INTRODUCTION

Ambulatory blood pressure monitoring (ABPM)—the measurement of blood pressure (BP) over a 24-h period—is the reference standard for BP measurement. ABPM results predict cardiovascular disease (CVD) events and mortality more accurately than clinic BP measurements. Additionally, ABPM allows for the identification of high-risk phenotypes—including nocturnal non-dipping of BP and heart rate (HR)—which cannot be diagnosed in the clinic.

People with HIV (PWH) have a twofold to fourfold higher incidence of CVD. This increased risk may be partly attributable to abnormalities in nocturnal BP and HR. We do not yet know whether these ABPM abnormalities observed in PWH differ by clinic BP status.

Therefore, we conducted a nested case-control study comparing ABPM in PWH with normal and high clinic BP and HIV-uninfected controls in Tanzania. Objectives of this research were as follows: 1) to compare nocturnal non-dipping of BP and HR between PWH and HIV-uninfected controls and 2) to determine...
correlates of nocturnal non-dipping of BP and HR in PWH and HIV-uninfected controls.

2 | METHODS

2.1 | Study cohort

This nested case-control study was conducted within a well-described prospective cohort of PWH attending an outpatient HIV clinic in Tanzania and HIV-uninfected controls.

2.2 | Study population

Cohort inclusion criteria include age 18-65 years, Tanzanian citizenship, and residing in Mwanza City. Exclusion criteria for both groups include previous history of CVD and a medical condition with a prognosis of <12 months.

2.3 | Study location

All study activities were performed in the outpatient HIV clinic at Bugando Medical Centre, in Mwanza, Tanzania.

2.4 | Study procedures

Study procedures have been described in detail previously. At each study visit, a standardized questionnaire and physical examination were administered. Automated BP was measured using an OMRON HBP-1300 (OMRON Healthcare) professional BP monitor. High clinic BP was defined as BP measurements (≥140/90 mmHg) on at least two consecutive visits according to the International Society of Hypertension (ISH) threshold.

2.5 | Ambulatory blood pressure monitoring study design

From February 2018 to June 2018, we performed ABPM on 50 consecutive cohort participants attending scheduled research clinic appointments with normal clinic BP. We also performed ABPM on all participants with high clinic BP.

2.6 | Ambulatory blood pressure measurement

Ambulatory blood pressure monitoring was performed using the validated SunTech Medical® Oscar 2 machine, programmed via the AccuWin Pro 4 software to measure BP for 24 h at an interval of 15 min. Initial readings were confirmed in-clinic. Participants were instructed to return to the clinic after 24 h. The following day self-reported sleep and wake times were recorded. All participants identified as hypertensive were referred to a physician and offered free hypertension treatment according to the Tanzanian guidelines. All ABPM met European Society of Hypertension (ESH) quality control guidelines for ABPM, which require >20 daytime and >7 nighttime measurements, and ≥70% valid measurements of expected measurements. Nocturnal non-dipping of HR/BP was defined as an asleep HR/BP reduction of ≥10% of awake values.

2.7 | Laboratory procedures

CD4⁺ T-cell count was measured using an automated BD FACS Calibur Machine (BD Biosciences) for PWH. Serum creatinine level was measured using the A25 Analyzer (Biosystems), calibrated by the creatinine Jaffé 2 method. An estimated glomerular filtration rate (eGFR) was calculated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) Equation. Urine albumin and creatinine were measured with the Siemens DCA Vantage Analyzer (Siemens Healthcare). High-sensitivity serum C-reactive protein (hsCRP) concentration was measured using R&D Systems Quantikine ELISA (R&D Systems). hsCRP measurements were classified according to cardiovascular risk, with hsCRP >3 mg/L representing high risk and hsCRP ≤3 mg/L representing low/intermediate risk.

2.8 | Statistical methods

Data were double entered into OpenClinica (OpenClinica LLC). Baseline participant characteristics were summarized using median and interquartile range for continuous variables and frequency and percent for categorical variables. For categorical variables, chi-squared tests or Fisher’s exact tests, as appropriate, were performed to evaluate the association between HIV status and BP/HR dipping status. Multivariate logistic regression analyses adjusted for clinic systolic blood pressure (SBP) were used to evaluate factors associated with nocturnal non-dipping of BP/HR. All analysis was conducted using Stata version 15.1 (STATACorp LLC).

2.9 | Ethics

The study was carried out in accordance with Good Clinical Practice and the Declaration of Helsinki. The study and consent forms were approved by the Weill Cornell Medicine (1506016328), the Tanzanian National Institute of Medical Research (NIMR/HQ/R.8c/Vol.1/1399), and Bugando Medical Centre (CREC/074/2015). All participants provided written informed consent.
3 | RESULTS

3.1 | Study population and characteristics

The baseline characteristics of all study participants are displayed in Table S1. Of the 137 participants selected, 50 had normal clinic BP (25 PWH and 25 HIV-uninfected) and 87 had high clinic BP (31 PWH and 56 HIV-uninfected). None of the participants had started anti-hypertensive medication at the time of ABPM measurement. All of the PWH were on ART. Mean duration of ART use was 1.46 years and ranged from 0 to 3.15 years. PWH and HIV-uninfected controls were similar in age, sex distribution, and BMI (Table S1). Analysis of the associations between HIV infection and ABPM results are in Table S2.

3.2 | Nocturnal non-dipping of BP/HR in all participants

Overall, PWH had a higher prevalence of nocturnal non-dipping of HR (39.3% [22/56] in PWH vs. 19.8% [16/81] in HIV-uninfected controls, \( p = .01 \)) than HIV-uninfected controls. Nocturnal non-dipping of BP was more common in PWH but this did not reach statistical significance (64.2% [36/56] in PWH vs. 53.1% [43/81] in HIV-uninfected controls, \( p = .19 \)).

3.3 | Nocturnal non-dipping of BP/HR in participants with normal versus high clinic BP

Prevalence of nocturnal non-dipping of HR/BP stratified by HIV status and clinic BP is displayed in Figure 1 and Table S3. Among participants with normal clinic BP, PWH had a higher prevalence of nocturnal non-dipping of BP (64.0% [16/25] in PWH vs. 36.0% [9/25] in HIV-uninfected controls, \( p = .048 \)). Among participants with high clinic BP, PWH had a higher prevalence of nocturnal non-dipping of HR (41.9% [13/31] in PWH vs. 21.4% [12/56] in HIV-uninfected controls, \( p = .043 \)) than HIV-uninfected controls.

3.4 | Correlates of non-dipping

Factors associated with nocturnal non-dipping of HR and BP independent of clinic SBP were similar in PWH and HIV-uninfected controls.
to data collection, data analysis, data interpretation, manuscript preparation, and revised manuscript for important intellectual content. AE contributed to study conception, design, data collection, and revised manuscript for important intellectual content. KR contributed to study conception, design, data collection, and revised manuscript for important intellectual content. SF contributed to data collection, data analysis, and revised manuscript for important intellectual content. CN contributed to study conception, design, data collection, and revised manuscript for important intellectual content. AE contributed to study conception, design, data collection, and revised manuscript for important intellectual content. KR contributed to study conception, design, data collection, and revised manuscript for important intellectual content. SF contributed to data collection, data analysis, and revised manuscript for important intellectual content. CN contributed to study conception, design, data collection, and revised manuscript for important intellectual content. AE contributed to study conception, design, data collection, and revised manuscript for important intellectual content. KR contributed to study conception, design, data collection, and revised manuscript for important intellectual content. SF contributed to data collection, data analysis, and revised manuscript for important intellectual content.

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CONFLICT OF INTEREST
The authors report no conflicts of interest.

AUTHOR CONTRIBUTIONS
CN contributed to study conception, design, data collection, and revised manuscript for important intellectual content. KR contributed to data collection, data analysis, data interpretation, manuscript preparation, and revised manuscript for important intellectual content. SF contributed to data collection, data analysis, and revised manuscript for important intellectual content.
data analysis, data interpretation, and revised manuscript for important intellectual content. CE contributed to data analysis, data interpretation, manuscript preparation, and revised manuscript for important intellectual content. JK contributed to study conception, study design, data collection, manuscript preparation, and revised manuscript for important intellectual content. CM contributed to study conception, study design, manuscript preparation, and revised manuscript for important intellectual content. ML contributed to study design, data analysis, data interpretation, manuscript preparation, and revised manuscript for important intellectual content. SK contributed to study conception, study design, data interpretation, manuscript preparation, and revised manuscript for important intellectual content. RP contributed to study conception, study design, data collection, data analysis, data interpretation, manuscript preparation, and revised manuscript for important intellectual content.

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SUPPORTING INFORMATION
Additional supporting information may be found online in the Supporting Information section.

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