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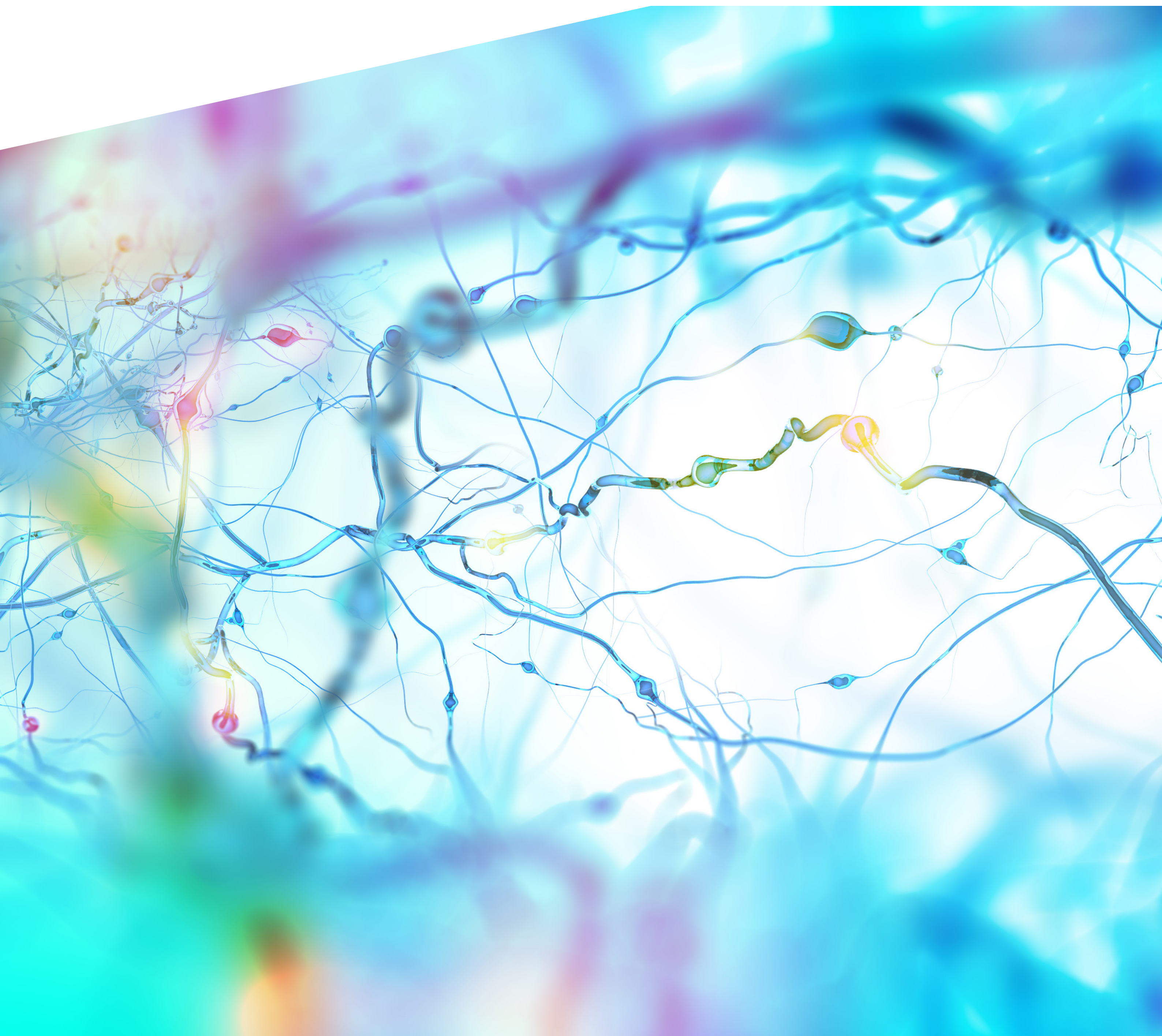

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Aims & Scope

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Original Articles

Case Report

Original Article

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Prognostic Significance of 24-Hour Ambulatory Blood Pressure and Holter Monitoring in Patients without Atrial Fibrillation

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Key Words
Blood pressure monitoring, ambulatory; Holter; Cardiovascular diseases; Stroke

Objectives: This study investigated the 24-hour ambulatory blood pressure monitoring (ABPM) and Holter parameters for evaluating their prognostic significance of cardiovascular events including stroke in population without atrial fibrillation (AF).
Methods: Among 3,199 patients that underwent ABPM, 335 who also underwent Holter recordings were selected in a tertiary hospital. Seventeen patients who had been documented with AF on Holter monitoring or diagnosed with AF were excluded, and finally 318 patients were analyzed. The association between cardiovascular events and ABPM/Holter parameters was analyzed by a logistic regression model, and the risk factors were estimated by a Cox hazard model. Age, sex, and histories of cardiovascular disease were adjusted by a multivariable analysis, and the cut-off values were suggested by a Kaplan-Meyer analysis.
Results: During the total follow-up (28.5±1.7 months), 13 (4.1%) stroke, 6 (1.9%) heart failure, and 12 (3.8%) acute coronary syndrome incidences were observed. In the univariate analysis of the ABPM parameters, an increment in the night systolic BP (hazard ratio=1.034, P=0.020) and night diastolic BP (hazard ratio=1.063, P=0.031) significantly elevated the risk of a stroke occurrence. According to the Kaplan-Meyer analysis, there was a significant difference in the stroke incidence between the groups divided by a cut-off value of the night systolic BP of 120 mmHg (P=0.014) and night diastolic BP of 75 mmHg (P=0.023).
Conclusion: In a population without AF, the nocturnal BP was a significant predictor of a stroke incidence. At this point, the cut-off value of mean 120/75 mmHg in 24 ABPM was advisable.

Introduction

Blood pressure (BP) monitoring and the electrocardiogram (ECG) are fundamental tools for assessing the risk of cardiovascular disease (CVD). Among them, 24-hour ambulatory BP monitoring (ABPM) and Holter monitoring are the most accurate diagnostic tools for measuring BP fluctuations and rhythm changes during the day [1–4]. The 24-hour ABPM is useful for predicting the risk of CVD by measuring the change in the continuous BP and the BP during sleep, and the Holter gives a lot of information on the ECG to diagnose arrhythmias [5]. In addition, the Holter contains information on the heart rate variability, which represents the activity of the sympathetic / parasympathetic nervous system, which is known to be highly related to the development of

CVD [6]. Nevertheless, measuring the patient's BP and ECG for 24-hour has the disadvantage of having to be attached to the body for a long time, so it is not easy to use them in the clinic. However, with the recent popularization of wearable devices, it is possible to measure the BP, heart rate, and ECG over 24-hour as well as during sleep [7]. Continuous ECG monitoring is useful in detecting arrhythmias including atrial fibrillation (AF) [8]. Continuous BP monitoring also has many clinical implications in chronic kidney disease. Compared to an office BP, the ABPM is recommended as a better tool in assessing a renal prognosis [9,10] and the cardiovascular risk of non-dialysis chronic kidney disease patients [11].

However, the ECG measured by a wearable device is just a single lead ECG, and the BP recorded through the wearable device is not accurate and is in an experimental stage as compared to the conventional BP monitoring [12]. Therefore, it seems to be of great significance to find the clinical implication of the continuous medical data measured by 24-hour ABMP and Holter monitoring in the development of CVD. So, we wanted to determine the relationship between heart failure (HF), acute coronary syndrome (ACS), AF, and the stroke incidence, which have been known as typical CVDs, and the parameters of 24-hour ABPM and Holter monitoring. Further, since AF is already known as the strongest risk factor for a stroke [13], we tried to find the risk factors for CVDs including strokes in patients without AF from 24-hour ABPM and Holter monitoring.

Methods

1. Study design

This study protocol was approved by the institutional review board of the Ewha Womans University Mokdong Hospital (IRB number: 2019-12-025-002). The study participants were selected from 3,199 patients who underwent ABPM at a tertiary general hospital (Ewha Womans University Medical Center, Seoul, Korea) from January 15, 2010 to November 27, 2018. The medical record dataset included information on the diagnosis based on the tenth revision of the International Classification of Disease (ICD-10) codes, admission, and treatment. A past history including congestive HF, hypertension, diabetes mellitus (DM), strokes, and ACS were analyzed by the existence of main diagnosis data with an ICD code (I50, I10-I15, E10-E14, I63-I66, I20-I25 respectively). For the analysis, patients who had been diagnosed with AF were excluded. Further, the study was conducted based on electronic medical records of 335 patients who also received Holter monitoring. Among them, 17 patients with documented AF on the Holter were excluded. At last, a final analysis was obtained in 318 eligible participants (Fig. 1). Finally the patients analyzed were followed up for 748.5 person-years in total. The average follow-up period was 28.6 months.

2. Study variables

The data of the independent variables were obtained from the ABPM and Holter monitoring. According to the ABPM results, a non-dipper was defined. A non-dipper was a subject whose mean BP did not decrease greater than 10% during sleep as compared to that during the daytime. Otherwise, the subject was defined as a dipper [14]. Covariates were collected based on the subject’s first interview, physical examination, and laboratory data executed for their cardiovascular examinations. Those covariates were the height, weight, body mass index, tobacco usage, and past histories of hypertension, type 2 DM, dyslipidemia, and AF. The lipid profiles of low density lipoprotein cholesterol and total cholesterol were gathered. The history of

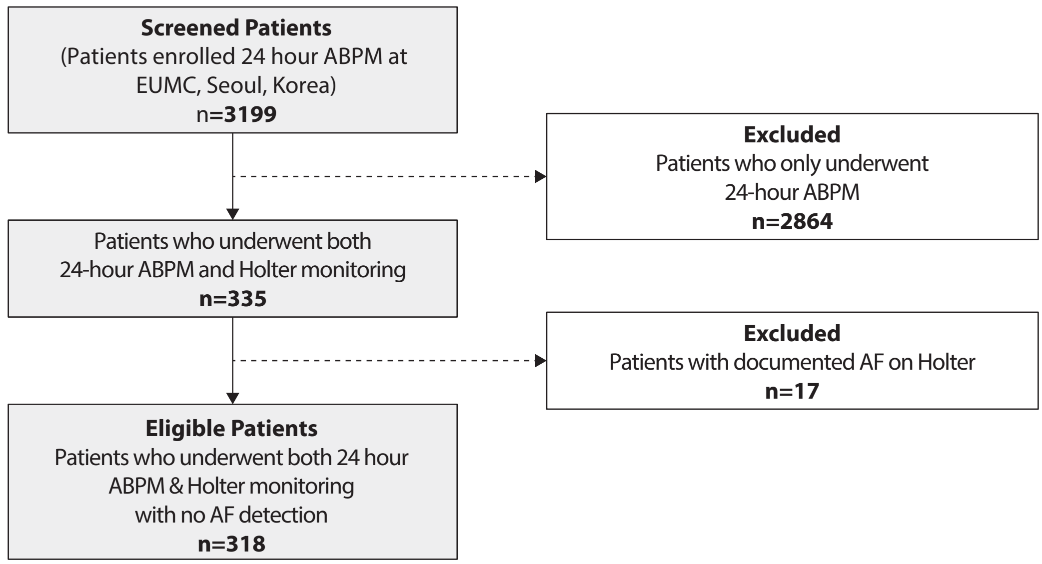

Fig. 1. Study design. By screening 3,199 patients who received 24 hr ABPM, 335 patients who also participated in Holter monitoring were enrolled. After excluding 17 patients with documented AF, 318 patients were eligible for the study analysis. ABPM, ambulatory blood pressure monitoring; AF, atrial fibrillation.

CVD such as a stroke, HF, or ACS was also collected.

The endpoint of this study was the occurrence of a stroke, HF, or ACS. All events were prespecified and coded according to the International Classification of Diseases 10th Revision (ICD-10). The total cardiovascular events in this study referred to the occurrence of either a stroke, HF, or ACS events.

3. Measurement (24-hour ambulatory blood pressure monitoring [ABPM], 24-hour Holter)

Both tests were performed on an inpatient or outpatient basis as the workups of the patients' clinical problems. BP measurements and ECG monitoring were recorded for 24-hour. A TM – 2430 (A&D, Tokyo, Japan) device was used for the ABPM. A SEER light (GE, Tokyo, Japan) device was used for the Holter monitoring. The data obtained did not include any unnecessary personal information to ensure the anonymity of the individuals. Also, the patient's information for the analysis was encrypted.

4. Statistical analysis

For the database management and statistical analysis, this study used IBM SPSS Statistics 25.0 software. A Student's t-test was used to compare the quantitative variables of the baseline characteristics. A Pearsons' chi-square test (χ^2 test) was used to analyze the qualitative variables. Moreover, the logistic regression model was used to find the significant parameters from the Holter and ABPM monitoring. In this analysis, the sex, age and other significant covariates were adjusted by the multiple regression model. Hazard ratios (HR) and CI were calculated by a Cox analysis. Finally, the survival curves of the significant ABPM parameters were estimated using a Kaplan Meier survival analysis.

Results

The baseline characteristics were analyzed in 335 individuals. The study population was

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composed of 52.8% (n=177) males and 47.2% (n=158) females. The average age of the population was 56.4±0.89 years. The mean body mass index was 24.5±3.48 kg/m^2, 13.4% (n=45) were current smokers, 25.0% (n=84) had a history of CVD, 54.0% (n=181) were diagnosed with hypertension, 5.0% (n=17) had known AF, 12.2% (n=41) had type 2 DM, and 13.1% (n=44) had dyslipidemia. The mean LDL cholesterol level was 97.43±41.86 mg/dL. The mean total cholesterol level was 168.79±49.21 mg/dL. The 24-hour mean BP of the study population was 129/79 mmHg (±16/10). The mean BP during the daytime and nighttime were 133/82 mmHg (±16/10) and 121/72 mmHg (±17/12), respectively (Table 1).

1. Comparison of the patients with and without cardiovascular events

Table 1 shows the clinical differences between the patients with or without primary events. During the follow up, 27 (8.4%) patients experienced 13 (4.0%) strokes, 12 (3.7%) ACSs, and 6 (1.8%) HF events. In comparison to those who remained free of disease, the patients who experienced CVD were older (P=0.026), and had a more frequent history of CVD (P<0.001) and AF (P<0.001; Table 1). The Supplemental Tables (Tables S1–S3) show the baseline characteristic analysis based on each disease. The stroke patients were older (P=0.028) and more often had AF (P=0.002) and dyslipidemia (P=0.018). They also had more histories of CVDs (P<0.001). Similarly, the ACS and HF patients had significantly more CVD histories than those without them (P=0.002, 0.004, respectively). The HF patients additionally had a more frequent history of AF (P=0.001; Tables S1–S3).

2. Analysis of the 24-hour ambulatory blood pressure monitoring (ABPM) and Holter variables

This study examined the association between each CVD (strokes, ACS, and HF) and the parameters of the ABPM/Holter. Tables 2–3 shows the results of the logistic regression analysis for the stroke incidence. In Table 2, the mean 24-hour systolic BP (sBP, odds ratios [OR]=1.040, 95% CI 1.006–1.075, P=0.020), daytime mean sBP (OR=1.038, 95% CI 1.003–1.074, P=0.032), night time sBP (OR=1.037, 95% CI 1.006–1.068, P=0.017), and night time diastolic BP (dBP,

Table 1. General characteristics of the study population analyzed by the cardiovascular disease morbidity

Characteristics		Non-CVD (n=308)	CVD (n=27)	P-value
Clinical features	Female [n (%)]	146 (47.4)	12 (44.4)	0.925
	Age (yrs±SD)	55.85±16.52	63.19±13.73	0.026*
	BMI (kg/m^2±SD)	24.56±3.51	24.25±3.08	0.664
Questionnaires	Tobacco use [n (%)]	40 (13.1)	5 (18.5)	0.388
	DM [n (%)]	36 (11.8)	5 (18.5)	0.354
	CVD Hx [n (%)]	64 (20.8)	20 (74.1)	<0.001***
	Known AF [n (%)]	12 (3.8)	5 (18.5)	<0.001***
	HTN Hx [n (%)]	163 (52.9)	18 (66.7)	0.227
	Dyslipidemia Hx [n (%)]	37 (12.0)	7 (25.9)	0.067
Biochemical data	LDL (mg/dL)	98.18±41.60	89.10±36.45	0.334
	Total cholesterol (mg/dL)	169.81±49.30	158.56±48.10	0.276

CVD, cardiovascular disease; BMI, body mass index; DM, diabetes mellitus; CVD Hx, cardiovascular disease history including acute coronary syndrome, heart failure, and stroke; AF, atrial fibrillation; HTN Hx, hypertension history; LDL, low density lipoprotein.
*,**,*** Statistical significance (P<0.05; P<0.01; P<0.001) of the difference between the two groups.

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Table 2. OR and 95% CIs of the stroke incidence according to the parameters of the 24-hour ABPM in people without atrial fibrillation

Variable of 24 hr ABPM		Unadjusted		Adjusted†	
		OR (95% CI)	P-value	OR (95% CI)	P-value
24 hr BP	Mean sBP (mmHg)	1.040 (1.006–1.075)	0.020*	1.040 (0.995–1.086)	0.080
	Mean dBP (mmHg)	1.031 (0.971–1.095)	0.319	1.080 (0.991–1.177)	0.080
Day BP	Mean sBP (mmHg)	1.038 (1.003–1.074)	0.032*	1.037 (0.993–1.083)	0.096
	Mean dBP (mmHg)	1.014 (0.952–1.080)	0.665	1.052 (0.971–1.140)	0.213
	Systolic load (%)	1.011 (0.990–1.032)	0.305	1.011 (0.986–1.036)	0.399
	Diastolic load (%)	0.999 (0.974–1.024)	0.931	1.009 (0.978–1.041)	0.558
Night BP	Mean sBP (mmHg)	1.037 (1.006–1.068)	0.017*	1.035 (0.994–1.078)	0.099
	Mean dBP (mmHg)	1.062 (1.003–1.124)	0.040*	1.118 (1.016–1.231)	0.022*
	Systolic load (%)	1.003 (0.998–1.008)	0.210	1.002 (0.997–1.007)	0.447
	Diastolic load (%)	1.026 (1.000–1.053)	0.053	1.032 (0.997–1.068)	0.072
	Dipper	0.237 (0.048–1.159)	0.075	0.244 (0.037–1.608)	0.143

Odds Ratios (OR) and CIs were estimated by a logistic regression analysis.
24 hr ABPM, 24 hours ambulatory blood pressure; sBP, systolic blood pressure; dBP, diastolic blood pressure.
*Statistical significance (P<0.05) of the difference between the two groups.
†The variables were adjusted for the sex, age, and known cardiovascular disease history.

OR=1.062, 95% CI=1.003–1.124, P=0.040) had significant associations with the stroke incidence. After an adjustment for the sex, age, and a history of CVD, only the night mean dBP had a significant association (OR=1.118, 95% CI 1.016–1.231, P=0.022).

Table 3 shows the correlation between the stroke incidence and Holter parameters. The significant parameters were the SD of all NN intervals (SDNN; P=0.030) and SD of the averages of the NN intervals (SDaNN; P=0.020). However, after the adjustment, they were not significant (Tables 2–3). The correlation between the ambulatory tests and ACS, HF, and total CVD events

Table 3. OR and 95% CIs of the stroke incidence according to the parameters of the 24-hour Holter examination in people without atrial fibrillation

Variable of 24 hr Holter		Unadjusted		Adjusted†	
		OR (95% CI)	P-value	OR (95% CI)	P-value
Arrhythmia	APC (%)	0.000	0.996	0.000	0.996
	PVC (%)	0.000	0.995	0.000	0.995
Time domain	Average HR (beat/m)	1.013 (0.954–1.076)	0.666	1.027 (0.959–1.099)	0.449
	Mean NN (ms)	1.000 (0.995–1.005)	0.906	0.998 (0.992–1.004)	0.502
	SDNN (ms)	0.979 (0.960–0.998)	0.030*	0.983 (0.957–1.008)	0.181
	SDaNN (ms)	0.974 (0.952–0.996)	0.020*	0.928 (0.955–1.010)	0.200
Heart rate variability	LF (ms)	1.004 (0.997–1.011)	0.257	1.004 (0.993–1.015)	0.460
	HF (ms)	0.874 (0.728–1.049)	0.149	0.888 (0.711–1.111)	0.299
	L/H (ms)	1.046 (0.210–5.198)	0.956	2.102 (0.410–10.781)	0.373

Odds Ratios (OR) and CIs were estimated by a logistic regression analysis.
APC, atrial premature complexes; PVC, premature ventricular contraction; HR, heart rate; beat/m, beat/minute; NN, normal to normal; ms, millisecond; SDNN, SD of all NN intervals; SDaNN, SD of the averages of the NN intervals; LF, low frequency; HF, high frequency; L/H, LF/HF.
*Statistical significance (P<0.05) of the difference between the two groups.
†The variables were adjusted for the sex, age, and known cardiovascular disease history.

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is presented in Tables S4–S9. In the single-variable analysis of the Holter parameters for the ACS incidence, the OR for atrial premature complexes (%) was 1.226 (CI: 1.017–1.478, P=0.032, Table S5) and the OR for PVCs (%) was 1.150 (CI: 1.007–1.314, P=0.040, Table S5). Further, in the 24-hour ABPM, the ORs for the mean 24-hour sBP (OR=1.053, CI: 1.005–1.104, P=0.031) and daytime mean sBP (OR=1.054, CI: 1.004–1.106, P=0.034) for HF (Table S6) were statistically significant (Tables S4–S9).

3. 24-hour ambulatory blood pressure monitoring (ABPM) as a predictor of the morbidity risk

Table 4 shows the Cox regression results of the ABPM parameters for strokes, ACS, and HF. In the case of a stroke, the risk increased significantly as the night mean sBP (HR=1.034, P=0.020) and night mean dBP (HR=1.063, P=0.031) increased. After the adjustment, only the nighttime mean dBP (HR=1.060, P=0.045) was statistically significant for predicting the risk of

Table 4. HR and 95% CIs of the incidence of cardiovascular disease according to the 24-hour ABPM parameters analyzed by a Cox proportional hazard model

Variable of 24 hr ABPM		Unadjusted		Adjusted	
		HR (95% CI)	P-value	HR (95% CI)	P-value
Stroke	24 Mean sBP	1.038 (1.005–1.71)	0.021*	1.031 (0.998–1.066)	0.064
	24 Mean dBP	1.033 (0.976–1.093)	0.263	1.053 (0.992–1.118)	0.091
	Day mean sBP	1.036 (1.002–1.070)	0.035*	1.033 (0.999–1.069)	0.057
	Day mean dBP	1.019 (0.961–1.080)	0.531	1.042 (0.980–1.109)	0.191
	Night mean sBP	1.034 (1.005–1.064)	0.020*	1.025 (0.996–1.056)	0.097
	Night mean dBP	1.063 (1.006–1.123)	0.031*	1.060 (1.001–1.121)	0.045*
	Dipper	0.261 (0.054–1.258)	0.094	0.361 (0.071–1.837)	0.220
ACS	24 Mean sBP	0.980 (0.938–1.025)	0.379	0.982 (0.943–1.023)	0.388
	24 Mean dBP	0.967 (0.911–1.026)	0.270	0.970 (0.916–1.027)	0.296
	Day mean sBP	0.795 (0.932–1.020)	0.277	0.976 (0.935–1.020)	0.279
	Day mean dBP	0.952 (0.883–1.027)	0.204	0.951 (0.882–1.027)	0.202
	Night mean sBP	0.991 (0.952–1.031)	0.642	0.987 (0.949–1.026)	0.509
	Night mean dBP	0.994 (0.939–1.052)	0.830	0.986 (0.937–1.038)	0.587
	Dipper	2.282 (0.57–9.129)	0.243	1.911 (0.453–8.055)	0.378
HF	24 Mean sBP	1.053 (1.002–1.106)	0.040*	1.052 (0.994–1.114)	0.078
	24 Mean dBP	1.069 (0.984–1.161)	0.114	1.090 (0.987–1.203)	0.088
	Day mean sBP	1.054 (1.005–1.106)	0.032*	1.089 (1.000–1.990)	0.050*
	Day mean dBP	1.060 (0.978–1.148)	0.157	1.083 (0.908–1.195)	0.116
	Night mean sBP	1.044 (0.997–1.093)	0.065	1.046 (0.994–1.101)	0.083
	Night mean dBP	1.094 (0.997–1.201)	0.057	1.085 (0.972–1.210)	0.146
	Dipper	0.830 (0.116–5.923)	0.853	2.726 (0.198–37.589)	0.454

Hazard ratios (HRs) and CIs were estimated by a Cox proportional hazard model. The variables were adjusted for the sex, age, and significant baseline characteristics related to each disease.
Significant baseline characteristics of ACS: known CVD history.
Significant baseline characteristics of a stroke: known CVD, AF history, and dyslipidemia Hx.
Significant baseline characteristics of HF: known CVD history and known AF history.
sBP, systolic blood pressure; dBP, diastolic blood pressure; ACS, acute coronary syndrome; HF, heart failure.
*Statistical significance (P<0.05) of the difference between the two groups.

stroke morbidity. There was no significant variable related to the development of the total CVD for the ABPM. As for the HF, in the multivariate analysis, a higher daytime mean sBP (HR=1.089, P=0.050) increased the HF risk (Table 4).

Being a dipper had a preventive effect on the incidence of the total cardiovascular events (HR=0.379, P=0.047; Table S10). The risk analysis of the Holter parameters are presented in Table S11. In the case of a stroke, the risk decreased as the SDNN (HR=0.973, P=0.009) and SDaNN (HR=0.966, P=0.008) increased in the Holter monitoring (Table S11). The risk of ACS increased significantly when the percent (%) of atrial premature complexes (HR=1.207, P=0.036) increased on the Holter (Table S11).

4. Night blood pressure (BP) cut-off value for a stroke prognosis prediction

According to the results of the Cox analysis, this study determined the cut-off value of the night mean BP, since it turned out to have a prognostic significance for strokes. In Fig. 2A, when the cut-off value of the night sBP was set to 120 mmHg (P=0.014), the stroke incidence was significantly predicted. In Fig. 2B, a night dBP of 75 mmHg (P=0.023) was a significant cut-off value. Taken together in Fig. 2C, when the two groups were divided based on a night BP of 120/75 mmHg (P=0.006), there was a significant difference in the stroke risk over time (Fig. 2A–C). Fig. 3 shows the relationship between the stroke distribution according to the night BP and a cut-off value of 120/75 mmHg based on Fig. 2.

Discussion

In this study, we analyzed the prognostic parameters of CVD events using data obtained from Holter and 24-hour ABPM monitoring in 335 patients. Through this analysis, we observed that in a population without AF, nocturnal BP emerged as a significant predictor of stroke incidence. Notably, we found that a mean nocturnal BP of 120/75 mmHg on 24-hour ABPM could serve as an advisable cut-off value.

1. Prognostic ability of the 24-hour ambulatory blood pressure monitoring (ABPM)

Previous studies on the relationship between 24-hour ABPM and CVD outcomes have been limited. The first study, conducted by Perloff and colleagues [15], involved 751 patients and assessed both daytime ABP and clinical blood BP measurements over a 5-year follow-up period. Their findings demonstrated that a combination of 24-hour ABPM and clinical BP values was a more accurate predictor of cardiovascular events compared to clinical BP alone. While this study faced some criticism, it pioneered the exploration of 24-hour ABPM's prognostic value. The second study, published by Verdecchia and colleagues [16], followed 1,187 hypertensive individuals and 205 normotensive men and women for an average duration of 3.2 years. The observed event rate was similar among normotensive individuals and those with white-coat hypertension, but significantly higher among individuals with sustained hypertension. The current study contributes additional insights into the prognostic value of 24-hour ABPM, specifically in patients with higher nocturnal BP, a high-risk group for cardiovascular complications.

In the case of a stroke, the nighttime BP was more related to the events than the daytime BP. When predicting the risk (HR), both a higher night sBP and the dBP, significantly increased the risk of a stroke occurrence in the univariate Cox regression analysis. The Night dBP was significant even after the adjustment, but the sBP was not. We also found that a cut-off of

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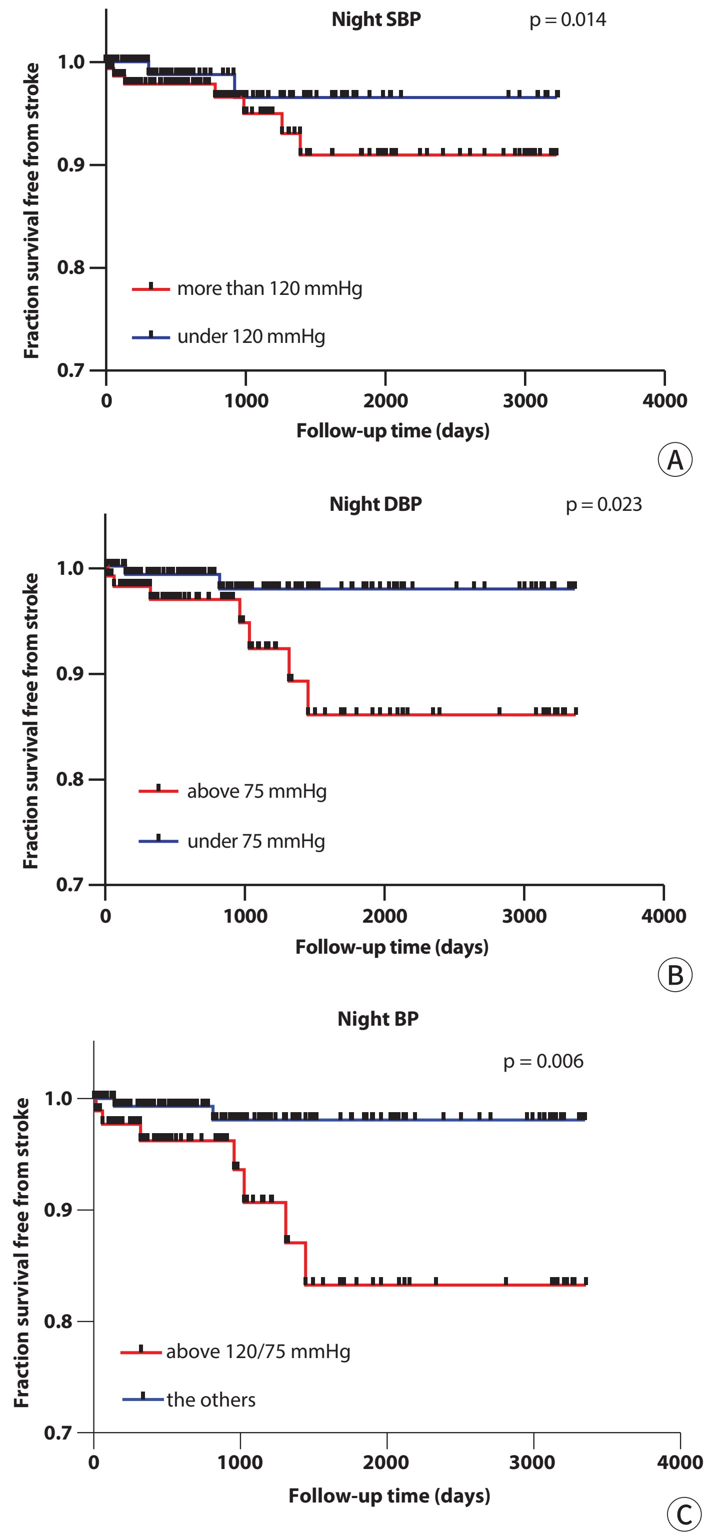

Fig. 2. Fraction survival free from strokes according to the cutoff value of the nighttime BP. (A) By a Kaplan-Meyer analysis, the significant difference in the stroke incidence between the groups divided by the cut-off value was a nighttime sBP of 120 mmHg. (B) In the case of the nighttime dBP, 75 mmHg was a significant cut-off value. (C) Also both the nighttime BP cut-off values of 120/75 mmHg were significant. SBP, systolic blood pressure; DBP, diastolic blood pressure; BP, blood pressure.

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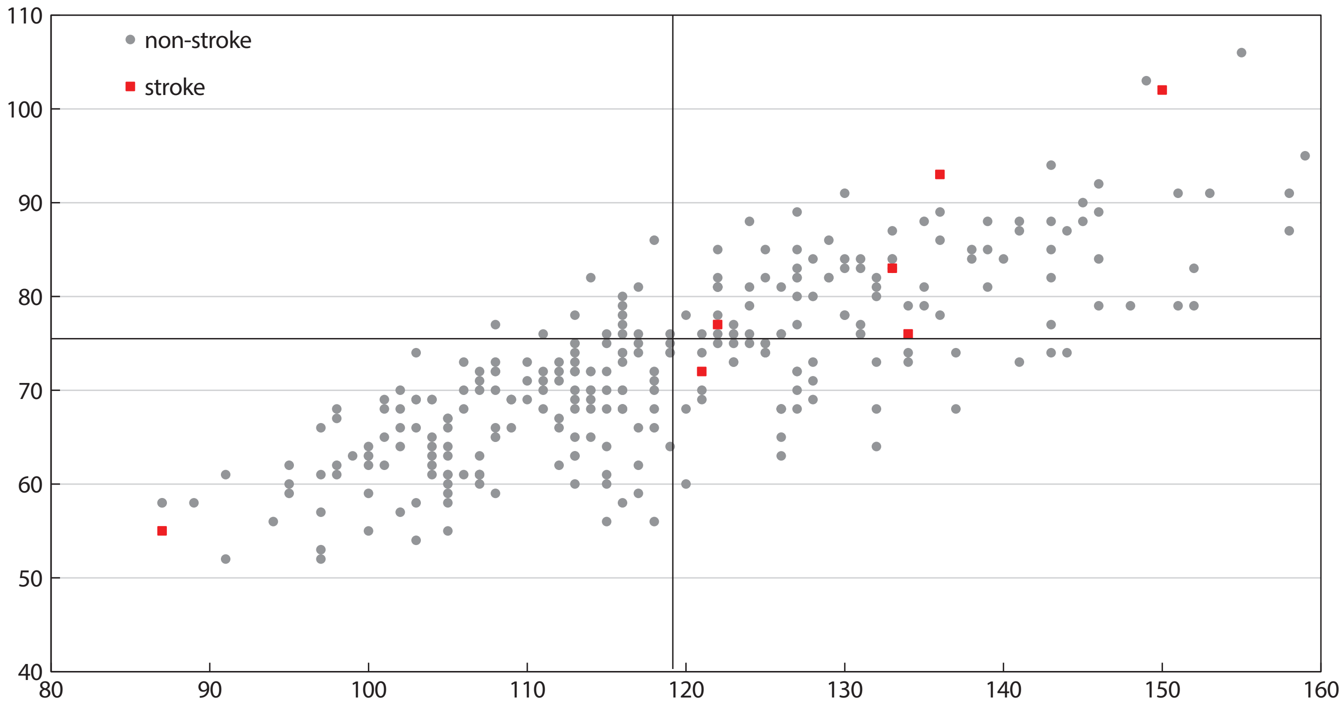

Fig. 3. Stroke incidence according to the nighttime BP cut-off value. The data of the 318 patients are distributed based on the nighttime sBP/dBP (mmHg). Nine patients with an occurrence of a stroke are marked as red boxes, and the grey circles mean the patients without a stroke. The cut-off of 120/75 mmHg was suggested by the Kaplan Meier survival analysis (P=0.006). BP, blood pressure; sBP, systolic blood pressure; dBP, diastolic blood pressure.

120/75 mmHg made a significant difference in the stroke occurrence between the two groups (P=0.006, Fig. 2). On the other hand, a dipper had no prognostic significance of a stroke. However, it should be considered that a dipping status has a low reproducibility and can be affected by antihypertensive drug treatment. However, there was no significant parameter that predicted the risk of ACS on the ABPM. On the other hand, in the case of HF, the mean daytime sBP predicted the risk of HF (HR=1.054, P=0.032; Table 4). It was significant even after the adjustment of a known CVD history and known AF history (HR=1.089, P=0.050; Table 4).

2. Night blood pressure (BP) and stroke risk

It has already been found that the nighttime BP has a closer relationship to cardiovascular risk [17,18]. In our study, the increase in the nighttime BP rather than the daytime BP increases the risk of a stroke, which is consistent with the fact that the nighttime BP is a more powerful prognostic factor. There are various hypotheses about the mechanism of why the nighttime BP had a better prognostic significance. Firstly, the decreased nocturnal arteriolar tone might lead to a greater impact on the small arteries supplying target organs during the elevation of the BP. When sleeping, organs need a minimal BP to get adequate perfusion, and the kidney's afferent arteriolar tone becomes lower. However, a high BP at night can exceed the level of adequate perfusion and damage target organs such as the heart, vasculature, and kidneys [19]. Secondly, there are some hypotheses that the harmful effect of increased sympathetic activity, sleep apnea, and BP dependent natriuresis are related [17,18]. Finally, the nighttime BP is less variable than the daytime BP, which can lead to accurate monitoring. During the daytime, physical

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and mental changes affect the BP, so the ABPM may not truly reflect the daytime averages [20]. Also, the daytime BP decreases and becomes less predictive because antihypertensive medications are taken during the daytime [18].

The 2017 American college of Cardiology / American Heart Association guidelines suggest that a nighttime BP of 120/70 mmHg in the ABPM corresponds to the hypertension criteria of 140/90 for the Clinic BP and this is based on the general population [21]. In our study, the cut-off of 120/75 mmHg for the nighttime ABPM was found to be a significant prognostic factor for a population without AF.

3. Limitations of the study

This study had limitations in terms of the retrospectively collected data. The patients were not free from the effects of the medications. In addition, the study population was small, which was all collected in one hospital. Moreover, as this study targeted patients who underwent both Holter and ABPM monitoring, they might be a high-risk group for cardiovascular events. More cardiovascular events might have occurred than in the general population. Finally, silent AF patients without symptoms might not have been included in this study, because they usually are not tested.

4. Strength of the study

However, there were several strengths of this study. First, we used 24-hour ABPM to predict the risk factor of CVD. There was a clinical implication in that we revealed the relationship between the nighttime BP and strokes on the ABPM, which is frequently used in the outpatient setting. Secondly, unlike other previous studies, the Holter and ABPM were analyzed at the same time. There have been few studies interpreting the results of both tests. This study took the advantages of both test's diagnostic sensitivity and accuracy. Finally, by excluding patients with AF, we offered a more reliable BP cut-off to predict strokes. AF itself is a strong risk factor for a stroke and its medications can affect the results.

5. Perspective

Further prospective studies should be performed to determine whether a tighter control of the nighttime BP affects the CVD morbidity and mortality reduction. Also, as this study suggested the nighttime BP cut-off in a population without AF, it is necessary to study the BP cut-off in a population with diagnosed AF. Considering that AF is a powerful risk factor of CVD, it might be necessary to select a different level of BP control.

6. Conclusion

In a population without AF, the nocturnal BP was a significant predictor of a stroke incidence. At this point, a cutoff value of 120/75 mmHg was advisable.

Acknowledgements

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Conflict of Interest
No potential conflict of interest relevant to this article was reported.

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Ethics Approval and Consent to Participate
This study protocol was approved by the institutional review board of the Ewha Womans University Mokdong Hospital (IRB number: 2019-12-025-002).

Supplementary Materials
Supplementary materials are available from: https://doi.org/10.12771/emj.2023.e6.

Supplementary Table S1. General characteristics of the study population analyzed by the stroke morbidity
Supplementary Table S2. General characteristics of the study population analyzed by the ACS morbidity
Supplementary Table S3. General characteristics of the study population analyzed by the heart failure morbidity
Supplementary Table S4. OR and 95% CI of the ACS incidence according to the parameters of the 24-hour AMBP in people without atrial fibrillation
Supplementary Table S5. OR and 95% CI of the ACS incidence according to the parameters of the 24-hour Holter examination in people without atrial fibrillation
Supplementary Table S6. OR and 95% CI of the heart failure incidence according to the parameters of the 24-hour AMBP in people without atrial fibrillation
Supplementary Table S7. OR and 95% CI of the heart failure incidence according to the parameters of the 24-hour Holter examination in people without atrial fibrillation
Supplementary Table S8. OR and 95% CI of the cardiovascular disease incidence according to the parameters of the 24-hour AMBP in people without atrial fibrillation
Supplementary Table S9. OR and 95% CI of the cardiovascular disease incidence according to the parameters of the 24-hour Holter examination in people without atrial fibrillation
Supplementary Table S10. HR and 95% CI of the incidence of the total cardiovascular disease according to the 24-hour AMBP parameters analyzed by a Cox proportional hazard model
Supplementary Table S11. HR and 95% CI of the incidence of the cardiovascular diseases according to the 24-hour Holter examination parameters analyzed by a Cox proportional hazard model

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Original Article

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A Proactive Testing Strategy to COVID-19 for Reopening University Campus during Omicron Wave in Korea: Ewha Safe Campus (ESC) Project

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Key Words
COVID-19; COVID-19-testing

Objectives: Ewha Womans University launched an on-campus Coronavirus disease-19 (COVID-19) response system called Ewha Safety Campus (ESC) Project in collaboration with the Seegene Inc. RT-PCR diagnostic tests for COVID-19 were proactively provided to the participants. This study examines the effectiveness of the on-campus testing strategy in controlling the reproduction number (R_t) and identifying student groups vulnerable to infection.

Methods: The ESC project was launched on March 2, 2022, with a pilot period from Feb 22 to March 1, 2022—the peak of the Omicron variant wave. We collected daily data on the RT-PCR test results of the students of Ewha Womans University from Mar 2 to Apr 30, 2022. We daily calculated R_t and compared it with that of the general population of Korea (women, people aged 20–29 years, and Seoul residents). We also examined the students vulnerable to the infection based on the group-specific R_t and positivity rate.

Results: A lower R_t was observed about 2 weeks after the implementation of the ESC Project than that of the general population. The lower R_t persisted during the entire study period. Dormitory residents had a higher R_t. The positivity rate was higher in students who did not comply with quarantine guidelines and did not receive the second dose of the vaccine.

Conclusion: The study provides scientific evidence for the effectiveness of the on-campus testing strategy and different infection vulnerabilities of students, depending on dormitory residence, compliance with the quarantine guidelines, and vaccination.

Introduction

As of Aug 12, 2022, more than 580 million confirmed cases of COVID-19 have been reported globally, more than 6 million of whom have died due to related complications (WHO Coronavirus

Dashboard - URL: http://covid19.who.int, access date: Aug 13, 2022) [1]. Clearly, South Korea (hereafter, Korea) was not an exception to the pandemic. In Korea, more than 21 million cases of confirmed COVID-19 and more than 25,000 related deaths were recorded by Aug 12, 2022 [1]. Although the number of confirmed cases in the country was <640,000 before the period of Omicron wave began (Jan 2022 onward), the spread of COVID-19 rapidly increased since then and the number of cumulative confirmed cases increased from 635,250 (Jan 01, 2022) to 17,237,878 (Apr 30, 2022) [2].

COVID-19 has drastically changed the education system worldwide. For example, in the US alone, >1,300 colleges and universities have suspended the traditional face-to-face classes, closed campuses, and/or have begun implementing different instruction approaches (in-person, online, and hybrid) [3]. Similarly, in Korea also, most educational institutions have started distance online learning classes. However, it remains to be seen whether and how campuses will reopen [4], and what is the impact of COVID-19 restrictions on the quality of education, student well-being, and public health, as well as returns to the local economy [5].

In the US, quarantine strategies including basic preventive measures (e.g., face coverings, physical distancing, and handwashing), on-campus arrival protocols (e.g., recommendation for asymptomatic COVID-19 testing and sequestration for the first 7 days of campus reopening), and periodic asymptomatic surveillance testing are recommended for campus reopening and restarting in-person classes [6]. The Ministry of Education of Korea announced the educational operation plan for the first semester of 2022 by utilizing the high vaccination rate of 20–29-year-old population (97.3%; at least once as of April 4). One of the main goals of campus reopening was the sustenance of in-person classes through autonomous quarantine strategies [7]. In accordance with the announcement, Ewha Womans University (Seoul, Korea) has launched an on-campus COVID-19 response system called the Ewha Safety Campus (ESC) Project [8]. This response project aimed to normalize the educational operation and implement in-person classes by reducing the transmission risk among students and staff and by establishing sustainable management plans against COVID-19. The core element of the ESC Project is the use of RT-PCR tests to diagnose COVID-19 for all members of Ewha Womans University at no cost for better accessibility of the testing [8], and the University announced the operation of ESC project to all school members both online and offline (the testing station was piloted on Feb 22, 2022).

This study evaluates the effectiveness of the ESC Project in reducing and containing the COVID-19 transmission. We calculate the daily reproduction number (R_t) of the confirmed cases to examine whether the ESC Project made any reduction in the transmissibility in the participants compared to that in the general population. We also investigate the transmission risk in vulnerable student groups to obtain epidemiological evidence for establishing differentiated on-campus COVID-19 action plans based on the residential type and compliance with quarantine policies and vaccination.

Methods

1. Study population

The ESC was launched on Mar 2, 2022. The pilot period was from Feb 22 to March 1. Any students of Ewha Womans University could participate in this project. The school strongly recommended using the ESC by mobile messages for students who were symptomatic, those who had close contact with confirmed cases, students in dormitories, or those who used crowded facilities; however, all students and school members voluntarily determined whether to use the ESC or the public community health centers to get a diagnostic test. All ESC exams had to be scheduled using the online reservation system via the Ewha Womans University Portal. During the study, we collected information on the date of testing, sex, age, dormitory residence, compliance with quarantine policies, and the vaccination stage of each participant. RT-PCR diagnostic tests for COVID-19 were provided to all participants of the project from Mar 2 to Apr 30, 2022. During the study period, 16,745 tests were performed on 6,240 students. We excluded 3,020 cases (1,166 students) that did not consent to participate in this research. Thus, our final study population includes 11,348 cases (3,220 students).

The variable on compliance with quarantine policies was self-reported and dichotomized to indicate whether a participant complied with all recommended quarantine policies, namely wearing a facial mask, washing hands, avoiding unnecessary social gatherings, and avoiding communal facilities. The vaccination-stage variable included the self-reported vaccination stage from none to the third dose of vaccine. We defined the fully vaccinated case as the participant who had received second and/or third dose of vaccine, regardless of the vaccine type.

2. COVID-19 case data of Ewha Safety Campus (ESC) cohort

RT-PCR tests with two different types of specimens were conducted on the ESC cohort for COVID-19 diagnosis. The test kits were provided by Seegene Medical Foundation free of cost [9]: 1) Combo Swab with self-collected specimens from the nasal and oral cavity under the supervision of a healthcare professional (hereinafter "Combo Swab RT-PCR"), and 2) nasopharyngeal swab (NPS) RT-PCR conducted by a medical professional (hereinafter "NPS RT-PCR"). The Combo Swab RT-PCR test was used for low-risk students who wanted to undergo a COVID-19 test. In contrast, the NPS RT-PCR test was used for high-risk students who tested positive for the Combo Swab test, were in contact with people with confirmed COVID-19, exhibited suspicious symptoms, and/or were exposed to other high-risk situations. These tests were performed at two separate testing stations, called Ewha Safety Stations (ESS). The ESS were open on weekdays and closed on weekends and holidays. Detailed testing procedures are shown in Fig. 1. Although two types of RT-PCR tests were conducted on the ESC cohort, we defined confirmed cases as only those who tested positive on NPS RT-PCR based on the guidelines of the Korean Society for Laboratory Medicine [10].

3. COVID-19 case data from the general population

We obtained daily counts of confirmed cases of COVID-19 of Korea from Mar 2 to Apr 30, 2022, by using the open data of the Korea Disease Control and Prevention Agency (KCDA) [2]. The data were stratified based on the residential region, age (0–19 yr, 20–39 yr, 40–59 yr, 60–79 yr, and 80+ yr), and sex of the patients. To increase comparability with the students of Ewha Womans University, we analyzed daily confirmed cases from the general population for women, people aged 20–39 years, and people living in Seoul.

4. Statistical analysis

We estimated the daily reproduction number (R_t) [11] during the study period following Cori et al.'s method (using the EpiEstim package in R version 4.0.3) [11,12]. R_t indicates the average number of new infections caused by a single infected person at time t in the people susceptible to infection. It denotes the power of transmission (i.e., transmissibility) [11,13]. R_t was calculated based on a combination of the observed daily confirmed cases and the distribution of the serial interval (the time interval between infection and subsequent transmission). Based on a previous

Omicron variant study in Korea, we calculated R_t with the serial interval assumed to follow a normal distribution with a mean of 3.78 days and a SD of 0.76 days [14] with a 14-day time window [11]. We calculated the R_t series of Ewha university students (via ESC cohort) and for each general population (women, people aged 20–29 years, and Seoul residents). We also estimated R_t for students living in dormitories, those complying with quarantine guidelines, and those who are fully vaccinated. In addition to R_t, to assess the different vulnerability to infection, we calculated the positivity rate (%) of the students based on their compliance with all quarantine guidelines and whether they are fully vaccinated.

Results

From Mar 2 to Apr 30, 2022, 11,348 applications (Combo-swab or NPS RT-PCR tests) were recorded on the ESC cohort (Fig. 1). A total of 711 confirmed cases of COVID-19 were reported (positivity rate: 6.27%; Table 1), with 264 cases for students living in dormitories (positivity rate: 3.52%), 679 cases for students who answered that they complied with all quarantine guidelines (positivity rate: 6.06%), and 697 cases for students who said that they were fully vaccinated (positivity rate: 6.22%; Table 2). During the same period, 5,524,226, 1,444,505, and 1,954,871 confirmed cases were reported for women, people aged 20–29 years, and people living in Seoul (Table 3).

Students who answered that they complied with all quarantine guidelines (6.06%) showed lower positivity rates than those who did not comply (20.0%) during the study period (Table 2).

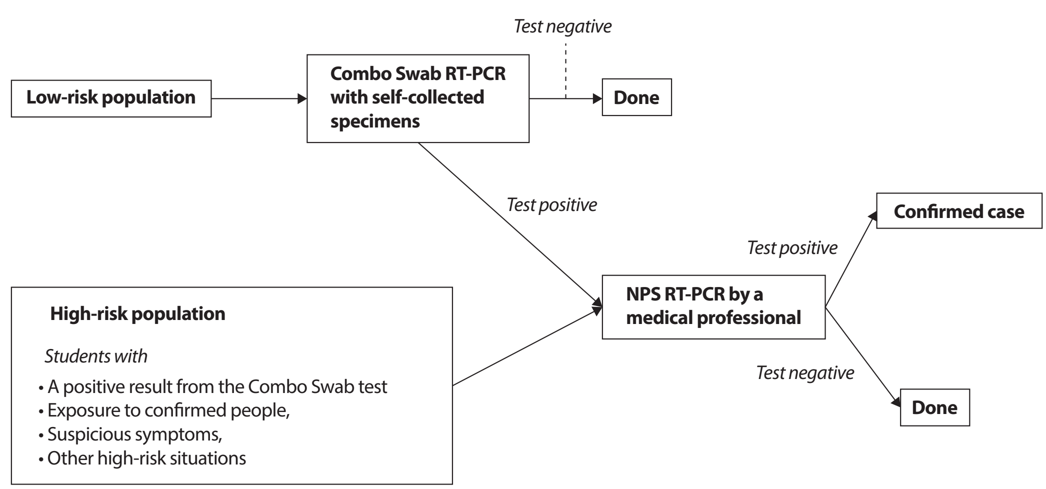

Fig. 1. Testing procedures of Ewha Safety Campus (ESC) cohort. NPS, nasopharyngeal swabs.

Table 1. Descriptive statistics for Ewha Safety Campus (ESC) project participants

Period	The number of confirmed cases	The number of applications	Positive rate (%)
Total period (Mar 02 to Apr 30, 2022)	711	11,348	6.27
March	607	6,519	9.31
April	104	4,829	2.15

The number of tests indicates the number of applications (Combo-swab, NPS RT-PCR, or both).
NPS, nasopharyngeal swab.

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Table 2. Positive rates by student groups registered in Ewha Safety Campus (ESC) cohort

Group	The number of confirmed cases	The number of applications	Positive rates (%)	Ratio of positive rates (95% CI)
Complied with all quarantine policies				
Yes	679	11,183	6.06	0.30 (−0.01, 0.62)
No	33	165	20	1.0 (ref)
Fully vaccinated (second dose or more)				
Yes	697	11,213	6.22	0.6 (0.1, 1.1)
No	14	135	10.37	1.0 (ref)
Dormitory usage				
Yes	264	7,504	3.52	0.3 (0.16, 0.45)
No	447	3,844	11.63	1.0 (ref)

Quarantine policies: wearing a facial mask, washing hands, avoiding unnecessary social gatherings, and avoiding communal facilities.

Table 3. Descriptive statistics for confirmed cases in the general population during the study period (Mar 02 to Apr 30, 2022)

Population	Total number of confirmed cases	Average confirmed cases/Day
Total	10,130,252	235,587.3
Females	5,524,226	128,470.4
Aged 20–29	1,444,505	33,539.1
Seoul residents	1,954,871	45,462.1

Students who were fully vaccinated (6.22%) also had lower positivity rates than those who were not (10.37%). Fig. 2 displays the temporal trends of daily confirmed cases (left) and daily number of diagnostic tests (right) for Ewha students through the ESC cohort. The infection peak was observed around Mar 5–10 (Fig. 2).

The initial R_t of Ewha students was slightly higher (or similar) than that of the general populations (Fig. 3). However, the R_t of Ewha students decreased faster and was smaller across all study periods after two weeks of the initiation of the ESC Project, compared to that in the general populations.

Among the ESC subgroups, changes in R_t are presented in Fig. 4. The R_t for student groups at Ewha Womans University and those living in dormitories was higher, indicating a higher transmissibility than that of the total students. However, we could not observe an evident difference in the R_t distribution based on compliance with quarantine guidelines and full vaccination.

Discussion

This study examined the effectiveness of the ESC Project that aims to reduce COVID-19 transmission in students by conducting proactive diagnostic tests. The results showed that the ESC Project might be effective in reducing the transmissibility among the students to a higher extent than that in general populations. Furthermore, the ESC Project also investigated student groups vulnerable to infection by assessing group-specific R_t or positivity rates and revealed

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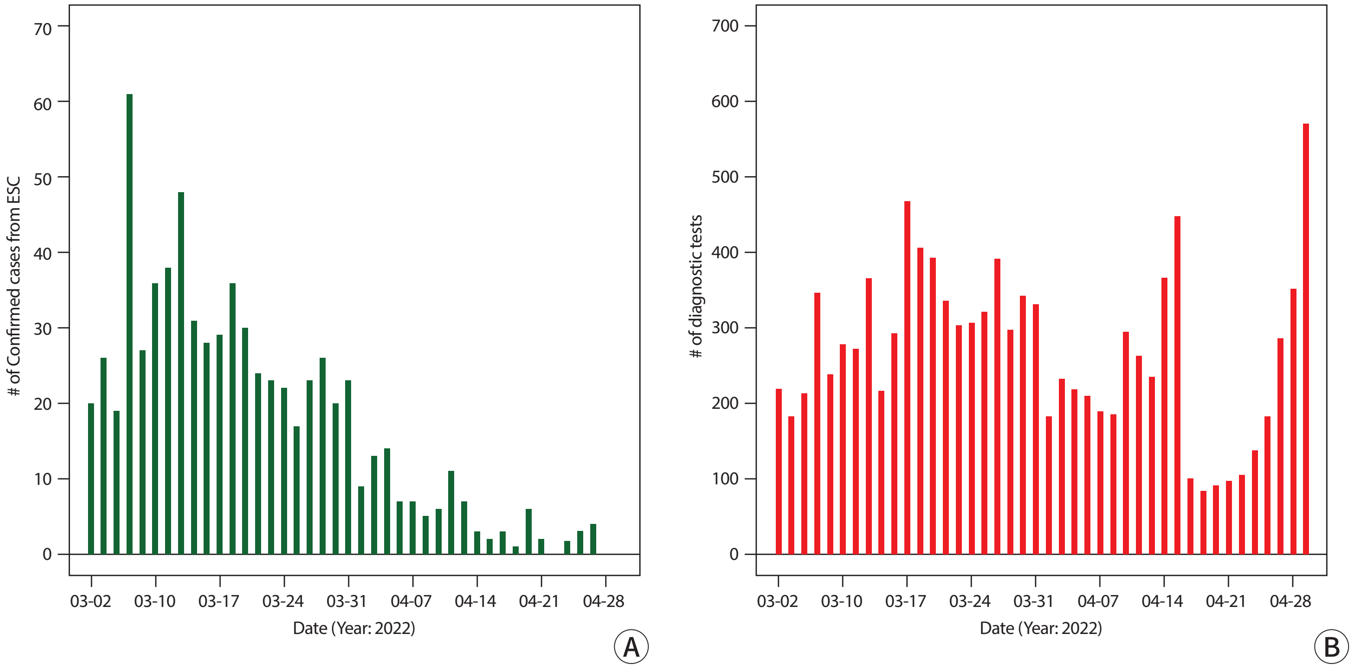

Fig. 2. Daily series of confirmed COVID-19 cases (A) and diagnostic tests (B) at Ewha Safety Campus cohort.

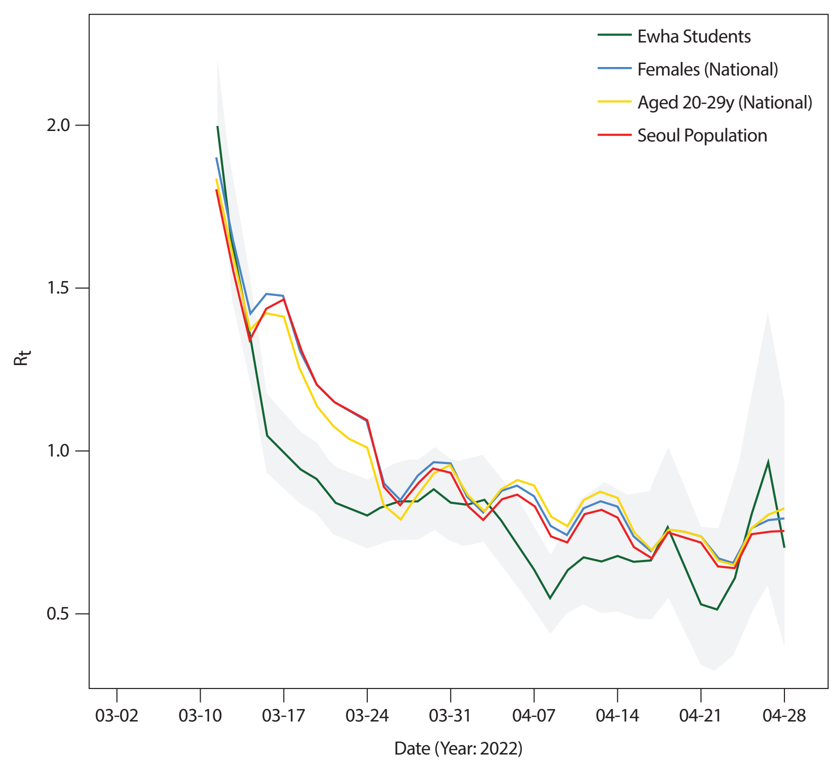

Fig. 3. Daily reproductive numbers (R_t) for Ewha students through the Ewha Safety Campus (ESC) cohort and general populations living in South Korea (females, people aged 20–29 years, and people living in Seoul). R_t: indicates the average number of new infections caused by a single infected individual at time t in the population susceptible to infection (i.e., the power of transmission; transmissibility).

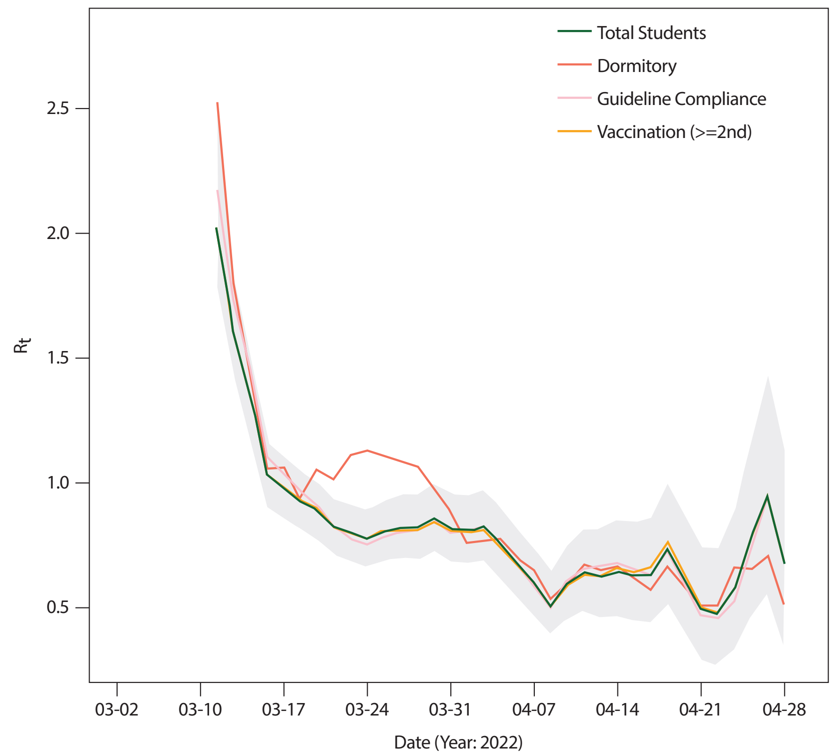

Fig. 4. Daily reproductive numbers (R_t) for Ewha students through the Ewha Safety Campus (ESC) cohort and general populations living in South Korea (females, people aged 20–29 years, and people living in Seoul). R_t: indicates the average number of new infections caused by a single infected individual at time t in the population susceptible to infection (i.e., the power of transmission; transmissibility).

that students who live in dormitories, those who did not comply with all quarantine guidelines, and those who were not fully vaccinated were more vulnerable to COVID-19 infection than other students.

To the best of our knowledge, this is one of the few studies that investigated the efficacy of an on-campus COVID-19 action plan and the resulting effectiveness of R_t based on proactive testing. R_t quantifies the contagiousness of the disease and estimates the incidence time series, which can be used to evaluate whether the intervention affected the transmission of infection. Estimation and comparison of R_t, which indicate the power of transmission (i.e., transmissibility), have been widely used in epidemiological studies to assess and provide insights into the effectiveness of intervention policies [11,13,15]. Thus, the results of this study may be used to demonstrate the effectiveness of the ESC cohort to reduce the spread of COVID-19 on campus.

In the case of South Korea, rapid diagnosis and rapid isolation are key to the prevention of transmission [16]. This was evaluated as a successful quarantine in 2020. Health authorities implemented a real-time RT-PCR analysis method to immediately detect SARS-CoV-2. In a study reported from another campus, when positive cases were quickly identified and quarantined, the transmission of infection greatly reduced. Furthermore, COVID-19 cases could be accurately confirmed by conducting repeat RT-PCR testing, which helped in quickly responding to cases such as prompt screening and in quarantining individuals who come in contact with cases [17–19]. The ESC Project also seems to have been effective in reducing the spread of infection on the Ewha campus as it recommended and implemented repeated RT-PCR tests, without any economical barrier, not only for symptomatic patients but also for the early detection of

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asymptomatic patients.

The effectiveness of the ESC cohort should be interpreted based on changes in the national COVID-19 diagnostic guidelines. Earlier, everyone in Korea was eligible for free RT-PCR tests at any national screening center. However, the Korean Disease Control and Prevention Agency changed the eligibility for free RT-PCR tests from Feb 04, 2022, in order to address the drastically increased confirmed cases due to the Omicron variant. Thus, only high-risk groups (people aged 60 or older, those referred from an epidemiological investigation or with the note of a medical doctor, those who received positive test results from rapid antigen tests, and/or those working at high-risk places such as hospitals) could undergo free RT-PCR tests during our study period at national screening centers. Students who were generally classified as the low-risk group ceased to be eligible for no-cost RT-PCR tests [10].

The ESC Project provided RT-PCR diagnostic tests at no cost to students. In addition, the ESC cohort tried to increase its accessibility by employing test recommendations based on the school's epidemiological inspections and internet-based application procedures. As a result, among a total of 1,205 confirmed students reported at Ewha Womans University through Apr 30, 2022 (including confirmed cases at external institutes such as screening centers operated by local governments), the ESC cohort detected 703 students with confirmed COVID-19 infection (58.3%). Increasing accessibility to accurate diagnostic tests has been consistently identified as a crucial factor to decrease the risk of infection and local transmissibility [12]. Thus, we conjecture that providing free and proactive RT-PCR tests considerably contributed in reducing the viral transmission in Ewha students compared to that in the general population.

The study has four limitations. First, since Mar 14, 2022, the period that was included in our study period, antigen tests performed by medical staff have been approved to confirm COVID-19. Therefore, the results regarding the general populations from this period should be interpreted carefully when it was compared with the ESC results based on PCR, and it should be acknowledged that there might be a risk of biases. However, the Korean CDC reported that because of a high prevalence of the Omicron variant, the sensitivity of the antigen tests performed in the Korean respiratory disease professional clinics in Feb 2022 was 94.7% compared to PCR tests (KCDC Press release on Mar 14, 2022; URL: https://www.kdca.go.kr/board/), thus we cautiously conjecture that the potential biases due to the antigen tests were not substantially large. Second, because we could not access the data of students who did not consent to participation in this research and who did not use ESS to have a diagnostic test, we cannot exclude the probability of selection bias resulting from voluntary participation. In particular, previous studies reported that voluntary participants can be younger, more professionally active, and more often had a history of contact with COVID-19 confirmed cases, and the factors generally negatively affect the generalizability of the study results via overestimation problems [20,21]. Third, variables used in this study regarding compliance with quarantine guidelines and vaccination relied on self-reported information. This might have led to an overestimate in the number of students who complied with quarantine guidelines and were fully vaccinated. Finally, only female students registered in a university in Seoul were included in the ESC cohort. Thus, our results are limited and it is difficult to extend them to university students and/or general population.

In this study, we assessed the effectiveness of an ESC cohort. Our study results provide scientific evidence for establishing autonomous, effective, and sustainable on-campus action plans against COVID-19 based on no-cost and proactive RT-PCR tests. Further, our results support the necessity of applying more intensive managing strategies for students who live in communal resident places, did not comply with quarantine guidelines, and who are not fully vaccinated.

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Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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Ethics Approval and Consent to Participate

This study was approved by the Ewha Institutional Review Board (protocol No: ewha-202211-0006-01). All data related to individual information and diagnostic test results were collected and analyzed with prior consent of the participants.

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Case Report

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Recurrent Colonic Perforation in Geriatric Patients with Sigmoid Colostomy: Two Case Reports

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Key Words
Intestinal perforation; Colostomy; Ischemic colitis; Fecal impaction

Recurrent colonic perforation in patients already having colostomy is extremely rare and only a few cases had been reported. Herein, we report 2 cases of recurrent colonic perforation at the proximal part of the colostomy in geriatric patients resulting from different causes, which might be caused by stercoral perforation and recurrent colonic ischemia, respectively. Based on our experience, surgeons should consider correcting chronic constipation even in patients who already have a colostomy. Additionally, transverse colostomy should be considered as a surgical treatment in patients with sigmoid colostomy for recurrent perforation due to colonic ischemia.

Introduction

Sigmoid colon perforations are usually treated using the Hartmann procedure with end colostomy. Recurrent colonic perforation in patients undergoing colostomy is extremely rare, with only a few cases reported. Previous studies have reported recurrent colon perforation due to fecalomas in patients with sigmoid colostomy [1–3]. Herein, we report two cases of recurrent colon perforation in geriatric patients with sigmoid colostomy. The first case was thought to be due to stercoral perforation, as previously reported, but the second case was thought to be due to ischemic colitis, considering the patient's history and operative findings. To the best of our knowledge, there have been no reports of recurrent colonic perforation due to colonic ischemia in patients with colostomy.

Case

1. Case 1

An 89-year-old bedridden woman with Parkinson's disease was admitted for septic shock with hypotension and hypoxia. The patient had abdominal pain for one day before admission, and physical examination revealed generalized abdominal tenderness, rebound tenderness, and rigidity. On admission, the initial blood pressure was 53/34 mmHg, pulse rate was 77 beats per minute, and body temperature was 34.9°C which was diagnostic of septic shock. Medical history revealed that the patient had undergone a Hartmann operation for stercoral perforation five years prior. Abdominopelvic computed tomography revealed a suspicious perforation in the sigmoid colon, proximal to the colostomy site (Fig. 1). In the operative field, typical findings of a stercoral perforation on the proximal part of the colostomy, such as a fecaloma and perforation on the antimesenteric side, were observed. We performed a segmental colon resection, including resection of the perforation site, followed by an end transverse colostomy. The patient died due to unrecovered septic shock the day after surgery.

2. Case 2

An 87-year-old man with hypertension, osteoarthritis, and dementia was admitted to the authors' hospital with severe lower abdominal pain. The initial vital signs were as follows: blood pressure 160/97 mmHg, pulse rate, 92 beats per minute; and body temperature, 36.8°C. Physical examination revealed diffuse abdominal tenderness and rebound tenderness, particularly in the lower abdomen. Laboratory examination revealed a white blood cell count of 860 cells/mm^3 suggesting leukocytopenia, a c-reactive protein of 0.65 mg/dL and a lactate level of 17.7 mg/dL. Two years ago, the patient underwent the Hartmann operation and reversal for a distal sigmoid colon perforation due to ischemic colitis. One year later, he underwent a second Hartmann operation for recurrent sigmoid colon perforation at another hospital. Abdominopelvic computed tomography on the third admission revealed a sigmoid colon perforation proximal to the previously built colostomy (Fig. 2). In the operative field, a 3 cm colon perforation was observed proximal to the colostomy, and colonic ischemia with fecal soiling was observed throughout the abdominal cavity. Segmental colon resection, including the perforation site and end transverse colostomy formation, was performed. The patient was discharged on the 17th postoperative day. During the 1-year follow-up period, the patient showed no recurrence of ischemic colitis.

Discussion

Recurrent colonic perforation has rarely been reported, and only a few cases of colonic perforation after colostomy have been reported. Serpell et al. [1] reported two cases of recurrent stercoral colon perforation proximal to the end colostomy in the postoperative period after

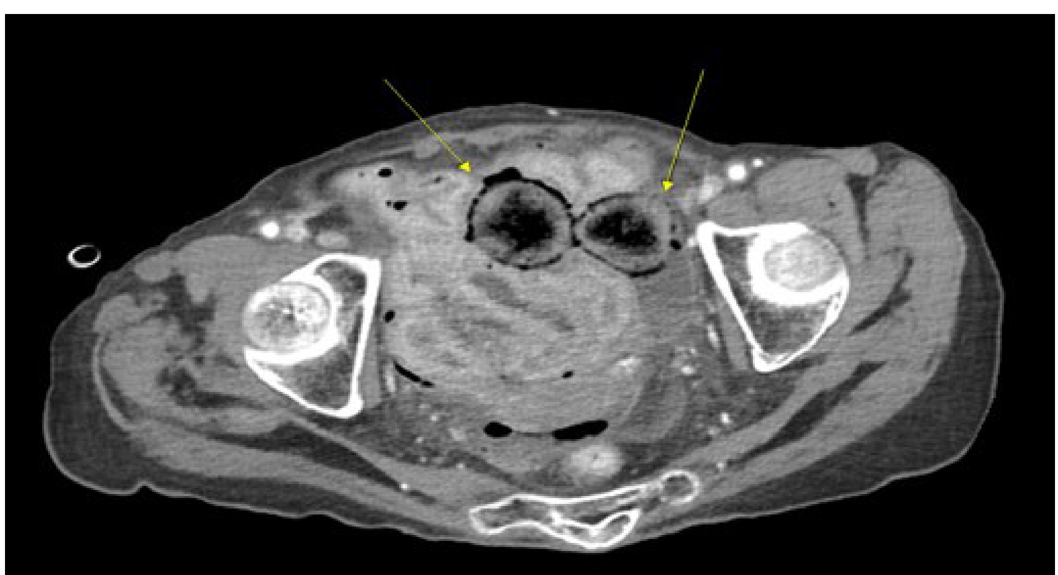

Fig. 1. Fecaloma was observed around the perforation site (yellow arrow).

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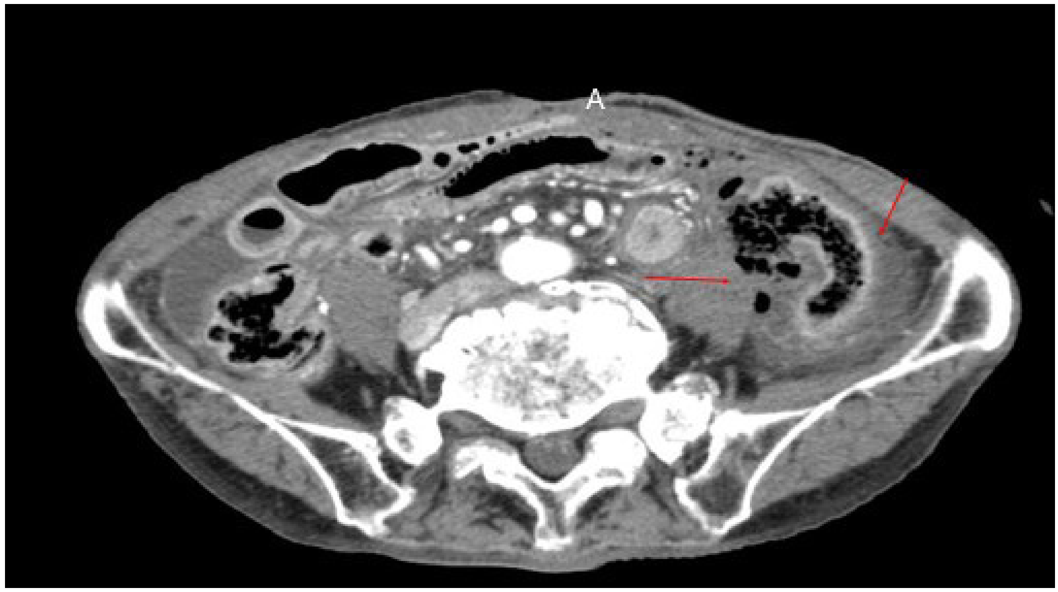

Fig. 2. The perforated colon wall was not enhanced in abdomino-pelvic contrast tomography, suggestive of ischemic colitis (red arrow).

undergoing Hartmann procedure for stercoral perforation. Kim et al. [2] also reported two cases of stercoral perforation in the colon proximal to a sigmoid colostomy in patients who underwent abdominoperineal excision for rectal cancer. Gekas and Schuster [3] presented a case of stercoral perforation in a patient, following transverse-end colostomy for traumatic colon perforation. The first case in our report is consistent with a previous report based on operative findings showing fecaloma and antimesenteric side perforation. In the second case, perforation due to ischemic colitis was suspected because of the past history of a previous perforation of the sigmoid colon and the operative findings of ischemia of the colon wall. Recurrent colonic perforation resulting from ischemic colitis in patients with colostomy has not yet been reported.

As we performed the transverse colostomy following segmental colon resection, including the perforation site in the second case, there was no recurrence of ischemic colitis, though the follow-up period was short. Surgeons should consider the existence of points vulnerable to ischemic injury, such as Griffith's and Sudek's points, when deciding on the point of resection. Although some surgeons have suggested that the watershed zone is not especially vulnerable [4], we thought that the transverse colon would be more suitable as the stoma site in patients with recurrent colon perforation, especially in recurrent colonic ischemia.

In conclusion, surgeons should consider preventive strategies to reduce the risk of recurrent perforation in geriatric patients who have already undergone colostomy. Appropriate management of constipation, including laxatives, enemas, and a high-fiber diet, is important to prevent recurrent stercoral perforation [2]. In addition, in cases of recurrent perforation due to colonic ischemia, the transverse colon may be considered for the stoma site.

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