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Association Between Declared Hurricane Disasters and Survival of Patients With Lung Cancer Undergoing Radiation Treatment

Natural disasters, such as hurricanes, can interrupt the provision of oncology care.[1] Radiotherapy is particularly vulnerable because it requires dependable electrical power and daily treatment.[2] Disruptions are especially concerning for patients undergoing treatment for locally advanced non-small cell lung cancer (NSCLC)[2] because treatment delays as little as 2 days negatively affect survival.[3]

We investigated whether hurricane disasters occurring during radiotherapy were associated with poorer survival for patients with NSCLC.

Methods | Patients undergoing definitive radiotherapy for nonoperative locally advanced NSCLC between 2004 and 2014 were selected from the hospital-based National Cancer Database, which captures approximately 70% of all cases in the United States and requires hospitals to have 90% annual follow-up of living patients.[4] All patients had at least 1 year of follow-up for vital status (up to December 31, 2015). Disaster declarations were identified from the Federal Emergency Management Agency for 2004 to 2014.[5]

Exposed patients were undergoing radiation treatment when a hurricane disaster was declared for the facility's area between the date when radiotherapy started and the date when radiotherapy ended. They were propensity score–matched[6] to unexposed patients, who completed treatment at the same facility at times when no disaster was declared, on radiotherapy start month, sex, age, stage, tumor spread to lymph nodes, and zip code–level median income quintile. Pearson χ^2 or *t* tests were used to compare groups.

Overall survival was defined as the interval between age at diagnosis and age at death or last contact. Multivariable Cox proportional hazards modeling included an indicator variable for hurricane disaster declared during radiotherapy, sex, race/ethnicity, income, geographic region,

Table. Characteristics of Patients Exposed to a Hurricane Disaster Declaration During Radiation Treatment for Locally Advanced Non–Small Cell Lung Cancer and Propensity-Matched Unexposed Patients

Patient Characteristics[a]	Exposed (n = 1734)	Unexposed (n = 1734)	*P* Value[b]
Age at diagnosis, mean (SD), y	66.5 (9.7)	66.4 (9.9)	.67
Sex, No. (%)			.97
Male	953 (55.0)	954 (55.0)	
Female	781 (45.0)	780 (45.0)	
Race/ethnicity, No. (%)[c]			.16
Non-Hispanic white	1355 (78.5)	1384 (80.0)	
Hispanic	70 (4.1)	53 (3.1)	
Non-Hispanic black	271 (15.7)	273 (15.8)	
Non-Hispanic other	30 (1.7)	19 (1.1)	
Median income quintile, No. (%), $			.05
<36 000	326 (19.2)	336 (19.8)	
36 000-43 999	342 (20.1)	324 (19.1)	
44 000-52 999	386 (22.7)	326 (19.2)	
53 000-68 999	336 (19.8)	381 (22.4)	
≥69 000	309 (18.2)	331 (19.5)	
Insurance, No. (%)			.43
Private	520 (30.6)	570 (33.3)	
Uninsured	73 (4.3)	61 (3.6)	
Medicaid	130 (7.6)	122 (7.1)	
Medicare	960 (56.4)	944 (55.1)	
Other	19 (1.1)	17 (1.0)	
Comorbidity, No. (%)			.52
0	1117 (64.4)	1133 (65.3)	
1	442 (25.5)	415 (23.9)	
≥2	175 (10.1)	186 (10.7)	
Tumor spread to lymph nodes, No. (%)	379 (21.9)	358 (20.6)	.38
Tumor size, mean (SD), mm	50.8 (46.5)	48.6 (38.6)	.17
Treatment duration, mean (SD), d	46.2 (25.6)	66.8 (77.8)	<.001
Region, No. (%)			.99
Northeast	622 (35.9)	625 (36.0)	
Midwest	20 (1.2)	20 (1.2)	
South	1092 (63.0)	1089 (62.8)	
Facility type, No. (%)			>.99
National Cancer Institute–designated	119 (7.3)	118 (7.2)	
Comprehensive	845 (51.7)	847 (51.8)	
Teaching	379 (23.2)	379 (23.2)	
Community	137 (8.4)	136 (8.3)	
Other	155 (9.5)	156 (9.5)	
Driving distance, mean (SD), miles	20.4 (42.6)	27.0 (103.6)	.02
Concomitant chemotherapy, No. (%)	485 (28.0)	497 (28.7)	.65
Fractions of treatment, No. (%)			.54
30	126 (22.7)	122 (20.5)	
33	145 (26.2)	164 (27.6)	
34	39 (7.0)	54 (9.1)	
35	138 (24.9)	130 (21.9)	
36	27 (4.9)	34 (5.7)	
37	59 (10.6)	61 (10.3)	
38	20 (3.6)	29 (4.9)	

(continued)

Table. Characteristics of Patients Exposed to a Hurricane Disaster Declaration During Radiation Treatment for Locally Advanced Non–Small Cell Lung Cancer and Propensity-Matched Unexposed Patients (continued)

Patient Characteristics[a]	Exposed (n = 1734)	Unexposed (n = 1734)	*P* Value[b]
Month radiotherapy started, No. (%)			.22
November-April	34 (2.0)	30 (1.7)	
May	56 (3.2)	43 (2.5)	
June	140 (8.1)	110 (6.3)	
July	437 (25.2)	428 (24.7)	
August	558 (32.2)	614 (35.4)	
September	273 (15.7)	273 (15.7)	
October	236 (13.6)	236 (13.6)	
Year radiotherapy started, No. (%)			.73
2004-2009	953 (55.0)	943 (54.4)	
2010-2014	781 (45.0)	791 (45.6)	

[a] Exposed patients were undergoing radiation treatment for locally advanced non–small cell lung cancer when a hurricane disaster was declared for the facility's area. Unexposed patients completed treatment at the same facility not during a disaster declaration. Unexposed patients were propensity-matched to exposed patients on month of initiation of radiation treatment, sex, age, lymph node involvement, and income. Patients were excluded if treated at a facility other than the reporting facility.

[b] Differences between exposed and matched unexposed patients were assessed using Pearson χ^2 test for categorical variables and *t* test for continuous variables.

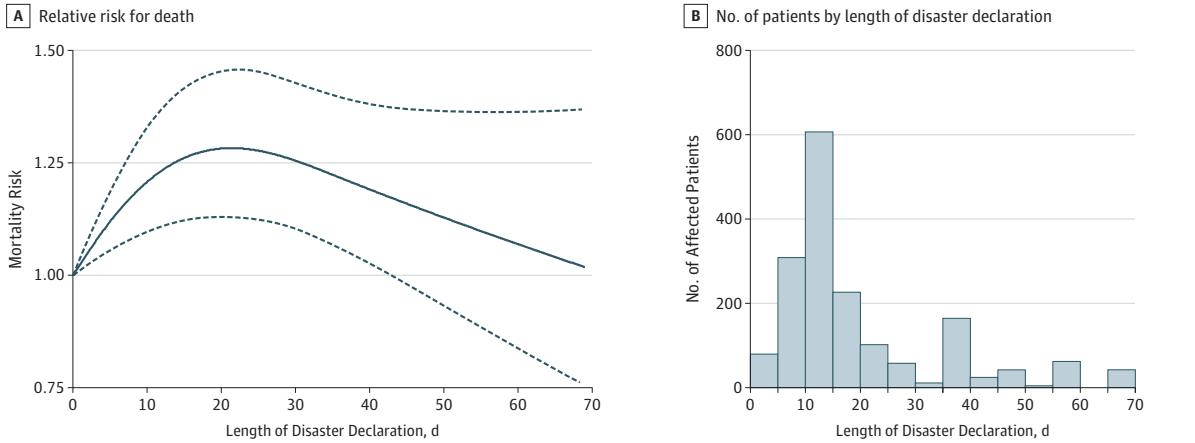
[c] Because race has a significant association with cancer outcomes, race was coded following the Surveillance, Epidemiology, and End Results program's coding manual, which uses patients' self-declared identification as the highest-priority source followed by documentation in the medical record and death certificate.

health insurance, comorbidities, tumor size, tumor spread to lymph nodes, facility type, driving distance to facility, receipt of concomitant chemotherapy, number of treatment sessions (fractions) received, and radiotherapy start month and year (2004-2009 and 2010-2014). Proportionality assumption, tested using Schoenfeld residuals, was met. Restricted cubic spline regression flexibly modeled the association between the number of days disaster declarations lasted and survival. Statistical significance was set at a 2-sided α = .05. All analyses were performed using SAS version 9.4. This study was granted exempt review by the institutional review board at the Morehouse School of Medicine.

Results | There were 1934 patients who had a hurricane disaster declared during radiation treatment and 129 080 who completed radiation treatment in the absence of a disaster declaration, with 1734 in the exposed group and 1734 in the unexposed group after matching characteristics were balanced (**Table**). The 101 disaster declarations lasted between 1 and 69 days.

The median observation time was 15 months. For the exposed group, the total number of deaths was 1408, mean survival time was 29 months, and 5-year survival estimate was 14.5%. For the unexposed group, the total number of deaths was 1331, mean survival time was 31 months, and 5-year survival estimate was 15.4%. Patients affected by a hurricane disaster had longer radiation treatment durations (66.9 vs 46.2 days; $P < .001$) and significantly worse overall survival than matched unexposed patients in both crude (hazard ratio [HR] for death, 1.11 [95% CI, 1.02-1.22]; $P = .02$) and adjusted (HR, 1.19 [95% CI, 1.07-1.32]; $P = .001$) analyses. The adjusted relative risk for death increased with the length of the disaster declaration (**Figure**, A), reaching 1.27

Figure. Association Between Length of Hurricane Disaster Declaration and Risk of Death in Patients With Lung Cancer Undergoing Radiation



In panel A, cubic spline regression modeled a 1-unit increase in the number of days the declaration lasted and the overall survival, adjusted for sex, race/ethnicity, income, geographic region, health insurance, comorbidities, tumor size, tumor spread to lymph nodes, facility type, driving distance to facility, receipt of concomitant chemotherapy, number of treatment sessions (fractions) received, and radiation treatment start month and year (2004-2009 and 2010-2014). Only the 1734 patients who were affected by a hurricane disaster declared during radiation treatment were included in this analysis. The solid line represents the relative risk and the dotted lines represent 95% CIs.

(95% CI, 1.12-1.44) for disasters lasting 27 days. The association became nonsignificant after 30 days, but only 19 declarations lasted that long (Figure, B).

Discussion | Having a hurricane disaster declared during radiotherapy was associated with worse overall survival in patients with locally advanced NSCLC. Longer declarations were associated with worse survival.

Strengths of this study include a large national sample with detailed sociodemographic, clinical, and treatment information and adequate follow-up periods. Limitations include lack of information about smoking history, performance status, treatment toxicity, reasons for or exact dates of treatment breaks, and other hurricane disaster–associated factors (eg, displacement, mental health status, physical functioning).

Because data on other potentially explanatory factors are lacking, the relative contribution of treatment delay to the observed association cannot be quantified. However, treatment delay is one of the few hurricane-related disruptions that can be prevented. Because no recommended correction for radiotherapy delays exists,[3] strategies for identifying patients, arranging for transferring treatment, and eliminating patient out-of-network insurance charges should be considered in disaster mitigation planning. Research is needed to evaluate other types of natural disasters, diseases, and treatments.

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COMMENT & RESPONSE

Intravenous Acetaminophen for Postoperative Delirium

To the Editor The DEXACET trial found a decreased incidence of postoperative delirium in older patients after cardiac surgery who received intravenous (IV) acetaminophen vs placebo combined with propofol or dexmedetomidine.[1] Dr Subramaniam and colleagues suggested that the difference in the primary outcome, incidence of delirium, may have been driven in part by reduction in opioid consumption in the acetaminophen group compared with the placebo group. The reduction in opioid requirements must therefore be carefully examined.

Of concern is the conversion factor used to calculate morphine equivalents. The authors used a conversion factor for fentanyl of 2.4, derived from the Centers for Disease Control and Prevention's recommendation for converting fentanyl transdermal patch in micrograms per hour to morphine equivalents in milligrams per day (ie, a 100-µg/h fentanyl patch = 240 mg/d of oral morphine).[2] This conversion is not applicable in postoperative cardiac surgery patients receiving IV fentanyl. The commonly accepted relative potency of fentanyl to morphine is 100× ; that is, 0.1 mg of IV fentanyl is equal to 10 mg of IV morphine.[3] Thus, the total morphine equivalents are imprecise in the study, and the authors' claim that a median reduction of 83 µg (0.083 mg) of morphine equivalents in 48 hours in the IV acetaminophen group may contribute to any meaningful clinical effect is inconceivable.

The standard of care for postoperative cardiac surgery patients includes multimodal pain regimens, which often consist of around-the-clock oral acetaminophen, whereas the DEXACET trial compared IV acetaminophen with placebo. Despite this design, no difference in pain scores was seen between the IV acetaminophen group and the placebo group. With a nominal, potentially inaccurate difference in opioid use and no difference in pain scores between groups, the mechanism by which delirium was reduced is unclear.

The clinical benefit of IV acetaminophen compared with standard practice (ie, multimodal pain regimens) remains unknown. The DEXACET trial joins a growing body of literature comparing IV acetaminophen with lack of nonopioid analgesia. Although IV acetaminophen offers an alternative in patients who may not tolerate other nonopioid