker *vs.* never smoker	1.65 (1.41–1.93)	2.02 (1.66–2.46)	1.59 (1.34–1.89)
Fractionation: Conventional *vs.* hypofractionation	1.67 (1.49–1.86) *p<0.0001*	1.85 (1.58–2.17) *p<0.0001*	1.51 (1.34–1.71) *p<0.0001*
Boost: Boost *vs.* No boost	1.30 (1.12–1.51) *p=0.0006*	1.29 (1.01–1.65) *p=0.04*	1.00 (0.84–1.18) *p=0.96*
SCV Nodal field treatment: Yes *vs.* no	1.02 (0.87–1.20) *p=0.81*	1.11 (0.91–1.36) *p=0.30*	0.86 (0.71–1.03) *p=0.10*

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