Letters

RESEARCH LETTER

Effect of Introducing a Default Order in the Electronic Medical Record on Unnecessary Daily Imaging During Palliative Radiotherapy for Adults With Cancer: A Stepped-Wedge Cluster Randomized Clinical Trial

Annually in the United States, about 250 000 patients with advanced cancer receive palliative radiotherapy to lessen pain, control bleeding, or improve quality of life. To ensure reproducible positioning, patients are immobilized on laser-aligned treatment tables and have standard weekly imaging during treatment. Daily imaging, using radiography or computed tomography, can augment positioning. Although daily imaging is often used for curative radiotherapy, national guidelines consider it unnecessary for palliative radiotherapy.[1,2] Unnecessary imaging can increase treatment time and expense for patients in distress.

Supplemental content

Default options, which leverage insights from behavioral economics, can change physician behavior but have focused less on deadoption of unnecessary care.[3,4] We conducted a stepped-wedge cluster randomized clinical trial to test the effectiveness of introducing a default imaging order in the electronic health record (EHR) vs usual practice to reduce unnecessary daily imaging during palliative radiotherapy.

Methods | The trial (NCT03110692) was conducted in the University of Pennsylvania Health System from February 10, 2016, to February 9, 2018, including a 1-year preintervention period. The trial protocol is available in Supplement 1. The sample comprised physicians from 5 radiation oncology practices (1 university practice in Philadelphia and 4 community practices in Pennsylvania and New Jersey). Eligible physicians prescribed at least 10 courses of palliative radiotherapy during the trial. Eligible patients were aged 18 years or older with bone, soft tissue, or brain metastases receiving 3-dimensional conformal radiotherapy. Single fraction radiotherapy was excluded. This study was approved as a quality improvement project by the University of Pennsylvania institutional review board and informed consent was waived.

The intervention introduced a default imaging order in the EHR that specified no daily imaging during palliative radiotherapy. Physicians could opt out, selecting another imaging frequency. Practices were classified into 2 groups: university or community based. Groups were randomly assigned by coin flip to cross over to the intervention in two 4-month predefined wedges (analyses included 1-month washout periods).

The primary outcome was a binary indicator of radiotherapy courses with daily imaging (defined as imaging during ≥80% of treatments). In intention-to-treat primary analyses, we fit models using generalized estimating equations

Table 1. Flow of Patients Who Received Palliative Radiotherapy Courses Through the Trial

Variable	Prestep Observation Period: February 10, 2016, to February 9, 2017, No.	Step 1: February 10, 2017, to June 9, 2017 (Intervention at University-Based Practice), No.	Step 2: June 10, 2017, to October 9, 2017 (Intervention at Community-Based Practices), No.	Poststep Observation Period: October 10, 2017, to February 9, 2018, No.
University-based practice				
Radiotherapy courses screened	441	173	150	194
Eligible	375	105	123	144
Ineligible	66	68	27	50
Single fraction	40	21	19	31
Physician with less than 10 radiotherapy courses	26	6	8	19
Washout month		41		
Community-based practices				
Radiotherapy courses screened	241	88	87	76
Eligible	220	84	67	70
Ineligible	21	4	20	6
Single fraction	12	4	4	6
Physician with less than 10 radiotherapy courses	9	0	0	0
Washout month			16	

Table 2. Analyses of the Effect of a Default Order Option on Daily Imaging During Palliative Radiotherapy

Variable	Preintervention Periods, No./Total (%)	Intervention Periods, No./Total (%)	Adjusted Odds Ratio (95% CI)	Adjusted Percentage Point Difference (95% CI)	*P* Value
Main analyses					
Primary model	463/679 (68.2)	165/509 (32.4)	0.43 (0.24 to 0.77)	−18.6 (−34.1 to −2.1)	.004
Also adjusted for patient and treatment characteristics	NA	NA	0.37 (0.19 to 0.72)	−18.8 (−34.2 to −2.4)	.003
Heterogeneity of Treatment Effects by Group[a]					
University-based practice	252/375 (67.2)	107/372 (28.8)	0.33 (0.14 to 0.76)	−22.3 (−44.0 to −5.9)	.01
Community-based practices	211/304 (69.4)	58/137 (42.3)	0.45 (0.22 to 0.89)	−27.5 (−46.5 to −11.1)	.02

Abbreviation: NA, not applicable.

[a] Primary model also adjusted for patient and treatment characteristics.

clustering on physicians, using group and period (4-month increments) fixed effects and adjusting for monthly temporal trends. In secondary analyses, we adjusted for age, sex, race, performance status, insurance type, fraction count, dose per fraction, prior radiotherapy, and target. We examined effects at university and community practices by interacting group with the intervention periods. We bootstrapped to obtain adjusted differences in percentage points. Analyses were conducted in SAS statistical software (version 9.4; SAS Institute Inc).

Results | The sample comprised 21 radiation oncologists and 1019 patients who received 1188 palliative radiotherapy courses (n = 747 at the university practice; n = 441 at the community-based practices) to bone (52.2%), soft tissue (19.9%), brain (15.7%), or multiple sites (12.3%). **Table 1** shows the flow of patients through the trial. Daily imaging was used in 68.2% (463/679) of courses in preintervention periods and 32.4% (165/509) of courses in intervention periods. The default intervention led to a significant reduction in daily imaging (adjusted odds ratio, 0.43; 95% CI, 0.24-0.77; adjusted difference in percentage points, −18.6; 95% CI, −34.1 to −2.1; *P* = .004) (**Table 2**). These findings were similar in analyses also adjusted for patient and treatment characteristics and across both university and community practices.

Discussion | In a network of 5 radiation oncology practices, introducing a default order in the EHR reduced unnecessary daily imaging during palliative radiotherapy. There was potential for spillover to community practices during the university intervention period; however, this would bias results toward the null. Our findings suggest that simple nudges, such as setting default orders, can meaningfully reduce unnecessary care.

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Tumor-Stroma Proportion as a Predictive Biomarker of Resistance to Platinum-Based Chemotherapy in Patients With Ovarian Cancer

Standard treatment for ovarian cancer is platinum-based chemotherapy; however, 15% to 30% of patients with ovarian cancer have primary platinum-resistant or refractory disease. Resistance to platinum-based chemotherapy is a clinical designation, assessed by time to recurrence or progression of malignant disease within 6 months after cessation of platinum-based treatment.[1] Refractory disease is defined as recurrence of disease during the course of platinum-based chemotherapy. There is evidence to support the hypothesis that stromatous components of malignant tumors stimulate growth and proliferation of malignant components of invasive tumors[2]; higher stromal content, referred to as *high tumor-stroma proportion*, has been associated with worse prognosis in many epithelial cancers.[3-5] We report the results of a prospective observational study examining tumor-stroma proportion as a predictive biomarker of chemoresistance in women diagnosed with ovarian cancer.

Video

Methods | This study followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guideline. Twenty-four women with newly diagnosed ovarian carcinoma were enrolled in this prospective study from April 1, 2014, to June 30, 2016. Patient data included age at diagnosis, histologic type of tumor, tumor grade and stage, tumor size, and baseline serum levels of cancer antigen 125 at diagnosis, before surgery or neoadjuvant chemotherapy. Data were analyzed between December 28, 2018, and February 28, 2019. This study was approved by the University of Minnesota Institutional Review Board, and written informed consent was obtained from all participants.

Two pathologists (M.K. and M.A.L.) examined hematoxylin/eosin-stained slides to confirm the diagnosis of ovarian carcinoma and identify sections of the primary tumor with the greatest proportion of tumor (×10 microscopic field, with tumor extending to all edges of the field). Tumor-stroma proportion was assessed as low (<50% stromal cells) or high (≥50% stromal cells); this cutoff was consistent with other published studies.[3,4,6] Pathologists were blinded to chemosensitivity status.

Demographic and clinical characteristics were summarized using descriptive statistics and compared by high or low tumor-to-stroma proportion using Fisher exact tests for categorical variables and *t* tests and Wilcoxon rank sum tests for continuous variables. Proportions of women with high and low tumor-stroma proportion and chemoresistance status were

Table 1. Patient Demographic and Clinical Characteristics of 24 Women With Newly Diagnosed Ovarian Cancer

Characteristic	No. (%)			*P* Value
	Overall	Low Stroma (<50%)	High Stroma (≥50%)	
No.	24	15	9	
Age, mean (SD), y	62.0 (8.1)	60.9 (8.8)	63.9 (6.7)	.37
Neoadjuvant chemotherapy				.06
No	17 (70.8)	13 (86.7)	4 (44.4)	
Yes	7 (29.2)	2 (13.3)	5 (55.6)	
Ovarian cancer type				.27
High-grade epithelial	21 (87.5)	12 (80.0)	9 (100.0)	
Low-grade epithelial	3 (12.5)	3 (20.0)	0 (0.0)	
Tumor grade				.42
G1	2 (9.1)	2 (15.4)	0 (0.0)	
G2	5 (22.7)	2 (15.4)	3 (33.3)	
G3	15 (68.2)	9 (69.2)	6 (66.7)	
Stage				.61
I-II	5 (20.8)	4 (26.7)	1 (11.1)	
III-IV	19 (79.2)	11 (73.3)	8 (88.9)	
Baseline CA-125, median (range), U/mL	416 (32-2782)	741 (32-2782)	396 (88-2336)	.45

Abbreviation: CA 125, cancer antigen 125.