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ORIGINAL RESEARCH

Effects of Extreme Humidity and Heat on Ventricular Arrhythmia Risk in Patients With Cardiac Devices

Corinna Keeler, PhD,[a] Stephanie E. Cleland, PhD,[b,c,d] K. Lloyd Hill, MS,[e] Anthony J. Mazzella, MD,[f] Wayne E. Cascio, MD,[a] Ana G. Rappold, PhD,[a] Lindsey A. Rosman, PhD[f]

ABSTRACT

BACKGROUND Climate change is increasing the frequency of high heat and high humidity days. Whether these conditions can trigger ventricular arrhythmias [ventricular tachycardia/ventricular fibrillation, VT/VF] in susceptible persons is unknown.

OBJECTIVES The purpose of this study was to determine the relationship between warm-season weather conditions and risk of VT/VF in individuals with pacemakers and defibrillators.

METHODS Baseline clinical and device data from 5,944 patients in North Carolina (2010-2021) were linked to daily weather data geocoded to individuals' residential addresses. Associations between extreme humidity, temperature, and VT/VF overall and by patient, community, and built environment factors were estimated using a case time-series design with distributed lag nonlinear models, adjusting for temporal trends and individual factors.

RESULTS VT/VF events occurred on 4,486 of the 484,988 person-days. Extreme humidity (95th percentile: 90% relative humidity) increased odds of VT/VF in the 7 days following exposure (aOR 1.23 [95% CI: 1.00-1.51]). Humidity-associated VT/VF risk was highest among those who were male (aOR: 1.38 [95% CI: 1.08-1.76]), age 67 to 75 years (aOR: 1.65 [95% CI: 1.16-2.35]) with coronary artery disease (aOR: 1.79 [95% CI: 1.25-2.57]), heart failure (aOR: 1.72 [95% CI: 1.2-2.46]), diabetes (aOR: 3.01 [95% CI: 1.99-4.56]), hypertension (aOR: 2.06 [95% CI: 1.48-2.88]), and prior myocardial infarction (aOR: 1.75 [95% CI: 1.23-2.48]). Communities with high socioeconomic deprivation (aOR: 1.83 [95% CI: 1.28-2.62]), high income inequality (aOR: 1.56 [95% CI: 1.19-2.04]), and urban areas with less greenspace (aOR: 1.29 [95% CI: 0.93-1.78]) also had increased VT/VF risk. High temperatures were not associated with VT/VF.

CONCLUSIONS In patients with preexisting cardiovascular disease, exposure to extreme humidity increased VT/VF risk, especially among vulnerable individuals, disadvantaged communities, and urban areas with less green space. These findings emphasize the need for policies that address environmental risks in susceptible individuals and communities. (JACC Adv. 2025;4:101463) © 2024 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

From the [a]U.S. Environmental Protection Agency, Center for Public Health and Environmental Assessment, Chapel Hill, North Carolina, USA; [b]ORISE at US Environmental Protection Agency, Center for Public Health and Environmental Assessment, Chapel Hill, North Carolina, USA; [c]Department of Environmental Sciences & Engineering, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina, USA; [d]Faculty of Health Sciences, Simon Fraser University, Chapel Hill, North Carolina, USA; [e]Oak Ridge Associated Universities at US Environmental Protection Agency, Center for Public Health and Environmental Assessment, Chapel Hill, North Carolina, USA; and the [f]Division of Cardiology, University of North Carolina School of Medicine, Chapel Hill, North Carolina, USA.

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ABBREVIATIONS AND ACRONYMS

CVD = cardiovascular disease

ICD = implantable cardioverter-defibrillator

VF = ventricular fibrillation

VT = ventricular tachycardia

Climate change is causing an increase in the frequency and intensity of extreme heat and humidity events.[1] Accumulating evidence suggests that both short- and long-term exposure to intense heat can exacerbate existing health conditions, especially among older adults[2] and those with established cardiovascular disease (CVD), who are more susceptible to weather-induced alterations in autonomic, metabolic, and hemodynamic processes.[3] Warmer temperatures may also limit time spent outdoors and engagement in daily physical activity, particularly during the summer months, thereby increasing the potential for adverse health outcomes.

Extreme heat has been linked to a higher incidence of myocardial infarction, stroke, heart failure, and cardiovascular mortality.[4-6] Relatively few studies have assessed the cardiovascular effects of rising humidity,[7] and even less is known about its impact on risk for potentially life-threatening ventricular arrhythmias. Published findings have been largely inconsistent and prone to confounding due to small sample sizes, short-duration of follow-up, use of surrogate outcomes, and lack of adjustment for important behavioral, clinical, and environmental factors.[8-11] It is also unclear whether intense heat and humidity disproportionately impact certain patient groups (based on their age, sex, race, and comorbidities)[12] and communities (eg, based on socioeconomic or structural disadvantage) that may be less capable of adapting to extreme weather conditions. Furthermore, characteristics of an individual's built environment (eg, urbanization, access to greenspace) have been shown to influence cardiovascular risk and health outcomes[13] and can be potentially modified through urban planning policies, but the effects of these contextual factors on heat-related risk of arrhythmia have not been studied. Given the projected increase in CVD and high heat events over the next decade,[1,3] it is essential to clarify the impact of extreme weather on the risk of ventricular arrhythmia in populations at greater risk of adverse health outcomes and to identify vulnerable subgroups who may benefit from tailored public health messaging and targeted interventions.

This study aimed to quantify both the day-to-day and cumulative risks of ventricular arrhythmias associated with exposure to extreme humidity and heat among adults at increased risk for such rhythm disturbances using retrospective data from a large, longitudinal cohort of patients with pacemakers and implantable cardioverter-defibrillators (ICDs). We also evaluated whether associations varied among individuals and communities, and by characteristics of built environment.

METHODS

STUDY POPULATION AND DATA SOURCES. This study included patients enrolled in the University of North Carolina Cardiovascular Device Surveillance Registry (UNC CDSR) from 2010 to 2021. The UNC CDSR[14,15] is a prospective and multicenter clinical research registry for patients with pacemakers and ICDs implanted at 11 hospitals located throughout North Carolina (Supplemental Figure 1). The registry collects daily information on arrhythmia episodes, therapies administered (ICD shocks and antitachycardia pacing [ATP]), and physiologic data (eg, minutes of physical activity per day) from all remote monitoring transmissions and routine follow-up visits for all consecutive implants, upgrades, and replacements. Device data are linked to patient-level sociodemographic and clinical information which are routinely abstracted from electronic health records (EHR) using standard procedures and validated algorithms.[16]

This study included all adults aged ≥18 years enrolled in the UNC CDSR who resided in North Carolina during the study period and had Medtronic (Minneapolis, Minnesota) or Boston Scientific (Marlborough, Massachusetts) ICDs or pacemakers, as physical activity data are measured similarly by these devices (description of physical activity data collection and validation in Supplemental Methods Part A).[17] Data from the first 5 years post-implant were abstracted from the registry for this study. Device data from the first 30 days post-implant were excluded from analysis to account for procedural recovery.[18] If a patient died during follow-up, data was censored 30 days prior to the recorded date of death. Individuals who received a left ventricular assist device (LVAD) at any point during follow-up were excluded. This study followed the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology)[19] reporting guideline (Supplemental Table 1). The UNC institutional review board approved the study and waiver of informed consent [IRB#21-1523].

TEMPERATURE AND HUMIDITY EXPOSURE. Exposures of interest were humidity (relative humidity [%]) and temperature (mean ambient air temperature [°C]). Meteorologic data were obtained from NOAA's National Climatic Data Center's Global Surface Summary of the Day database. Daily meteorologic observations were interpolated to census tract population centroids using thin plate splines and then

aggregated to the zip code tabulation area (ZCTA) using population weighting. Supplemental Figure 2 illustrates spatial and descriptive patterns in warm-season temperature and humidity.

Daily estimates of humidity and temperature were assigned to each patient for each patient-day of follow-up, matched spatially based on the ZCTA of their geocoded residential address. Each patient-day in the registry was categorized as occurring in either the warm season (April 16th-October 15th) or the cool season (October 16th-April 15th). As in prior studies,[20,21] we limited the study period to the warm season to represent high heat and high humidity exposure in North Carolina.

OUTCOME ASCERTAINMENT. Validated detection algorithms embedded within the CIEDs[22] were used to determine the occurrence of ventricular arrhythmias defined as 1 or more device-detected ventricular tachycardia (VT) or ventricular fibrillation (VF) episode on a given day, hereafter referred to as a VT/VF-day. Episodes were classified according to device-specific detection settings (Supplemental Methods Part B). As in other studies,[23] VT/VF episodes were not mandated to be of any certain duration, as ICDs are often programmed to deliver therapies prior to traditional 30-second cutoffs defining sustained VT or VF.[24] Device-categorized non-sustained VT/VF episodes were not included in the primary analysis, as non-sustained episodes, including ventricular ectopy, do not meet detection criteria (described in Supplemental Methods Part B). Additionally, to further explore the clinical relevance of associations, we conducted a sensitivity analysis that included only the most clinically severe VT/VF episodes that were treated with device therapy (ATP or shock).

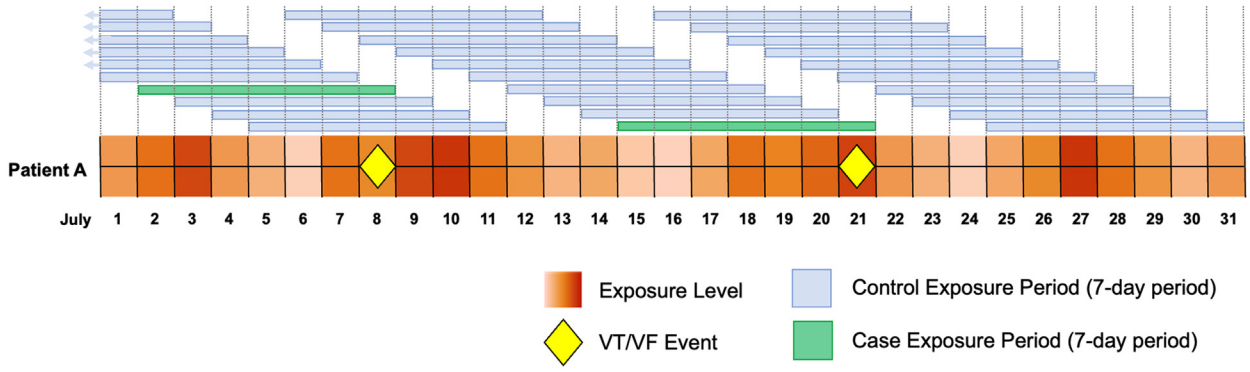
COVARIATES. Baseline comorbidities were considered present and assumed to persist if the International Classification of Diseases, Tenth Revision (ICD-10) code for that specific condition was recorded in the EHR at the time of implant; diagnoses that subsequently occurred during follow-up were classified as such. Community-level factors for each patient were determined using their geocoded residential address and included: income inequality (measured by the Gini coefficient[25]), health insurance rates, and neighborhood socioeconomic deprivation (measured by the Area Deprivation Index [ADI]).[26] Built environment was assessed with a composite measure of urbanicity and tree canopy cover within a 1 km radius of a patient's residence (categorized as: urban-low tree cover, and urban-high tree cover). See Supplemental Methods Part C for detailed description of spatial data sources and processing for community-level factors.

STATISTICAL ANALYSIS. As shown in **Figure 1**, we used a case time-series design[27] to estimate associations between daily meteorological conditions (exposure) and VT/VF (outcome). Case time-series designs have been extensively used in the analysis of observational data with time-varying, transient exposures.[28,29] In the case time-series design, each patient serves as their own control and the baseline risk is stratified between and within subjects, effectively eliminating potential confounding from non-time-varying individual characteristics (eg, age, comorbidities, device type and settings) and allowing for flexible control of time-varying characteristics (eg within person changes in baseline risk due to progression of disease or aging).

The case time-series modeling framework allows for different outcome and exposure distributions (ie, binary vs continuous) and estimation of the non-linear and time distributed effects of exposure. Here, we apply logistic regression for the binary indicator of a VT/VF event-day and model the effects of temperature and humidity using a distributed lag non-linear model (DLNM). Daily temperature and humidity were operationalized independently as continuous exposure variables. DLNMs are a well-established framework that quantify both the cumulative and day-by-day effects of exposure on the outcome of interest over a specified time period, allowing for non-linear and time-lagged associations.[30,31] We consider exposures over a 7-day period, beginning 6 days prior to the outcome (lag 6) to the day of the outcome (lag 0). The exposure-response associations were modeled as non-linear functions of time and exposure level, allowing for a non-linear response at each lag and cumulatively across all 7 lags (model specifications described in detail in Supplemental Methods Part D). Results were reported as the cumulative 7-day (lags 0-6) odds ratio (OR) of a VT/VF event at the 95th percentile of temperature or humidity versus the 50th percentile. The 95th percentile was selected to represent extreme conditions during the warm season.[20,21] Individual-lag effects (lag 0, lag 1, etc.) were also reported.

All models were adjusted for prespecified time-varying covariates: time since device implantation, patient-level number of prior VT/VF events, seasonality (via a natural cubic spline of day of season with 4 degrees of freedom), and a model term capturing within-person monthly variations in risk. Additionally, since physical activity has been associated with

FIGURE 1 Illustration of Case Time-Series Study Design



For a sample month, figure illustrates the case time-series study design where each individual has the potential to contribute both nonexposed (control) patient-days and exposed (case) patient-days, allowing each individual to act as their own control. The 7-day lag period, with day 0 being day of exposure and day 6 being end of the exposure period, is shown using blue bars (7-day period without patient-level VT/VF event) and green bars (7-day period with patient-level VT/VF event). This figure is based on the work of Gasparrini A. The case time series design. *Epidemiology*. 2021;32(6):829-837.

risk of VT/VF[32] and patients may alter their activity patterns in response to weather conditions, we adjusted for minutes of daily activity using accelerometer data from patients' cardiac device.[17]

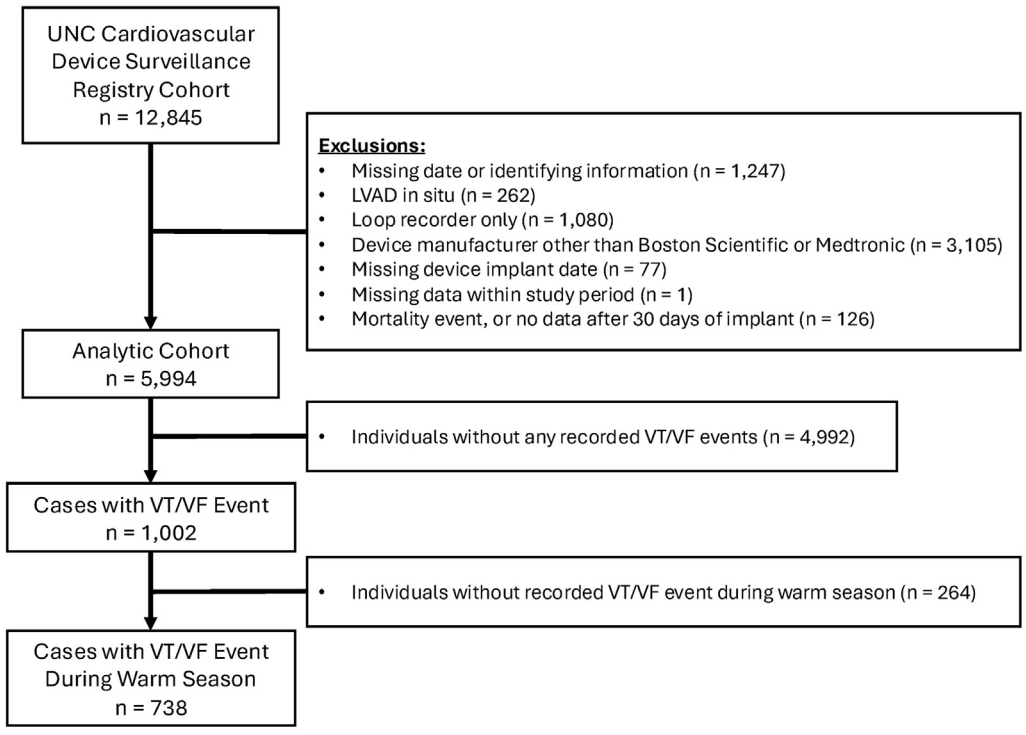
Stratified analyses were performed to explore whether effects varied by individual and community-level factors, and by built environment. Individual-level factors included age (<65, 65-75, >75 years), sex (male, female), race (Black, White), and baseline diagnoses of coronary artery disease, heart failure, hypertension, and myocardial infarction. Community-level factors included income inequality (Gini coefficient <0.4, >0.4), uninsured rate (below median [<14%], above median [>14%]), and neighborhood socioeconomic deprivation (ADI scores for low [1-3], moderate [4-7], high deprivation [8-10]). Built environment was analyzed as "urban, low tree cover" and "urban, high tree cover".

Sensitivity analyses were performed to assess the robustness of the modeling parameters (Supplemental Methods Part D). We also performed an additional analysis with a more specific outcome of VT/VF episodes resulting in device intervention (ATP or shock). Additionally, we repeated the main analysis of humidity with additional statistical adjustment for daily temperature. We also examined relationships between heat index and VT/VF in a supplemental analysis because heat index incorporates both heat and humidity; for this supplemental analysis, daily heat index was derived from the daily temperature and relative humidity data described above using the *Weathermetrics* package in R.[33] VT/VF data were missing on 21,645 of 458,828 (4.7%) of patient-days, and the DLNMs flexibly handled missing patient-days of data without eliminating individuals from the analysis. Data cleaning, analyses, and visualization were conducted between March 2023 and January 2024 using R statistical software (version 4.3.1).

RESULTS

Of the 12,485 individuals in the UNC CDSR registry, 5,944 met study inclusion criteria (see **Figure 2** for cohort eligibility flow diagram). Characteristics of the study cohort at baseline and at the end of study follow up are summarized in **Table 1**. Among those, 1,002 (16.9%) experienced an episode of VT/VF during follow up and 738 (12.4%) experienced a VT/VF event during the warm season. There were 4,488 patient-days with a VT/VF event, accounting for 0.14% of all patient-days. The mean age of all patients at baseline was 74.9 ± 12.9 years with VT/VF events occurring more frequently among men, Black adults, and those who developed cardiovascular comorbidities during follow up. Community-level factors and characteristics of built environment were similar among those who experienced VT/VF during the warm season and patients who never experienced an event (**Table 2**). Warm-season temperature and humidity were not strongly correlated with each other on patient days included in the analysis. Similarly, geographic patterns in warm-season temperature and humidity differed spatially across the study area (Supplemental Figure 2). Across the study period and study area, the 95th percentile and 50th percentile levels for relative

FIGURE 2 Cohort Construction Diagram



LVAD = left ventricular assist device; VF = ventricular fibrillation; VT = ventricular tachycardia.

humidity were 90% and 73.8% respectively; for temperature these levels were 28.5 °C and 24.3 °C.

Exposure to extreme humidity increased the odds of a VT/VF event by 23% over a 7-day period (aOR: 1.23, 95% CI: 1.00-1.51) with highest odds of a VT/VF event occurring the same day as the exposure to extreme humidity (Lag 0) (aOR: 1.04, [95% CI: 1.00-1.08]) (**Central Illustration**). The risk of VT/VF monotonically increased at higher levels of humidity (Supplemental Figure 3).

Figure 3 and Supplemental Table 2 present the effect of extreme humidity on VT/VF modified by individual and community-level factors, and by built environment. The cumulative risk of VT/VF due to extreme humidity exposure was greatest among adults aged 65 to 75 years (aOR: 1.65 [95% CI: 1.16-2.35]), men (aOR: 1.38 [95% CI: 1.08-1.76]), and White patients (aOR: 1.33 [95% CI: 1.03-1.72]) (**Figure 3**). Among patients who were aged 65 to 75, male, and White, effects of extreme humidity on VT/VF were strongest on the day of the exposure (lag 0). Among adults aged 65 to 75 years, we observed a 28% increase in odds of VT/VF at lag 0 and 14% at lag 1 (Supplemental Table 2). Individuals diagnosed with coronary artery disease (aOR: 1.79 [1.25-2.57]), heart failure (aOR: 1.72 [2-2.46]), hypertension (aOR: 2.06 [95% CI: 1.48-2.88]) and myocardial infarction (aOR: 1.75 95% CI: 1.23-2.48]) during follow-up also demonstrated a higher cumulative risk of VT/VF events. Individual lags with the highest odds of VT/VF after humidity exposure varied between clinical factors.

When we examined community-level factors, we found the highest risk of VT/VF among those with higher income inequality (aOR: 1.56 [95% CI: 1.19-2.04]), higher uninsurance rates (aOR: 1.46 [95% CI: 1.11-1.94]), and higher socioeconomic deprivation (aOR: 1.83 [95% CI: 1.28-1.62]). The individual lags with the highest odds of VT/VF after exposure to humidity varied between community strata except for areas with higher socioeconomic deprivation where individual-lag odds of VT/VF remained high and uniform across the entire 7-lag period. Additionally, we found evidence of effect modification by built environment. The risk of VT/VF was higher among individuals residing in urban areas with low tree cover (aOR: 1.29 [95% CI: 0.93-1.78]). The risk was highest on the day of exposure (aOR: 1.08 [95% CI: 0.95-1.22]) and

TABLE 1 Characteristics of the Study Population

Characteristics	Baseline		End of Follow-Up[a]	
	VT/VF Events[b] (n = 738)	No VT/VF Events (n = 5,206)	VT/VF Events[b] (n = 738)	No VT/VF Events (n = 5,206)
Demographics				
Age	69.3 ± 13.2	75.7 ± 12.6	–	–
Sex				
Female	209 (28.3%)	2,340 (44.9%)	–	–
Male	520 (70.5%)	2,836 (54.5%)	–	–
Race				
Black	225 (30.5%)	1,030 (19.8%)	–	–
White	473 (64.1%)	3,938 (75.6%)	–	–
Other	29 (3.9%)	191 (3.7%)	–	–
Device type				
CRT-D	267 (35.9%)	936 (17.9%)	–	–
CRT-P	10 (1.3%)	329 (6.3%)	–	–
ICD	376 (50.5%)	1,073 (20.6%)	–	–
Pacemaker	88 (11.8%)	2,792 (53.5%)	–	–
Lifestyle factors				
Daily minutes of physical activity	119.7 (78.0)	144.3 (104.0)		
BMI at implant, kg/m^2	30.1 (7.4)	29.0 (6.8)	–	–
Alcohol use	232 (31.4%)	1,472 (28.3%)	–	–
Smoking				
Current	113 (15.3%)	411 (7.9%)	–	–
Former	369 (50.0%)	2,452 (47.1%)	–	–
Never	248 (33.6%)	2,293 (44.0%)	–	–
Clinical history				
Hypertension	63 (8.5%)	1,025 (19.7%)	379 (51.4%)	3,363 (56.6%)
Previous myocardial infarction	139 (18.8%)	1,170 (22.5%)	415 (56.2%)	3,066 (51.6%)
Congestive heart failure	43 (5.8%)	638 (12.3%)	310 (42.0%)	2,437 (41.0%)
Coronary artery disease	118 (16.0%)	1,070 (20.6%)	391 (53.0%)	2,969 (49.9%)
Diabetes	42 (5.7%)	575 (11.0%)	194 (26.3%)	1,600 (26.9%)
Sleep apnea	63 (8.5%)	499 (9.6%)	134 (18.2%)	1,007 (16.9%)
Stroke	58 (7.9%)	468 (9.0%)	85 (11.5%)	789 (13.3%)
Dyslipidemia	202 (27.4%)	1,950 (37.5%)	459 (62.2%)	3,796 (63.9%)
Chronic kidney disease	51 (6.9%)	418 (8.0%)	117 (15.9%)	868 (14.6%)
COPD	92 (12.5%)	718 (13.8%)	246 (33.3%)	1,701 (28.6%)
Pulmonary hypertension	68 (9.2%)	348 (6.7%)	96 (13.0%)	531 (8.9%)
Depression	53 (7.2%)	390 (7.5%)	130 (17.6%)	944 (15.9%)
Arrhythmias and conduction defects				
Atrial fibrillation/flutter	70 (9.5%)	809 (15.5%)	405 (54.9%)	2,977 (50.1%)
Prior sudden cardiac arrest	61 (8.3%)	184 (3.5%)	95 (12.9%)	354 (6.0%)
Medications				
ACE inhibitor or ARB	496 (67.2%)	3,158 (60.7%)	602 (81.6%)	4,400 (74.0%)
Beta-blocker	484 (65.6%)	3,308 (63.5%)	674 (91.3%)	4,949 (83.3%)
Statin	446 (60.4%)	3,225 (61.9%)	562 (76.2%)	4,443 (74.7%)
Calcium-channel blockers	177 (24.0%)	1,756 (33.7%)	231 (31.3%)	2,461 (41.4%)
Antiarrhythmic	167 (22.6%)	1,003 (19.3%)	293 (39.7%)	1,626 (27.4%)
Anticoagulant	194 (26.3%)	1,672 (32.1%)	370 (50.1%)	2,937 (49.4%)
Platelet inhibitors	473 (64.1%)	3,385 (65.0%)	593 (80.4%)	4,605 (77.5%)
Diuretics	479 (64.9%)	3,155 (60.6%)	605 (82.0%)	4,440 (74.7%)
SGLT2i	20 (2.7%)	153 (2.9%)	71 (9.6%)	423 (7.1%)

Values are mean ± SD or n (%). [a]Clinical characteristics including comorbid conditions and medication use were measured at baseline (ie time of device implantation) and at the end of follow up for all individuals and are presented here for both time points. Demographic and lifestyle factors were measured only at baseline. [b]Individuals with VT/VF events are defined here as individuals in the case-only cohort with eligible warm-season VT/VF events.

ACE = angiotensin-converting enzyme; ARB = angiotensin receptor blocker; BMI = body mass index; COPD = chronic obstructive pulmonary disease; CRT-D = cardiac resynchronization therapy-defibrillator; CRT-P = cardiac resynchronization therapy - pacemaker; ICD = implantable cardioverter-defibrillator; SGLT2i = sodium glucose transport protein 2 inhibitor; VT/VF = ventricular tachycardia/ventricular fibrillation.

attenuated with time for those residing in areas with urban areas with low tree cover (Supplemental Table 2).

Exposure to high temperatures was not associated with an increased risk of VT/VF (Supplemental Table 3), therefore subgroup analyses were not performed. Additionally, we observed no relationship between heat index and VT/VF (Supplemental Table 3). Sensitivity analyses were conducted for humidity exposure. Results were robust to different model specifications for the DLNMs (Supplemental Table 4) and findings for relative humidity were not affected by adjustment for temperature (Supplemental Table 4). Analyses limited to VT/VF events terminated with device therapy (Supplemental Table 5) did not substantially change the results.

TABLE 2 Community-Level and Built Environment Characteristics of the Study Population

	VT/VF Event (n = 738)	No VT/VF Event (n = 5,206)
Community-level factors		
Income inequality (Gini coefficient)		
High	481 (65.2%)	3,444 (66.2%)
Low	257 (34.8%)	1,761 (33.8%)
Uninsured rate		
Above median	390 (52.8%)	2,623 (50.4%)
Below median	348 (47.2%)	2,582 (49.6%)
Socioeconomic Deprivation (Area Deprivation Index)		
High	228 (31.0%)	1,282 (24.7%)
Moderate	254 (34.5%)	1,844 (35.5%)
Low	254 (34.5%)	2,070 (39.8%)
Built environment		
Urban, high tree cover	232 (31.4%)	1,702 (32.7%)
Urban, low tree cover	270 (36.6%)	1,872 (36.0%)

Values are n (%).

DISCUSSION

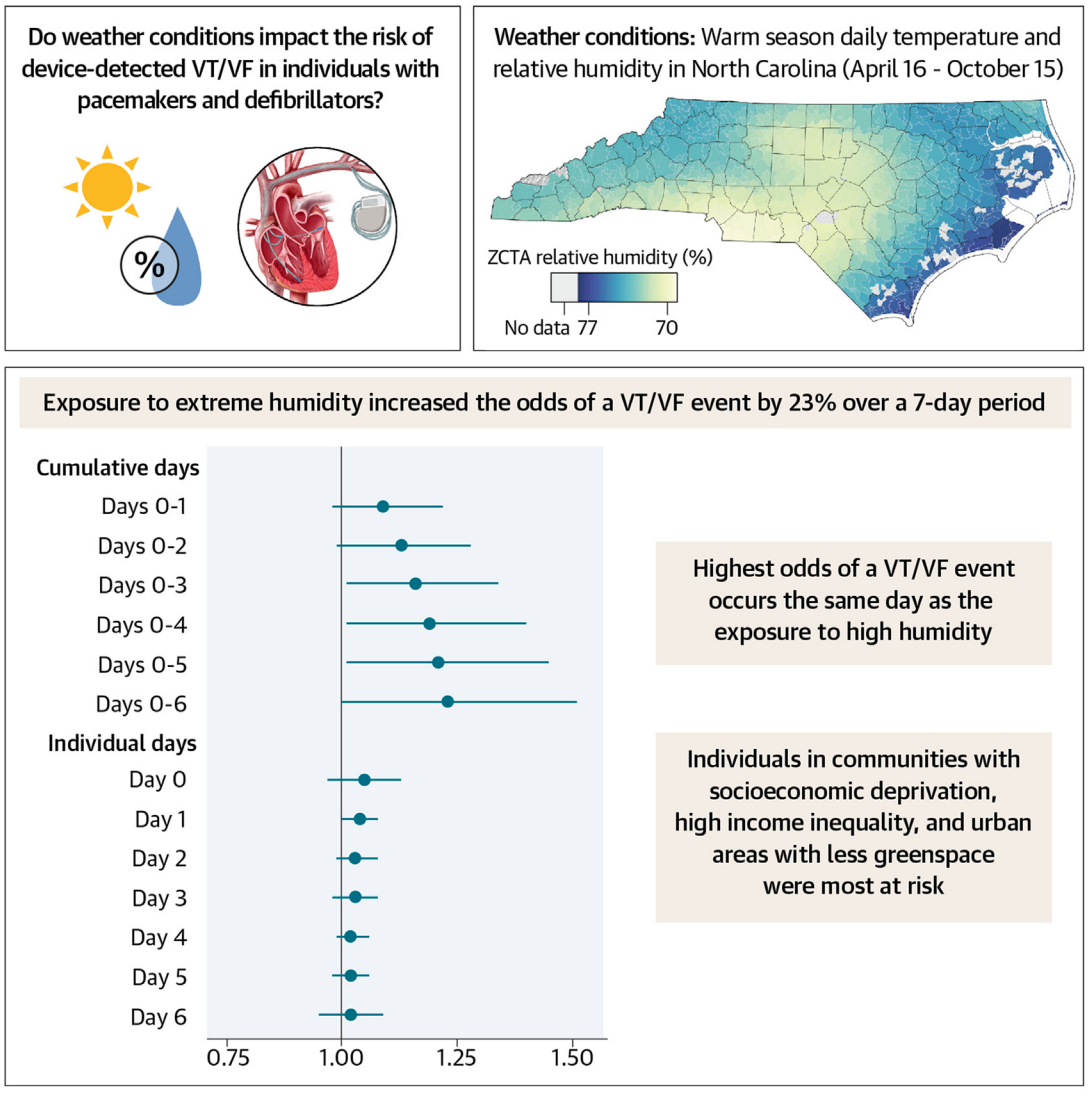
In this large cohort of patients with implanted cardiac devices, we observed that exposure to extreme humidity was associated with a 23% increase in the risk of VT/VF. This excess risk was strongest immediately following the initial humidity exposure and at higher levels of humidity and was independent of known clinical confounders and behavioral risk factors that may be altered in response to warmer temperatures. We also observed a higher risk of humidity-related VT/VF among distinct patient groups (men, elderly adults, white individuals, those with comorbidities), socioeconomically disadvantaged communities, and urban areas with less tree cover. Conversely, we observed no association between high heat temperatures and VT/VF.

The finding of a robust association between exposure to extreme humidity and an increased risk of VT/VF has important clinical and public health implications. VT/VF is a predominant cause of sudden cardiac death in healthy adults and those with chronic health conditions.[34] While patients in this study were more susceptible to irregular heart rhythms and many had ICDs capable of treating potentially fatal ventricular arrhythmias, the potent health effects of humidity found here may extend to other populations and potentially contribute to an increased risk of sudden cardiac death in the general population. Our finding of an association between extreme humidity and clinically meaningful VT/VF events terminated by device therapy supports this potential scenario. Therefore, additional research is needed to determine the health impacts of extreme humidity in other populations, as this information will be essential to support the inclusion of environmental risk factors in medical education and future clinical guidelines. Furthermore, because chronic exposure to acute health risks may accumulate and potentially increase in magnitude over time, there is an urgent need for research on the long-term effects of chronic exposure to extreme humidity on arrhythmia burden across the lifespan.

Another important contribution of this study was the examination of individual and contextual factors that modify susceptibility to humidity-related risk of VT/VF. These findings reveal that men, white individuals, elderly adults, persons with multiple chronic health conditions, and those living in socioeconomically disadvantaged communities were more vulnerable to the adverse cardiovascular effects of extreme humidity. Characteristics of a person's built environment were also found to have a substantial effect on risk of VT/VF. Among individuals living in urban areas, those with more access to greenspace had a lower risk of VT/VF than those residing in areas with less greenspace. These findings are consistent with prior studies that found an increase in cardiovascular morbidity associated with urban heat islands.[35,36] Another recent study of 93 European cities reported that approximately 2,644 premature deaths could be prevented by increasing city tree coverage to 30%.[37] Collectively, these data suggest that increasing green infrastructure in urban areas could be a potentially important public health intervention to attenuate adverse health consequences of climate change in vulnerable communities.[38,39]

North Carolina, along with some of the world's most populous cities, including Sao Paulo, Brazil,

CENTRAL ILLUSTRATION **Effects of Extreme Humidity and Heat on Ventricular Arrhythmia Risk in Patients With Cardiac Devices**



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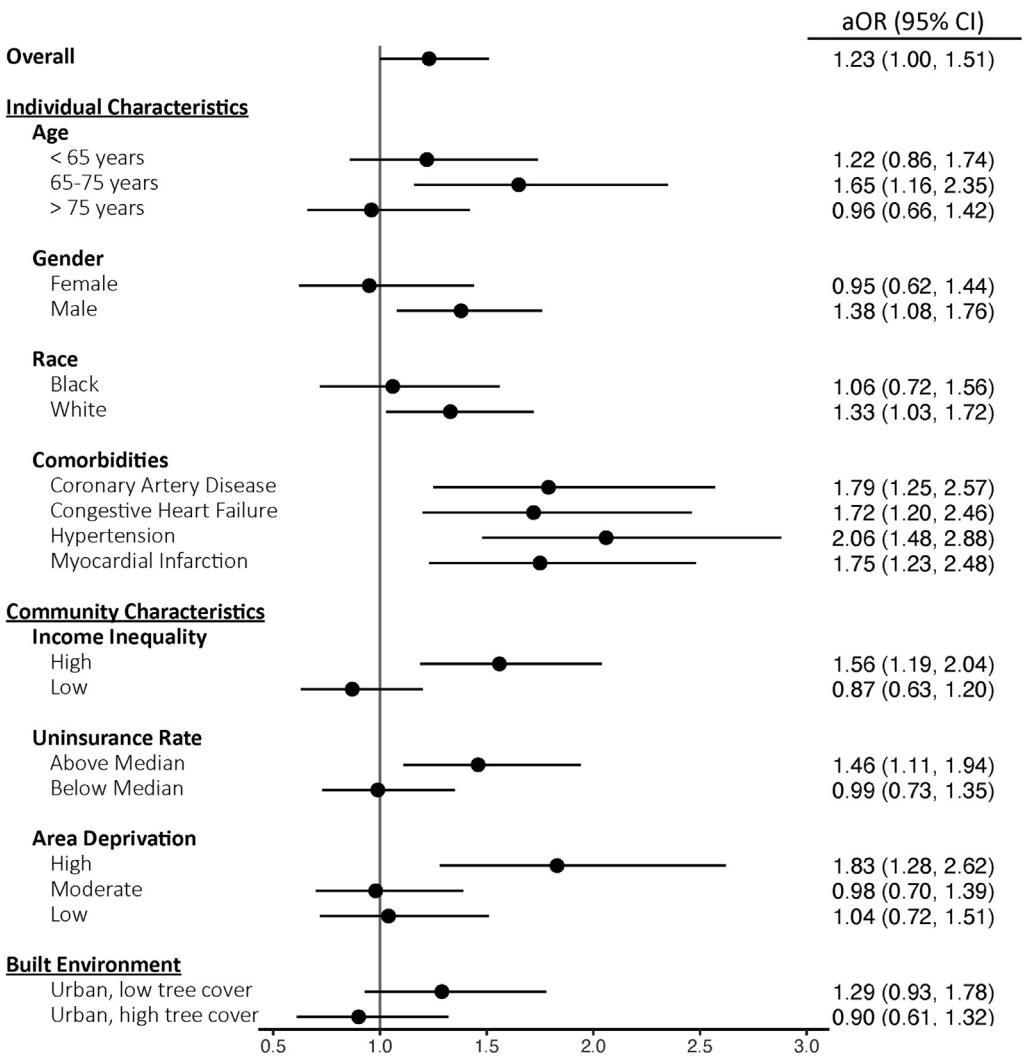
ORs represent the odds of a VT/VF event at the 95th percentile humidity level versus the 50th percentile humidity level. Models were adjusted for patient-level days since device implantation, prior VT/VF events, daily physical activity, and seasonality. Cumulative lags represent the cumulative odds of VT/VF across multiple days following extreme humidity. Individual lags represent the odds of VT/VF on each individual day following extreme humidity.

Beijing, China and Delhi, India, is located in a humid subtropical zone.[40] and experiences greater variability in humidity than temperature during the warm season (Supplemental Figure 2). This may, in part, explain why we did not observe a relationship between extreme heat and VT/VF in this study whereas prior investigations conducted in other climate zones have found associations between higher temperatures and cardiac arrhythmias.[10,41] These findings emphasize the need for further research into the differential effects of weather conditions on cardiovascular outcomes across geographic regions and climate zones with greater temperature variation. This work will be crucial to determine the extent to which there is heterogeneity not only in exposure, but also vulnerability, and will inform the development of multilevel interventions that simultaneously target individuals, communities, and physical

FIGURE 3 Associations Between Extreme Humidity and VT/VF by Individual and Community-level Characteristics and by Built Environment



ORs were estimated for each group separately and represent the 7-day cumulative odds of a VT/VF event at the 95th percentile humidity level versus the 50th percentile humidity level. Models were adjusted for patient-level days since device implantation, prior VT/VF events, daily physical activity, and seasonality.

environments to reduce the adverse health impacts of climate change.

Mechanistically, a wide range of pathways may promote arrhythmogenesis in response to extreme humidity. High humidity can lead to intervascular volume depletion and electrolyte perturbances[42] which can trigger arrhythmia and maintain arrhythmogenic substrate.[43] Increased humidity also blunts the compensatory effects of perspiration, thereby increasing heat-related stress on the cardiovascular system.[44,45] Excess heat stress can also induce vasodilation, increase cardiac output, and increase susceptibility to arrhythmia. Elderly adults and those with comorbid chronic health conditions may have less tolerance for these demands.[44] Increased heat stress can also exacerbate side effects and reduce the overall efficacy of commonly prescribed cardiovascular medications (ie, antihypertensives, antiarrhythmic drugs, and diuretics), thereby increasing health risks.[46] Other plausible mechanisms include altered metabolic processes, oxidative stress, chronic inflammation, and behavioral and environmental factors that may interact synergistically with established cardiovascular risk factors to further increase

the risk of arrhythmia among susceptible individuals.[12,13]

STRENGTHS AND LIMITATIONS. This study has several strengths, including the consideration of both the cumulative and day-by-day risks of heat and humidity exposure and the analysis of multiple sources of high-dimensional health data from a large, prospective patient registry. We also had access to continuous arrhythmia data over a 5-year period, allowing us to precisely define the date of onset of VT/VF. Our analyses were further strengthened by the addition of fine-resolution spatiotemporal meteorological data and detailed information on community socioeconomic conditions linked to patients' residential addresses. Additionally, the case time-series study design controlled for all non-time-varying patient characteristics. Thus, effect estimates are not driven by between-patient differences in clinical history or long-term health behaviors.

Despite these advantages, our study has limitations. First, because this was a retrospective observational study, no causal relationship should be inferred. Second, although the study design and rich dataset permitted adjustment for a wide range of baseline characteristics and time-varying confounders, the influence of unknown confounders that vary quickly over time (eg, acute stress) cannot be excluded. Third, humidity was operationalized as relative humidity, a metric used in weather forecasts that is familiar to clinicians and patients. There are multiple ways to measure humidity (eg relative humidity, vapor pressure, absolute humidity) and recent scholarship has highlighted the importance of selecting the appropriate measure[47]; in our study area the extreme levels of summer relative humidity, with 90% relative humidity at the 95th percentile, inherently also represent a high level of absolute humidity and vapor pressure. Similarly, we were also unable to adjust for air pollution which has been shown to trigger cardiac arrhythmias in prior studies.[48] While exposures were based on geocoded residential addresses and therefore had a high degree of spatial precision, we did not directly measure individuals' exposure to outdoor weather conditions. The use of daily weather data limited the temporal resolution of this analysis to days. Fourth, arrhythmia episodes were classified by validated device detection algorithms. Although this may have resulted in occasional misclassification of events, it is unlikely to have affected our results, as misclassification would have occurred consistently within individual patients. Electrograms were also not available for adjudication and information on device programming was not available. Fifth, this study was not powered to ascertain the effects of extreme humidity on device therapies during the warm season. Therefore, effects on devices therapies were analyzed as a secondary endpoint. Finally, this analysis was limited to patients with established CVD who were implanted with CIEDs from 2 of the largest device manufacturers in the United States (Medtronic and Boston Scientific). The extent to which these results are generalizable to other populations or geographies is uncertain; however, they provide a strong foundation for larger studies in more diverse populations exposed to greater fluctuations in daily humidity and temperature.

CONCLUSIONS

Findings from this investigation suggest that exposure to extreme humidity is associated with an increased risk for potentially life-threatening arrhythmias among adults with preexisting CVD. These associations were strongest among vulnerable patient groups, disadvantaged communities, and urban areas with less green space; external community-level and built-environment factors are potentially modifiable through policy to increase adaptive capacity for extreme weather. Future investigations need to determine whether targeted multi-level interventions, such as increasing green space in socially vulnerable communities, decrease cardiovascular risk and increase resilience to climate change.

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ADDRESS FOR CORRESPONDENCE: Prof Lindsey A. Rosman, Division of Cardiology, Department of Medicine, University of North Carolina at Chapel Hill, 160 Dental Circle - CB 707527599-7075, Chapel Hill, North Carolina 27514 USA. E-mail: Lindsey_Rosman@med.unc.edu.

PERSPECTIVES

COMPETENCY IN MEDICAL KNOWLEDGE: Climate change is increasing the frequency of high heat and high humidity days. Exposure to extreme weather conditions has been associated with adverse cardiovascular outcomes but has not been evaluated as a risk factor for ventricular arrhythmias (VT/VF) in persons with pre-existing cardiovascular risk. In this large cohort of patients with implanted cardiac devices, exposure to extreme humidity during the warm season was associated with an increased risk of ventricular arrhythmias, with the highest risks observed among vulnerable patient groups, socioeconomically disadvantaged communities, and urban areas with less green space. This study suggests that extreme humidity may be an important risk factor for potentially lethal cardiac arrhythmias in persons with established cardiovascular risk.

TRANSLATIONAL OUTLOOK: Further research is needed to determine whether cardiovascular risk in susceptible individuals and communities can be reduced, and outcomes improved by increasing awareness of risk and motivating the at-risk population to reduce exposure.

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APPENDIX For supplemental methodological details as well as supplemental tables and figures, please see the online version of this paper.