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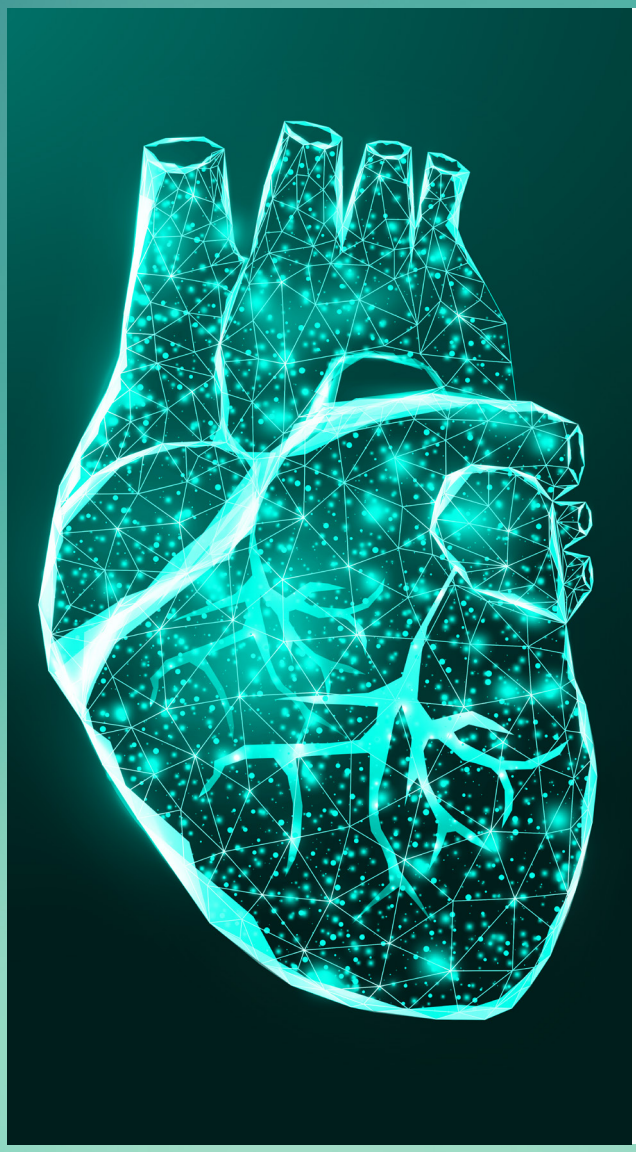

## RESEARCH ARTICLES



## CASE REPORT





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## CASE REPORT

RESEARCH ARTICLE

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Int J Cardiovasc Acad 2023;9(3):52-59

# Self-monitoring of Blood Pressure: Awareness, Practice, Perceived Barriers and Associated Sociodemographic Factors Among Adult Hypertensives Attending a Tertiary Hospital in South-South Nigeria

**Ejiroghene Martha Umuerri[1], Ehimwenma Judith Ogbemudia[2], Patrick Oyibo[3,4]**

[1]Department of Medicine, Cardiology Unit, Delta State University Teaching Hospital, Oghara, Nigeria
[2]Department of Medicine, Cardiology Unit, University of Benin Teaching Hospital, Benin-City, Nigeria
[3]Department of Community Medicine, Delta State University Faculty of Medicine, Abraka, Nigeria
[4]Division of Health Services Research and Management, School of Health and Psychological Sciences, City University of London, London, United Kingdom

## Abstract

**Background and Aim:** Self-monitoring of blood pressure (SMBP) is helpful in blood pressure (BP) status categorization and emerging evidence shows its beneficial impact on BP control. The study assessed the awareness and practice of SMBP and its associated sociodemographic factors among adult hypertensives in Southern Nigeria.

**Materials and Methods:** The study was cross-sectional and questionnaire based. Eligible adult hypertensive patients attending a tertiary hospital in South-South Nigeria were randomly recruited from the cardiology clinic over one year.

**Results:** Of the 364 hypertensive adults studied, the mean (± standard deviation) age was 59.34 (±14,308) years, males (192, 52.7%) and urban dwellers (273, 75%). A total of 287 (78.8%) were aware of SMBP, and 240 (65.9%) practiced it. Most (75, 60.5%) of the respondents who did not practice SMBP had no specific reason not to. Of the respondents who practiced SMBP, 226 (94.2%) owned a BP monitoring device, and 135 (56.3%) kept records of their BP readings, out of which 83% (112/135) cross-checked with clinic readings. The practice of SMBP was significantly associated with marital status ($P = 0.038$), education ($P < 0.001$), residence ($P = 0.011$), average monthly income ($P = 0.020$), and access to healthcare insurance ($P = 0.042$) but not with age, sex, and occupation.

**Conclusion:** The awareness and practice of SMBP were high in this study. However, almost half of the respondents who practiced SMBP neither kept records nor cross-checked home BP with clinic readings, thus limiting the added clinical support offered by SMBP. Healthcare providers must continue educating patients to maximize the benefits of SMBP.

**Keywords:** Self-monitoring of blood pressure, self-measured blood pressure, hypertension, out-of-office blood

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**Address for Correspondence:** Assoc. Prof. Ejiroghene Martha Umuerri, Department of Medicine, Cardiology Unit, Delta State University Teaching Hospital, Oghara, Nigeria
**E-mail:** umuerriejiro@gmail.com
**ORCID ID:** orcid.org/0000-0001-8372-8328

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## INTRODUCTION

About 1.39 billion adults globally live with hypertension, making it the foremost modifiable cardiovascular risk factor worldwide.[1] Despite efforts to prevent and control hypertension, the proportion of persons with uncontrolled blood pressure (BP) is daunting.[2] The burden of hypertension in Nigeria is high and still growing, and it remains difficult to estimate the exact burden with burden.[3] However, a recent nationwide survey in Nigeria reported an age-standardized prevalence of 38.1% for hypertension. [4]

Hypertension is a leading cause of non-communicable disease-related premature mortality and morbidity. It accounts for 8.5 million deaths worldwide, chiefly from stroke, ischaemic heart disease, and chronic kidney disease.[5] However, there is an uneven spread in the burden of hypertension across regions and nations.[2] There are burden-related disparities between high-income and low- and middle-income countries. Indeed, the monstrous health-related and economic consequences of hypertension noted in many low- and middle-income countries are attributable to the low awareness, treatment, and control rates compared with high-income countries.[6]

As part of efforts to improve BP control, several organizations including the International Society of Hypertension,[6] the European Society of Hypertension,[7] and the Nigerian Hypertension Society[8] have included out-of-office BP monitoring in their practice guidelines for the management of hypertension. Self-monitoring of blood pressure (SMBP) is a form of out-of-office BP monitoring. It involves the regular measurement and recording of BP by an individual outside the clinical or public settings using a personal monitoring device. Several factors may hinder the effective practice of SMBP. These factors include lack of awareness, ownership of measuring devices, BP measurement without record keeping, and lack of clinical support.

SMBP aids the categorization of BP status. It helps to identify individuals with masked and white-coat hypertension separate from true hypertensives and true normotensives. SMBP is also helpful in decision making regarding treatment, whether by self-titration of antihypertensive medications or with support from healthcare practitioners. Indeed, emerging evidence supports the beneficial impact of SMBP on BP control, especially with clinical support.[9]

Easily operated validated electronic BP devices are recommended for home-based SMBP. Although these devices are becoming increasingly available and accessible, there is inadequate data on the knowledge and practice of SMBP in many low- and middle-income countries, such as Nigeria. More data on SMBP among persons with hypertension in Nigeria need to be collected. This study aims to close some gaps by providing data on the knowledge, practice and perceived barriers to SMBP and the associated sociodemographic factors among adult hypertensive patients receiving tertiary healthcare in Delta State, Nigeria.

## MATERIALS AND METHODS

**Study design:** The study was cross-sectional and descriptive in design.

**Study setting:** The study setting was Delta State University Teaching Hospital, Oghara, Nigeria. Oghara, a suburban town, is the capital of the Ethiope West local government area, one of 25 in the state. Delta State University Teaching Hospital is a 150-bedded public tertiary healthcare facility owned by the Delta State Government. It receives medical referrals from other hospitals within the State and neighboring States (Anambra, Bayelsa, and Edo). Cardiology clinics run weekly on Mondays and Wednesdays at the Consultant Medical Outpatient Department (MOPD). An average of 40 patients with hypertension are seen weekly at the Delta State University Teaching Hospital MOPD.

**Study population:** Hypertensive patients attending the Delta State University Teaching Hospital Consultant Medical Outpatient Department (Delta State University Teaching Hospital MOPD), Oghara, who met the study eligibility criteria, were recruited. The diagnosis of hypertension was as per the patient's medical record, and it is defined as a BP reading of 140/90 mmHg and above or the use of antihypertensive medications irrespective of BP reading. Hypertensive patients aged 18 years and above who had attended at least two cardiology clinic visits at Delta State University Teaching Hospital MOPD and provided written informed consent participated in the study. Patients visiting the MOPD for the first time, presenting to the clinic after being lost to follow-up for at least one year, adjudged incapable of self-care, and declined to partake in the study were excluded. The Delta State University Teaching Hospital Health Research Ethics Committee on Jul 13, 2021 provided ethics approval [approval number: HREC/PAN/2021/016/0327] to conduct the study. The general conduct of the study was guided by the Helsinki Declaration as revised in 2013.[10]

**Sample size determination and sampling procedure:** The calculated minimum sample size employed the Cochrane formula[11]: $n = 1.96^2p\ (1 - p)/d^2$. Using the prevalence of hypertension among adults in the Delta State of 29.3%,[12] and assuming a 95% confidence interval (CI), 5% error margin, and 10% non-response rate, the calculated minimum sample size was 350.

A list of potential study participants was extracted from the case files on each cardiology clinic day. Eligible study participants were then randomly selected by balloting. Informed consent was obtained from the selected patients before administering

the study questionnaire. The case files of recruited patients were marked to avoid reselection. The study participant identification and a recruitment process continued until the sample size was attained. Data collection spanned between July 2021 and June 2022.

**Study instrument and data collection:** Data collection was by self-administered and interviewer-administered (for patients who were not literate) questionnaires. The study questionnaire comprised three sections that elicited data on (a) sociodemographic characteristics, (b) risk factors/comorbidities, and (c) SMBP, defined as the measurement of BP by the patient outside clinic settings, either at home or within the community. The sociodemographic characteristics assessed included respondents' age, sex, educational status, marital status, occupational status, monthly income, and access to health insurance. The second part of the questionnaire assessed behavioral risk factors such as smoking, alcohol consumption, unhealthy diet consumption, and comorbidities such as diabetes mellitus, renal disease, and stroke. The last part of the questionnaire assessed the awareness, attitude, practice and perception of SMBP.

**Dependent and independent variables:** The dependent variables were awareness of SMBP, ownership of a personal BP monitor, attitude toward SMBP, perception of SMBP, and the practice of SMBP.

Independent variables were age, sex, marital status, educational level, place of residence, occupational status, monthly income, health insurance, comorbidities, and duration of hypertension.

### Statistical analysis

Obtained data were coded and analyzed using the International Business Machine Statistical Package for Scientific Solutions (IBM SPSS) version 23 (IBM SPSS Corp., Armonk, NY, USA). Descriptive and inferential analysis of the data collected was performed. Categorical and continuous variables were presented as frequency, percentage, and mean and standard deviation of the mean, respectively. Bivariate analysis using chi-square and student t-tests tested the association between categorical variables and the difference in means, respectively. A statistically significant *P*-value was <0.05.

## RESULTS

Of the 380 questionnaires distributed, 364 (95.8%) were completed.

### Sociodemographic characteristics

The study population's age range was 20-94 years, with a median age of 61 years. The mean (± standard deviation) age was 59.34 (±14.31) years, and the 95% CI for the mean was 57.87-60.82 years. The modal age group was 60-69 years; 102 (28.0%) respondents. A total of 192 (52.7%) of the respondents were males. The majority of the respondents were married (*n* = 274; 75.3%), had a tertiary level of education (*n* = 205; 56.3%), lived in urban settings (*n* = 273; 75.0%), were gainfully employed (*n* = 188; 51.6%), and had no access to healthcare insurance (*n* = 296; 81.3%) (Table 1). The mean duration of hypertension is 7.18 (± 8.09) years.

### Behavioral risk factors and comorbidities

Eight (2.2%) respondents were current smokers, while 72 (19.8%) admitted drinking alcohol. One hundred and thirty-eight (37.9%) respondents exercised at least thrice weekly, while 63 (17.3%) added salt to already cooked meals. The following comorbidities were reported to be present: diabetes mellitus (*n* = 73; 20.1%), dyslipidemia (*n* = 95; 26.1%), eye disease (*n* = 62; 17.0%), heart disease (*n* = 102; 28.0%), kidney disease (*n* = 12; 3.3%) and stroke (*n* = 18; 4.9%).

### The source of information and awareness of SMBP

Most respondents (*n* = 197; 54.1%) reported healthcare providers as the source of information on SMBP. Other sources of information on SMBP included family/friends (*n* = 76; 20.9%), the internet (*n* = 11; 3.0%), school/seminar/conferences (*n* = 7; 1.9%), and unsure (*n* = 73; 20.1%).

A total of 287 (78.8%) of the respondents were aware of SMBP, while 240 (65.9%) reported they checked their BP outside the clinic setting (Figure 1). Among respondents who were aware of SMBP, 231 (80.5%) put it into practice. The association between awareness and practice of SMBP was statistically significant ($\chi^2$ = 127.94, df = 1; *P* < 0.001).

### Ownership of BP monitoring device and practice of SMBP

Of the respondents who practice SMBP, 226 (94.2%) reported they had personal BP monitors: electronic (*n* = 187; 82.7%), anaeroid (*n* = 12; 5.3%), and mercury (*n* = 27; 11.9%) sphygmomanometers. The remaining 14 (5.8%) respondents

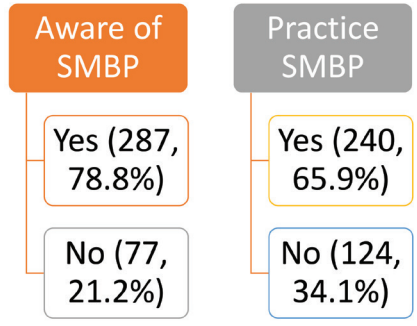


**Figure 1:** Awareness and practice of self-monitoring of blood pressure

*SMBP: Self-monitoring of blood pressure*

that did not have personal BP monitors had access to one within their community: seven (50.0%) had access to an electronic device, one (7.1%) to anaeroid, and six (42.9%) to mercury sphygmomanometer. All the respondents that did not practice SMBP had no personal BP monitoring device. The association between ownership of a BP monitoring device and the practice of SMBP was statistically significant ($\chi^2$ = 307.99, df = 1; $P < 0.001$).

### Reasons for and pattern of the practice of SMBP

Table 2 shows the practice of SMBP as reported by the respondents. One hundred and eleven (46.3%) respondents who practiced SMBP were personally motivated to do so, while 85 (35.8%) reported they did so because of advice from their healthcare providers. Ninety (37.5%) of the respondents checked their BP at home at least once daily, while 59 (24.5%) reported irregular SMBP. While 86 (35.8%) had no specific time of the day when they checked their BP, 90 (37.5%) did so in the mornings. One hundred and thirty-five (56.3%) respondents kept a record of their BP checks, out of which 112 (83.0%) cross-checked the self-monitored BP with clinic records. As shown in Table 2, 21 (18.8%) of the respondents who cross-checked SMBP with clinic records do so always, while 10 (8.9%) rarely cross-check.

### Barriers to the practice of SMBP

As shown in Figure 2, 124 (34.1%) of the respondents do not practice SMBP. Seventy-five (60.5%) respondents had no specific

**Table 1. Sociodemographic profile of the study population**

| Variable | Category | Frequency (*n*=364) | Percentage (%) |
|---|---|---|---|
| The age group (years) | <40 | 34 | 9.3 |
| | 40-49 | 55 | 15.1 |
| | 50-59 | 81 | 22.3 |
| | 60-69 | 102 | 28.0 |
| | ≥70 | 92 | 25.3 |
| Sex | Male | 192 | 52.7 |
| | Female | 172 | 47.3 |
| Marital status | Single | 20 | 5.5 |
| | Married | 274 | 75.3 |
| | Widowed | 67 | 18.4 |
| | Divorced | 3 | 0.8 |
| Education | No formal | 23 | 6.3 |
| | Primary | 59 | 16.2 |
| | Secondary | 77 | 21.2 |
| | Tertiary | 205 | 56.3 |
| Residence | Urban | 273 | 75.0 |
| | Rural | 91 | 25.0 |
| Occupation | Employed | 188 | 51.6 |
| | Unemployed | 66 | 18.1 |
| | Retired | 105 | 28.8 |
| | Student | 5 | 1.4 |
| Average monthly income (NGN) | <30,000 | 132 | 40.9 |
| | 30,000-100,000 | 133 | 41.2 |
| | ≥100,000 | 58 | 18.0 |
| | Missing | 41 | - |
| Access to healthcare insurance | Yes | 68 | 18.7 |
| | No | 296 | 81.3 |
| The duration of hypertension (years) | <5 | 149 | 47.0 |
| | 5 - 10 | 105 | 33.1 |
| | >10 | 63 | 19.9 |
| | Missing | 47 | - |

NGN: Nigerian Naira

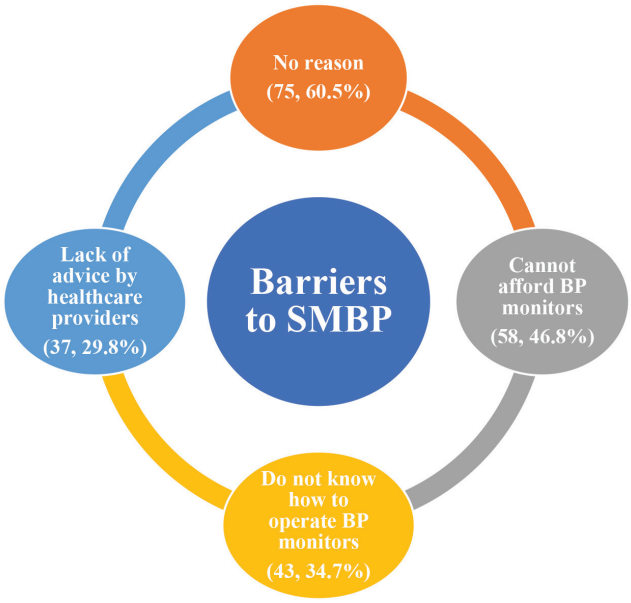


**Figure 2:** Barriers to the practice of self-monitoring of blood pressure

*SMBP: Self-monitoring of blood pressure, BP: Blood pressure*

**Table 2. The practice of self-monitoring of blood pressure (SMBP)**

| Practice of SMBP | Category | Frequency (%) (*n*=240) |
|---|---|---|
| Reasons for SMBP | Personal motivation | 111 (46.3) |
| | Advice by healthcare providers | 86 (35.8) |
| | Advice from family/friends | 27 (11.2) |
| | Own a BP monitoring device | 16 (6.7) |
| Frequency of SMBP | At least once daily | 90 (37.5) |
| | At least once weekly | 77 (32.1) |
| | At least once monthly | 14 (5.8) |
| | Irregularly | 59 (24.5) |
| Timing of SMBP | Morning | 90 (37.5) |
| | Evening | 16 (6.7) |
| | Morning and evening | 48 (20.0) |
| | No specific time | 86 (35.8) |
| Keep a record of BP checks | Yes | 135 (56.3) |
| | No | 105 (43.7) |
| Cross-check SMBP record with clinic BP* | Yes | 112 (83.0) |
| | No | 23 (17.0) |
| How often do you cross - Check SMBP with clinic BP records** | Always | 21 (18.8) |
| | Sometimes | 81 (72.3) |
| | Rarely | 10 (8.9) |

*$n$=135, **$n$=112, SMBP: Self-monitoring of blood pressure, BP: Blood pressure

reason for not practicing SMBP. Other barriers are shown in Figure 2 (multiple responses applied).

### Perception and attitude toward SMBP

Three hundred and ten (86.4%) and 303 (83.2%) respondents thought self-monitoring of BP was important and beneficial, respectively. A significantly higher proportion of respondents who did not know if SMBP was important (39, 32.5%) or beneficial (41, 33.1%) did not monitor their BP at home (Table 3). While 206 (56.6%) of the respondents felt that SMBP was accurate, 41 (11.3%) thought it was not accurate, and 117 (32.1%) respondents were unsure of its accuracy. Two hundred and fifty-nine (71.2%) respondents stated they would recommend the practice of SMBP to others, 22 (6.0%) would not, and 83 (21.8%) were undecided. The association between the perception of SMBP and its practice was statistically significant (Table 3).

### Association between the practice of SMBP and sociodemographic profile

The practice of SMBP did not differ based on age, sex, and occupation. The sociodemographic characteristics significantly associated with the practice of SMBP were marital status ($P$ = 0.038), education ($P < 0.001$), residence ($P$ = 0.011), average monthly income (0.020), and access to healthcare insurance (0.042) (Table 4). A significantly higher proportion of respondents who had been hypertensive for at least five years practiced SMBP (Table 4), and the mean duration of hypertension was significantly higher among those who practiced SMBP than those who did not ($P < 0.001$).

## DISCUSSION

This study shows that almost four-fifths (78.8%) of the study population were aware of SMBP. Edah et al.,[13] in a study of hypertensive patients attending Jos University Teaching Hospital, Nigeria, reported a 73.7% awareness rate of SMBP. However, a lower SMBP awareness rate of 43.4% was reported by Konlan et al.[14] among hypertensive patients receiving a tertiary level of care in Korle-Bu, Ghana. In this study, the majority (54.1%) of the respondents received information on SMBP from healthcare providers. Konlan et al.[14] Also reported that most (46.4%) of their study population received information on SMBP from their healthcare providers. The practice of SMBP was significantly associated with its awareness in this study. Thus, there is a need to increase awareness by all means possible: healthcare providers, family/friends, and the mass media.

Two-thirds (65.9%) of the respondents in this study practiced SMBP. Despite the similar SMBP awareness rate, the practice of SMBP in this study was higher than the 44.6% reported by Edah et al.[13] The explanation for the observed difference in the prevalence rate of SMBP is not immediately apparent.

However, a sizeable (46.3%) number of the respondents in this study who practiced SMBP attributed it to personal motivation. In contrast, three-fifths (60.5%) of the respondents who did not practice SMBP had no reason for not doing so. This underscores the need to keep creating awareness among patients with hypertension, as the gains of practicing SMBP are well established.

Although a majority (94.2%) of the respondents who practiced SMBP owned a BP monitoring device, less than a tenth (6.7%) reported they did so because of ownership of the device. In the same vein, respondents who did not practice SMBP were ascribed to lack of funds to buy a BP monitor (46.8%) and the inability to operate the monitor (34.7%). Indeed, it is noteworthy that the practice of SMBP was significantly associated with its awareness and ownership of BP monitoring devices. Although not explored in this study, the content of the information on SMBP available to the general public, and hypertensive patients in particular, should emphasize the use of validated electronic sphygmomanometers, which are relatively cheap and easy to operate as no special skills are needed.

Although there are no consensus guidelines on the schedules for SMBP, some studies have recommended that home BP be checked at least four times in the week preceding the clinic visit. The BP readings should be recorded, averaged, and cross-checked with the clinic BP reading.[15] This recommendation implies that measuring BP at home without clinical support is not enough. Almost half of the respondents in this study did not keep records of BP. Also, some respondents who kept their BP records did not cross-check with the clinic readings. Thus, many respondents who practiced SMBP may not get the added value from clinical support.[9] The non-adherence to recommended schedules may be because the respondents needed to be better versed in maximizing the benefits of SMBP, especially as about a fifth were unsure of their source of information. Also, the inertia of getting clinical support may be fueled by the perception of the accuracy of SMBP. Only about half of the respondents in this study thought SMBP was accurate.

The mean age of those who practiced SMBP and those who did not was similar in this study. Indeed, the practice of SMBP was similar by the age group. In the same vein, sex was not significantly associated with SMBP practice. This observation was similar to the reports from similar study populations in Northern Nigeria and Ghana.[13,14]

Like the study by Konlan et al.,[14] the practice of SMBP in this study was significantly higher among married respondents. Previous reports have also linked the practice of SMBP with the level of education.[13,14] While the practice of SMBP was significantly higher among respondents with a tertiary level of education in this study, Edah et al.[13] reported a significant association for those with at least secondary education. However, it is not known if the observation by Edah et al.[13] would have mirrored this study if the level of education was further subclassified, as in this study. Indeed, there is no evidence that formal education positively influences health-seeking behaviors, as observed in these studies.

A significantly higher proportion of urban dwellers practiced SMBP, whereas a higher proportion of rural dwellers did not. The observed association was statistically significant. Similarly, respondents' monthly incomes was significantly associated with the practice of SMBP. A higher proportion of those who earned less than the monthly minimum wage (₦30,000) did not practice SMBP and vice-versa. Konlan et al.[14] also reported

**Table 3. Association between practice and perception and attitude toward SMBP**

| Variable | Category | Frequency | Practice SMBP | | Chi-square | *P*-value |
|---|---|---|---|---|---|---|
| | | | Yes *n*=240 (%) | No *n*=124 (%) | | |
| **Is SMBP important?** | Yes | 310 (86.4) | 227 (94.6) | 83 (66.9) | 54.917 | <0.001 |
| | No | 6 (1.6) | 4 (1.7) | 2 (1.6) | | |
| | Don't know | 48 (13.2) | 9 (3.8) | 39 (32.5) | | |
| **Is SMBP beneficial?** | Yes | 303 (83.2) | 224 (93.3) | 79 (63.7) | 52.406 | <0.001 |
| | No | 7 (1.9) | 3 (1.3) | 4 (3.2) | | |
| | Don't know | 54 (14.8) | 13 (5.4) | 41 (33.1) | | |
| **Is SMBP accurate?** | Yes | 206 (56.6) | 178 (74.2) | 28 (22.6) | 113.013 | <0.001 |
| | No | 41 (11.3) | 29 (12.1) | 12 (9.7) | | |
| | Don't know | 117 (32.1) | 33 (13.8) | 84 (67.7) | | |
| **Will you recommend SMBP to others?** | Yes | 259 (71.2) | 208 (86.7) | 51 (41.1) | 92.747 | <0.001 |
| | No | 22 (6.0) | 13 (5.4) | 9 (7.3) | | |
| | Undecided | 83 (22.8) | 19 (7.9) | 64 (51.6) | | |

SMBP: Self-monitoring of blood pressure

**Table 4. Association between the practice of SMBP pressure and sociodemographic profile and duration of hypertension of respondents**

| Variable | Category | Practice SMBP | | Chi-square (*P*-value) |
|---|---|---|---|---|
| | | Yes (*n*=240) | No (*n*=124) | |
| The age group (years) | <40 | 18 (7.5) | 16 (12.9) | 6.482 (0.166) |
| | 40-49 | 37 (15.4) | 18 (14.5) | |
| | 50-59 | 59 (24.6) | 22 (17.7) | |
| | 60-69 | 71 (29.6) | 31 (25.0) | |
| | ≥70 | 55 (22.9) | 37 (29.8) | |
| | Mean age (± SD) | 59.3 (±13.98) | 59.5 (14.97) | -0.129† (0.332) |
| Sex | Male | 129 (53.8) | 63 (50.8) | 0.284 (0.594) |
| | Female | 111 (46.3) | 61 (49.2) | |
| Marital status | Single | 14 (5.8) | 6 (4.8) | 8.446 (0.038) |
| | Married | 190 (79.2) | 84 (67.7) | |
| | Widowed | 34 (14.2) | 33 (26.6) | |
| | Divorced | 2 (0.8) | 1 (0.8) | |
| Education | No formal | 10 (4.2) | 13 (10.5) | 35.065 (<0.001) |
| | Primary | 25 (10.4) | 34 (27.4) | |
| | Secondary | 45 (18.8) | 32 (25.8) | |
| | Tertiary | 160 (66.7) | 45 (36.3) | |
| Residence | Urban | 190 (79.2) | 83 (66.9) | 6.523 (0.011) |
| | Rural | 50 (20.8) | 41 (33.1) | |
| Occupation | Employed | 128 (53.3) | 60 (48.4) | 6.660 (0.084) |
| | Unemployed | 36 (15.0) | 30 (24.2) | |
| | Retired | 74 (30.8) | 31 (25.0) | |
| | Student | 2 (0.8) | 3 (2.4) | |
| Average monthly income (NGN) | <30,000 | 80 (36.0) | 52 (51.5) | 7.811 (0.020) |
| | 30,000-100,000 | 96 (43.2) | 37 (36.6) | |
| | ≥100,000 | 46 (20.7) | 12 (11.9) | |
| | Missing | 18 | 23 | |
| Access to healthcare insurance | Yes | 52 (21.7) | 16 (12.9) | 4.133 (0.042) |
| | No | 188 (78.3) | 108 (87.1) | |
| The duration of hypertension (years) | <5 | 88 (41.7) | 61 (57.5) | 11.046 (0.004) |
| | 5-10 | 71 (33.6) | 34 (32.1) | |
| | >10 | 52 (24.6) | 11 (10.4) | |
| | Missing | 29 | 18 | |
| | Mean (± SD) | 8.8 (9.11) | 4.9 (4.81) | 3.639† (<0.001) |

†Student t-test, SMBP: Self-monitoring of blood pressure, SD: Standard deviation, NGN: Nigerian Naira

that the practice of SMBP was associated with income level, increasing with higher incomes.[14] This association is not surprising considering that owing a BP monitor comes at a financial cost. Indeed, 46.8% of those who did not practice SMBP in this study reported lacking money to buy BP monitors. Added to the burden of low income is out-of-pocket spending on health. In this study, less than one-fifth of the respondents had access to healthcare insurance and a significantly higher proportion of respondents without access to healthcare insurance did not practice SMBP.

### Study limitations

The study is limited in its questionnaire-based cross-sectional design because recall bias cannot be ruled out. Thus, the generalizability of the study inferences is limited. This study is also limited in not measuring respondents' BP to determine their control status and how it relates to the practice of SMBP.

## CONCLUSION

This study has a high awareness rate of SMBP and owning a BP monitoring device. Although two-thirds of the respondents checked their BP outside the clinic settings, about half needed to keep records and cross-check with clinic readings. The lack of record keeping and comparison of home BP checks with clinic readings can limit the added clinical support offered by SMBP. Thus, healthcare providers must continue to inform the public of the importance of including SMBP in the care of hypertensive patients and emphasize the added benefits if correctly done.

The practice of SMBP in this study was significantly higher among respondents who were married, had a tertiary level of education, lived in urban areas, had access to healthcare insurance, and earned more than the minimum monthly wage in Nigeria of thirty thousand naira (₦30,000).

### Ethics

**Ethics Committee Approval:** The Delta State University Teaching Hospital Health Research Ethics Committee on Jul 13, 2021 provided ethics approval [approval number: HREC/PAN/2021/016/0327] to conduct the study.

**Informed Consent:** Informed consent was obtained from the selected patients before administering the study questionnaire.

**Peer-review:** Externally peer-reviewed.

### Authorship Contributions

Surgical and Medical Practices: E.M.U., E.J.O., P.O., Concept: E.M.U., E.J.O., P.O., Design: E.M.U., E.J.O., P.O., Data Collection or Processing: E.M.U., E.J.O., P.O., Analysis or Interpretation: E.M.U., E.J.O., P.O., Literature Search: E.M.U., E.J.O., P.O., Writing: E.M.U., E.J.O., P.O.

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RESEARCH ARTICLE

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# Endovascular Revascularization of Lower Extremity Arteries: A Single-center Retrospective Report on Long Lesions (>100 mm)

**İbrahim Çağrı Kaya[1], Halil Bulut[2], Merih Özbayburtlu[1], Alper Selim Kocaoğlu[1]**

[1]University of Health Sciences Turkey, Eskişehir Health Practice and Research Hospital, Clinic of Cardiovascular Surgery, Eskişehir, Turkey
[2]Department of Cardiology, İstanbul University-Cerrahpaşa, Cerrahpaşa Faculty of Medicine, İstanbul, Turkey

## Abstract

**Background and Aim:** Lower extremity peripheral artery disease (PAD) is a prevalent condition characterized by the accumulation of plaque in the arteries of the lower extremities. Traditionally, open surgery has been the conventional method for managing complex lesions in these patients. However, there is a growing trend toward using endovascular therapy as the preferred approach. This study aimed to assess the feasibility and effectiveness of endovascular revascularization in patients with a lower extremity PAD, specifically those with long lesions exceeding 100 mm. By focusing on this subgroup, the study sought to provide insights into the potential benefits of endovascular treatment for this particular patient population.

**Materials and Methods:** This retrospective cohort study included 41 patients with long lesions who underwent endovascular revascularization. The study received ethical approval and patient data were collected and analyzed. Statistical analyzes were conducted to summarize the data.

**Results:** In the analyzed cohort, the study reported that most patients undergoing PAD treatment was males. The average age of the patients was 62.4 years. The prevalence of common comorbidities was as follows: coronary artery disease in 43.9% of patients, hypertension in 43.9%, type 2 diabetes mellitus in 41.5%, and tobacco use in 51.2%. Medication usage included aspirin (97.6% of patients), clopidogrel (82.9%), angiotensin-converting enzyme inhibitors (29.3%), cilostazol (29.3%), statins (36.6%), insulin (24.4%), and oral antidiabetics (17.1%). Lesion characteristics revealed that 41.5% of patients had complete occlusion, while most procedures involved drug-coated balloons (90.2%). Complications were reported in a small percentage of cases (9.8%). Revascularization outcomes showed high rates of technical success (87.8%) and hemodynamic success (97.8%), with favorable primary patency rates at both 30-day (97.8%) and 6-month (87.8%) follow-ups.

**Conclusion:** This study highlights the effectiveness of endovascular treatment for long lesions in lower extremity arteries, with favorable outcomes in terms of primary patency and hemodynamic success.

**Keywords:** Peripheral arterial disease, advanced lesions, drug coated balloon angioplasty, stent angioplasty

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**Address for Correspondence:** MD. Halil Bulut, Department of Cardiology, İstanbul University-Cerrahpaşa, Cerrahpaşa Faculty of Medicine, İstanbul, Turkey
**E-mail:** halilibrahim.bulut@ogr.iuc.edu.tr
**ORCID ID:** orcid.org/0000-0002-9076-8296

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## INTRODUCTION

Lower extremity-peripheral artery disease (PAD) is a prevalent atherosclerotic condition affecting a significant number of individuals worldwide, with estimated 200 million patients affected.[1] The disease is characterized by the diffuse spread of plaques, often progressing from the iliac bifurcation to the femoral artery and even to the popliteal artery in symptomatic patients.[2]. While open surgery has traditionally been used for complex lesions falling into the anatomically advanced class, endovascular therapy has rapidly become a standardized approach for treating PAD.[3]

In recent years, there have been increasing reports suggesting that even complex lesions can be effectively revascularized through endovascular means.[4-6] Particularly, the focus has been on addressing long lesions, defined as cohesive plaques longer than 100 mm. However, vascularizing these longer segments poses challenges as interventions covering an extended area elevate the risk of complications and treatment failure.[7]

Given the evolving landscape of endovascular treatment for lower extremity PAD, it is crucial to contribute to the existing literature by reporting the outcomes of endovascular interventions in patients with long lesions. This study aims to explore the feasibility and efficacy of endovascular revascularization in this specific patient population, shedding light on the success rates, complications, and overall treatment outcomes (Figure 1).

## MATERIALS AND METHODS

### Study design

This retrospective cohort study explored the feasibility and efficacy of endovascular revascularization in patients with lower extremity - PAD lesions exceeding 100 mm in length.

### Ethical considerations

The study and its methodology, conducted in adherence to the principles of the Declaration of Helsinki, received approval from the Clinical Trials and Ethics Committee of the Eskişehir City Hospital. The ethics committee approval number for this study is "ESH/GOEK 2022/9" (date: 21.12.2022).

### Patients

From January 2021 to January 2023, 41 patients with atherosclerotic lesions exceeding 100 mm in length who underwent endovascular revascularization were enrolled in this study.

### Procedure

A single interventionist conducted the procedures within a designated angiography laboratory, using a Canon Infinix-I INFX 8000-V single-plane Toshiba angiography system, complemented by a movable interventional table. Before starting the intervention, all patients received a routine oral dose of 300 mg of clopidogrel. To maintain an activated clotting time of more than 200 s, intraarterial injections of 70 to 100 U/kg of unfractionated heparin were administered.

Patients were positioned either supine or prone depending on the puncture site and manually adjusted on a sliding table to achieve the appropriate field of view. A standard posterior anterior projection was consistently used, with occasional implementation of an oblique projection to confirm stenosis presence or evaluate the outcome of angioplasty. Magnification was employed sparingly, primarily at the interventionist's discretion and mostly for below-the-knee interventions.

For all therapeutic interventions, a 7F sheath was utilized, and lesion predilation with an uncoated balloon was performed as

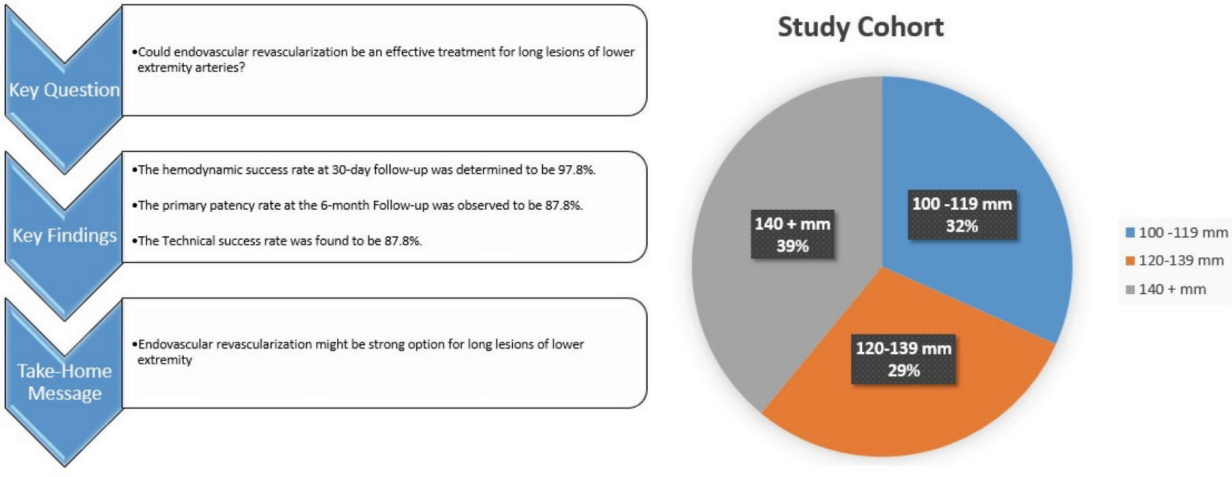


**Figure 1:** Graphical abstract of the study

a standard procedure. The size and length of paclitaxel drug-eluting balloons (DEBs), crucial for determining the total drug load, were carefully selected based on measurements using a ruler placed behind the patient's leg, with diameter sizing set at a 1:1 ratio to the reference vessel. The inflation of the DEB occurred for a minimum of 120 s, starting 10 mm proximal and extending 10 mm distal to the target lesion. When multiple balloons were necessary, a 5 mm overlap was allowed to ensure uniform drug elution in the treated vessel.

Self-expandable stent implantation was performed in cases of progressive stenosis or when a dissection flap was observed during the control phase after balloon dilation. For therapeutic interventions using a retrograde approach, digital subtraction angiography was conducted through a pigtail catheter. A manual injection of the iohexol contrast medium (Omnipaque 350, GE HealthCare, Ireland) into the arterial system was performed by the interventionist. On average, 100 $mm^3$ (175 mg/mL) of contrast medium was used for patients undergoing aortoiliac therapeutic interventions.

### Report standardization definitions

The terminology used in this report, including lesion characteristics, complications, and outcomes, adheres to the Society for Vascular Surgery reporting standards.[8] The comorbidities of patients during the preprocedural period were obtained by examining the National Health Database. Follow-up data at 1 month and 6 month intervals were assessed during postprocedural follow-up appointments with the patients.

The collected data were anonymized and transferred to an electronic database for analysis. All analyzes were conducted within this anonymous database.

### Statistical analysis

Descriptive statistics were employed to summarize the demographic and clinical characteristics of the study population. Continuous variables were presented as means based on the distribution of the data. Categorical variables were reported as percentages.

## RESULTS

### Patient characteristics

Table 1 presents the patient characteristics of the cohort. The cohort consisted of 17.1% ($n$ = 7) females, with a mean age of 62.4 ± 10.5 years. The prevalence of comorbidities in the cohort was as follows: coronary artery disease was present in 43.9% ($n$ = 18) of patients, hypertension in 43.9% ($n$ = 18), type 2 diabetes mellitus in 41.5% ($n$ = 17), and tobacco use in 51.2% ($n$ = 21). Regarding the clinical symptoms, the patients exhibited varying degrees of claudication, with a mean distance of 250 ± 110 meters. The Rutherford classification system was used to assess the severity of PAD, with the following distribution: 24.4% ($n$ = 10) of patients were categorized as stage I category II, 14.6% ($n$ = 6) as stage I category III, 17.1% ($n$ = 7) as stage II, 31.7% ($n$ = 13) as stage III, and 12.2% ($n$ = 5) as stage IV. For Rutherford-chronic limb ischemia staging, 48.8% (20) of patients were classified as stage I, 12.2% ($n$ = 5) as stage II, and no patients were categorized as stage III. In terms of medication

**Table 1: Patient characteristics**

| **Cohort ($n$=41)** | **mean ± SD** | **% ($n$)** |
|---|---|---|
| Gender (female) | | 17.1 (7) |
| Age | 62.4±10.5 | |
| CAD | | 43.9 (18) |
| HT | | 43.9 (18) |
| T2DM | | 41.5 (17) |
| Tobacco use | | 51.2 (21) |
| **Clinical symptoms** | | |
| Claudication (m) | 250±110 | |
| **Rutherford** | | |
| Stage I category II | | 24.4 (10) |
| Stage I category III | | 14.6 (6) |
| Stage II | | 17.1 (7) |
| Stage III | | 31.7 (13) |
| Stage IV | | 12.2 (5) |
| **Rutherford chronic limb ischemia** | | |
| Stage I | | 48.8 (20) |
| Stage II | | 12.2 (5) |
| Stage III | | 0.0 (0) |
| **Medications** | | |
| ASA | | 97.6 (39) |
| Clodiprogel | | 82.9 (34) |
| ACE inhibitors | | 29.3 (12) |
| Cilostazol | | 29.3 (12) |
| Statin | | 36.6 (15) |
| Insulin | | 24.4 (10) |
| Oral antidiabetics | | 17.1 (7) |
| **Laboratory results** | | |
| HGB | 13.7±2.4 | |
| HCT | 41.8±5.8 | |
| MON | 2.0±2.5 | |
| LDL | 116.5±36.2 | |
| HDL | 39.6±8.5 | |
| TC | 208±66 | |
| TG | 227.4±126.0 | |

SD: Standard deviation, CAD: Coronary artery disease, HT: Hypertension, T2DM: Type 2 diabetes mellitus, ASA: Acetylsalicylic acid, ACE: Angiotensin-converting-enzyme, HGB: Hemoglobin, HCT: Hematocrit, MON: Monocyte, LDL: Low density lipoprotein, HDL: High density lipoprotein, TC: Total cholesterol, TG: Triglyceride

usage, a high percentage of patients were prescribed aspirin (acetylsalicylic acid) (97.6%, *n* = 39) and clopidogrel (82.9%, *n* = 34). Other medications included angiotensin-converting enzyme inhibitors (29.3%, *n* = 12), cilostazol (29.3%, *n* = 12), statins (36.6%, *n* = 15), insulin (24.4%, *n* = 10), and oral antidiabetics (17.1%, *n* = 7). Laboratory results revealed the following mean values: hemoglobin 13.7 ± 2.4 g/dL, hematocrit 41.8 ± 5.8%, monocyte count 2.0 ± 2.5 x $10^9$/L, low density lipoprotein cholesterol 116.5 ± 36.2 mg/dL, high density lipoprotein cholesterol 39.6 ± 8.5 mg/dL, total cholesterol 208 ± 66 mg/dL, and triglycerides 227.4 ± 126.0 mg/dL.

### Lesion characteristics

Table 2 presents the lesion characteristics. The cohort exhibited a mean lesion length of 126 ± 18 mm and mean lesion diameter of 5.8 ± 1.1 mm. Analysis of the stenosis rate revealed that 26.8% (*n* = 11) of the lesions had a stenosis rate between 50% and 74%, while 31.7% (*n* = 13) exhibited a stenosis rate ranging from 75% to 99%. Notably, a significant proportion of lesions, accounting for 41.5% (*n* = 17) of the cohort, demonstrated complete occlusion with a stenosis rate of 100%. In terms of lesion distribution, the majority of patients (70.7%, *n* = 29) presented with femoropopliteal disease, while a smaller subset (29.3%, *n* = 12) displayed aorta-iliac disease. Multivessel involvement was observed in 17.1% (*n* = 7) of the patients.

### Periprocedural outcomes

Table 3 provides insights into the procedural characteristics. The majority of procedures involved the use of drug-coated balloons (DCB), accounting for 90.2% (*n* = 37) of the cases. A smaller proportion of patients, 9.8% (*n* = 4), underwent treatment with bare metal stents.

Analysis of the complications arising from these procedures revealed that 9.8% (*n* = 4) of the patients experienced a dissection. However, no instances of bleeding, rupture, micro embolization, macro embolization, arteriovenous fistula, or infection related to the device were reported in any of the patients. Additionally, device malfunction was observed in only 2.2% (*n* = 1) of the cases.

### Revascularization outcomes

Table 4 presents the outcomes. Technical success, defined as the successful completion of the procedure without any immediate complications, was achieved in 87.8% (*n* = 36) of the cases. Hemodynamic success, indicating the restoration of normal blood flow, was achieved in 97.8% (*n* = 40) of the patients at the 30 day follow-up.

Assessing the primary patency rates, defined as the absence of significant restenosis or occlusion, the 30 day primary patency rate was reported as 97.8% (*n* = 40), indicating a high rate of procedural success in maintaining vessel patency. At the 6 month follow-up, the primary patency rate remained favorable at 87.8% (*n* = 36).

## DISCUSSION

PAD requires lifelong management to preserve the extremities and prevent complications. In recent years, endovascular treatment has emerged as the primary therapeutic option, with surgical or endovascular interventions reserved for secondary or tertiary approaches depending on the specific

**Table 2: Lesion characteristics**

| Cohort (*n*=41) | | mean ± SD | % (*n*) |
|---|---|---|---|
| Lesion length (mm) | | 126±18 | |
| The lesion diameter (mm) | | 5.8±1.1 | |
| Stenosis rate | 50-74% | | 26.8 (11) |
| | 75-99% | | 31.7 (13) |
| | 100% | | 41.5 (17) |
| Femoropopliteal disease | | | 70.7 (29) |
| Aorta-iliac disease | | | 29.3 (12) |
| Multivessel involvement | | | 17.1 (7) |

SD: Standard deviation

**Table 3: Procedure**

| Cohort (*n*=41) | mean ± SD | % (*n*) |
|---|---|---|
| DCB | | 90.2 (37) |
| BMS | | 9.8 (4) |
| Intervened length (mm) | 146.3±19.3 | |
| Complications | | |
| Dissection | | 9.8 (4) |
| Bleeding | | 0.0 (0) |
| Device malfunction | | 2.2 (1) |
| Rupture | | 0.0 (0) |
| Microembolization | | 0.0 (0) |
| Macroembolization | | 0.0 (0) |
| Arteriovenous fistula | | 0.0 (0) |
| Infection (device) | | 0.0 (0) |

SD: Standard deviation, DCB: Drug-coated balloons, BMS: Bare-metal stents

**Table 4: Outcomes**

| Variable | mean ± SD | % (*n*) |
|---|---|---|
| Technical success 30 day | 87.8 (36) | |
| Hemodynamically success 30 day | 97.8 (40) | |
| Primary patency 30 day | 97.8 (40) | |
| Primary patency 6 month | 87.8 (36) | |
| Need for open surgical revascularization 6 month | | 0.0 (0) |

SD: Standard deviation

clinical scenario.[9] However, due to the unique anatomical and histological characteristics of peripheral arteries compared with coronary arteries, several anatomical and structural limitations in the current treatment practices still warrant further investigation and clarification.[10] Long lesions, defined as lesions exceeding a length of 100 mm, pose particular challenges in endovascular management.[8,11] Initially, the 100 mm threshold for endovascular treatment was established in 2007.[12] However, subsequent randomized controlled trials, including FAST, ABSOLUTE, BASIL, and EMINENT, have provided compelling evidence supporting the efficacy and feasibility of endovascular interventions for long lesions.[11,13-15]

Notably, the 2018 report from the American College of Cardiology, American Heart Association, Society for Cardiovascular Angiography and Interventions, Society of Interventional Radiology, and Society for Vascular Medicine acknowledged the growing body of evidence supporting endovascular treatment as a viable option for lesions longer than 100 mm.[11] This recognition further solidified the role of endovascular interventions in managing long lesions of the lower extremity arteries. The inclusion of endovascular treatment in the management of long lesions signifies a shift in the treatment paradigm, reflecting a patient-centered approach that aims to maximize therapeutic options while minimizing invasiveness. By considering endovascular treatment as a primary option for long lesions, clinicians can reduce the need for extensive surgical procedures, offering patients a less invasive and more efficient therapeutic pathway.

Our study investigated the outcomes of endovascular treatment for long lesions, and the findings align with existing literature,[11-15] highlighting promising results in terms of primary patency. In addition, our study demonstrated superior hemodynamic success rates compared to both surgical and endovascular cohorts reported in the current-15). Particularly noteworthy is the high rate of primary technical success (88%) achieved in challenging cases involving long, diffuse, and calcific lesions, half of which occurred in diabetic patients and the other half in individuals with chronic ischemia. Additionally, the subsequent secondary endovascular intervention achieved a remarkable 100% technical success rate at the 30 day follow-up, underscoring the feasibility of endovascular therapy in this complex patient population. These encouraging findings pave the way for further exploration of endovascular treatment as a promising option in managing long lesions, particularly in patients with challenging comorbidities and chronic ischemia.

### Study limitations

This study has certain limitations that warrant a careful consideration when interpreting the findings. The primary limitation lies in the relatively small sample size which may limit the generalizability of the results to larger populations. Furthermore, the retrospective design of the study introduces inherent selection bias, potentially impacting the validity and reliability of the results. Given these limitations, it is crucial to emphasize the necessity for large-scale randomized controlled trials, accompanied by comprehensive treatment guidelines, to establish the optimal revascularization approach for patients with PAD and long complex lesions. Such studies would not only shed light on the risk factors associated with treatment failure but also provide valuable insights into refining and individualizing the management of patients with PAD.

## CONCLUSION

In conclusion, our study reinforces the growing body of evidence supporting the effectiveness of endovascular treatment for long lesions in lower extremity arteries. The findings demonstrate favorable outcomes in terms of primary patency and hemodynamic success, indicating the feasibility of endovascular interventions in this challenging patient population. However, the limitations of our study, including the small sample size and retrospective design, highlight the need for large-scale randomized controlled trials to further validate these results and guide treatment strategies. Future research should identify risk factors for treatment failure and develop comprehensive guidelines for managing patients with long and complex lesions in PAD.

### Ethics

**Ethics Committee Approval:** The study and its methodology, conducted in adherence to the principles of the Declaration of Helsinki, received approval from the Clinical Trials and Ethics Committee of the Eskişehir City Hospital. The ethics committee approval number for this study is "ESH/GOEK 2022/9" (date: 21.12.2022).

**Informed Consent:** Retrospective cohort study.

**Peer-review:** Externally and internally peer-reviewed.

### Authorship Contributions

Surgical and Medical Practices: İ.Ç.K., M.Ö., A.S.K., Concept: H.B., Design: İ.Ç.K., H.B., Data Collection or Processing: İ.Ç.K., M.Ö., A.S.K., Analysis or Interpretation: İ.Ç.K., H.B., M.Ö., A.S.K., Literature Search: H.B., Writing: İ.Ç.K., H.B.

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RESEARCH ARTICLE

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# Gender Differences in Periprocedural and Long-term Outcomes in Patients with Hypertrophic Cardiomyopathy Treated with Alcohol Septal Ablation Therapy: A Single Center Retrospective Study

**Ayşe Çolak[1], Ahmet Anıl Başkurt[2], Zeynep Kumral[1], Hüseyin Dursun[1], Ebru Özpelit[1], Bahri Akdeniz[1], Nezihi Barış[1], Özer Badak[1], Özhan Göldeli[1]**

[1]Department of Cardiology, Dokuz Eylül University Faculty of Medicine, İzmir, Turkey
[2]Department of Cardiology, Bakırçay University Faculty of Medicine, İzmir, Turkey

## Abstract

**Background and Aim:** We aim to demonstrate the periprocedural and long-term results of alcohol septal ablation (ASA) treatment in patients with hypertrophic cardiomyopathy (HCM) and specify the differences between female and male patients.

**Materials and Methods:** We enrolled 53 consecutive patients with HCM who underwent ASA treatment. Preprocedural demographic data, pre- and postprocedural characteristics and complications, echocardiographic data, and long-term results, including all-cause mortality and major adverse cardiovascular events (MACE), were recorded. MACE was defined as sudden cardiac death due to ventricular arrhythmias or heart failure (HF) and rehospitalizations due to HF or atrial fibrillation after the procedure.

**Results:** The mean age was 56.4 ± 12.1 years and 29 (54.7%) of the patients were female. Age at the time of ablation was higher ($P = 0.04$), and the presentation New York Heart Association functional class ($P = 0.03$) was worse in female patients. The median volume of ethanol usage was higher in male patients ($P = 0.03$) and the median duration of intensive care unit stay was higher in female patients ($P = 0.02$). The overall survival rates after ASA at 1, 5, 10, and 12 years were 96%, 87%, 76%, and 76%, respectively. There was no difference in the overall survival rates between genders (log-rank $P = 0.4$) and MACE was significantly higher in women patients (log-rank $P = 0.03$).

**Conclusion:** Women patients with HCM were older and had a worse functional capacity during the ASA procedure. Despite the similar mortality rates between genders, MACE was higher in women after the procedure. Earlier evaluation and treatment in female patients might decrease MACE during follow-up after ASA treatment.

**Keywords:** Gender differences, sex differences, hypertrophic cardiomyopathy, alcohol septal ablation, mortality, major adverse cardiovascular events

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**Address for Correspondence:** Asst. Prof. Ayşe Çolak, Department of Cardiology, Dokuz Eylül University Faculty of Medicine, İzmir, Turkey
**E-mail:** aysecolak1@windowslive.com
**ORCID ID:** orcid.org/0000-0002-1958-6158

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## INTRODUCTION

Hypertrophic cardiomyopathy (HCM) is one of the most prevalent hereditary cardiac disorders characterized by left ventricular outflow tract (LVOT) obstruction.[1] First-line therapy for reducing LVOT obstruction is medical treatment with negative inotropic drugs. In patients who are resistant to medical treatment, the recommended strategy to relieve LVOT obstruction is septal reduction therapy with surgical septal myectomy or alcohol septal ablation (ASA) therapy.[2,3]

A recent meta-analysis demonstrated that both surgical septal myectomy and ASA procedures have identical short-term and long-term risks for stroke, sudden cardiac death (SCD), all-cause, and cardiovascular (CV) mortality. However, compared with surgical septal myectomy, the ASA procedure is linked with a reduced risk of periprocedural complications but an increased risk of pacemaker implantations and repeated interventions.[4]

Evidence on differences in short- and long-term outcomes after ASA procedures between male and female patients is limited in the literature. women patients with HCM presented in later stages of the disease than men and had more refractory heart failure (HF) symptoms. However, there are inconsistencies about the overall survival between genders.[5] Some studies have demonstrated worse long-term outcomes after ASA in women[6], whereas after propensity score matching analysis of the Euro-ASA Registry, women and men had similar short- and mid-term outcomes after ASA treatment.[7]

Therefore, in this study, we aim to demonstrate the discrepancies in the periprocedural and long-term results of the ASA procedure between female and male patients and specify the differences in major adverse cardiovascular events (MACE) between genders after ASA treatment.

## MATERIALS AND METHODS

### Study population

We retrospectively enrolled 56 consecutive patients with HCM who underwent ASA procedure due to symptomatic LVOT obstruction despite maximally tolerated medical treatment between January 2010-December 2022. Inclusion criteria were; 1) interventricular septum (IVS) thickness 15 mm; 2) resting or provoked LVOT gradient 50 mmHg, and 3) New York Heart Association (NYHA) functional class II despite optimal medical therapy (OMT).[2,3] The mitral valve abnormalities requiring surgical intervention or any other indication for cardiac surgery were excluded from the study. Informed consent was obtained from all subjects before the procedure. The study protocol was approved by the Dokuz Eylül University Non-invasive Research Ethics Committee (approval number: 2022/33-08, date: 19.10.2022).

### Data collection

Institutional electronic medical records were analyzed for data collection. Preprocedural baseline patient characteristics, symptomatic status, comorbidities, medical therapies, and echocardiographic and electrocardiographic (ECG) data were recorded. Postprocedural data including ECG, echocardiographic parameters, and symptomatic status were documented. Mortality data were obtained from death certificates and causes of mortality were noted. MACE was defined as SCD because of ventricular arrhythmias or HF and rehospitalizations due to HF or AF after the procedure.

### Alcohol septal ablation

Standard diagnostic coronary angiography was performed for all subjects to determine the coronary heart disease that may need coronary bypass surgery and to assess the appropriateness of the septal perforator artery for an ASA procedure. All procedures were conducted under local anesthesia. A temporary pacemaker was inserted via the femoral vein before the procedure except for patients who had a previously implanted permanent cardiac pacemaker. A pigtail catheter and a 7 French (F) left coronary guiding catheter were inserted via two different femoral arteries. The pigtail catheter was used for measuring the outflow gradient before and after the procedure. After the identification of the septal perforator artery supplying the obstructing part of the septum, it is cannulated by a 0.014-inch guidewire. Afterwards, an over-the-wire (OTW) balloon is advanced into this target septal artery. The OTW balloon is inflated to isolate the septal artery from the other coronary arteries. Radiographic contrast was injected through the OTW balloon to exclude backflow into the left anterior descending (LAD) artery and to opacify the septum area involved in the systolic anterior motion (SAM) contact point. Continuous echocardiographic screening was performed to document the opacification of the septum. Under continuous ECG, echocardiographic, fluoroscopic, and hemodynamic monitoring, a small volume (1-3 mL) of absolute alcohol was injected slowly through the balloon catheter. Balloon occlusion was maintained for at least 10 min. After deflating the OTW balloon, a coronary angiogram was performed to establish complete occlusion of the septal perforator artery and to confirm normal flow in the LAD artery. Transthoracic echocardiography (TTE) and left heart catheterization via a pigtail catheter were used for measuring the LVOT gradient during and after the procedure.

### Follow-up

Patients stayed in the coronary intensive care unit (ICU) and were observed carefully for a minimum of 24 h after the intervention. TTE and ECG were performed immediately after the procedure to check for pericardial effusion and complete

heart block (CHB). Cardiac markers (creatinine kinase-myocardial band) and troponin T were measured every 8 h on the first day and daily thereafter until discharge. If a CHB was absent, the temporary pacemaker was removed after 24 h.

### Statistical analysis

A statistical software (SPSS version 26; SPSS, Inc., Chicago, IL) was used. The normality of continuous variables was checked with histograms and the Kolmogorov-Smirnov test. The categorical data were presented as numbers and percentages, and continuous data were presented as means standard deviations and median (interquartile range). Pre- and post-treatment echocardiographic data were evaluated with the Paired t-test and Wilcoxon test for continuous data and McNemar tests for categorical data. Survival estimates were calculated using the Kaplan-Meier method. MACE and survival comparisons between genders were made using the log-rank test. A *P*-value of <0.05 was considered significant.

## RESULTS

### Patient population

ASA could not be performed in three patients because of procedural reasons. The reasons were as follows; septal artery perforation, unable to advance the OTW balloon into the target septal artery, and septal artery tortuosity. After excluding these patients, 53 patients were analyzed. The baseline characteristics of all subjects and the differences in demographics between genders are outlined in Table 1. The mean age of the entire cohort was 56.4 ± 12.1 years and 29 (54.7%) of the patients were female. All subjects were symptomatic despite OMT, including beta-blockers (88.7%) and calcium channel blockers (15.1%). The majority of patients were in sinus rhythm (88.7%) and conduction abnormalities were noted in 3 (5.7%) patients, including left bundle branch block (LBBB) and right bundle branch block (RBBB). None of the patients had a history of surgical myectomy. Four patients (7.5%) had previous coronary revascularization via percutaneous coronary intervention, and none had a history of prior coronary artery bypass surgery. Two patients (3.8%) had a history of ICD implantation and one patient (1.9%) had a history of permanent pacemaker implantation. Age at the time of ablation was higher (59.5 ± 12.3 vs 52.7 ± 10.8, $P = 0.04$), and the presentation NYHA functional class ($P = 0.03$) was worse in female patients (Table 1). Additionally, the percentage of furosemide usage among women was higher than among male patients ($P = 0.04$).

### Procedural characteristics

The ASA procedure was performed on 53 patients. There was no procedural death. ASA reduced the resting LVOT gradient from 85 (70-109) to 20 (10-40) mmHg in the overall cohort ($P < 0.001$) (Figure 1). Additionally, the reduction in resting LVOT gradients was comparable between women and men [83 (70-115) to 20 (10-40) in women vs 85 (66-100) to 20 (15-40), $P < 0.001$ for both] (Figure 2). The median volume of ethanol injected was 1.6 (1.1-2.0, interquartile range) mL (Table 2). Intraprocedural CHB was observed in 18 (34%) patients and intraprocedural ventricular arrhythmia was observed in 1 (1.9%) patient (Table 2). In one patient (1.9%), left main coronary artery dissection was observed and treated with successful percutaneous stent implantation during the procedure. Among procedural characteristics, only the median volume of ethanol usage was higher in male patients [2.0 (1.5-2.0) vs 1.5 (1.0-2.0), $P = 0.03$].

### Post-procedural characteristics

Post-procedure serum troponin I level peaked at 24.7 (12.1-31.9) ng/mL x 1000 (Table 2). Patients were routinely monitored in the cardiac ICU for 59 (48-96) hours with a total median duration of hospital stay of 7 (6-8) days. Persistent or recurrent CHB was observed in 10 (18.9%) patients and 6 (11.3%) patients required internal cardioverter defibrillator (ICD) implantation before discharge. Post-procedural pericardial effusion was observed in 3 (5.7%) patients, however, there was no cardiac tamponade. Femoral vascular

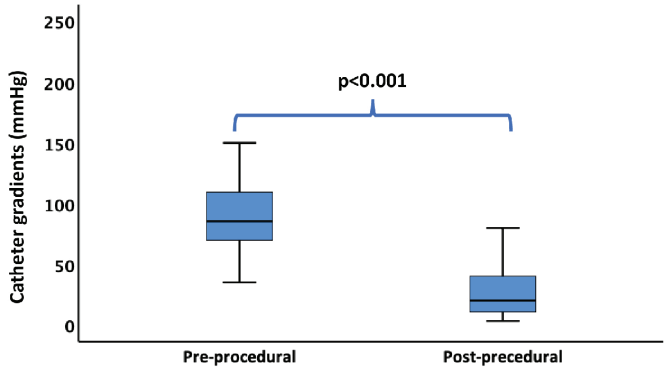


**Figure 1:** Comparison of pre-and post-procedural gradients

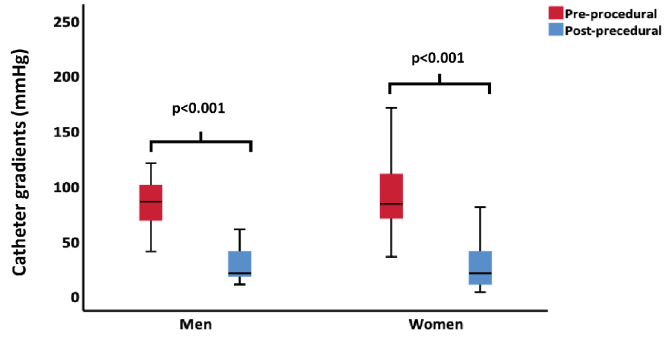


**Figure 2:** Comparison of pre-and post-procedural gradients in women and men

complications such as hematoma were in 4 (7.5%) patients, and no pseudoaneurysm was noted. The administration of erythrocyte suspension was needed in 3 (5.7%) patients. Post-procedure LBBB was present in 3 (5.7%) patients, RBBB was present in 16 (30.2%) patients, and left anterior fascicular block (LAFB) was present in 8 (15.1) patients (Table 2). Among post-procedural characteristics, the median duration of ICU stay was higher in female patients (p=0.02) (Table 2). Although not statistically significant, most other post-procedural complications were more prevalent in female patients (Table 2). The presence of post-procedural LBBB, RBBB, and LAFB were comparable between women and men.

Two (3.8%) patients died during the hospital stay. One patient died 3 days after the procedure of acute renal failure secondary to CHB. One patient died 29 days after the procedure because of septic shock.

## Echocardiographic data

The comparison of pre- and postprocedural echocardiographic data of the female and male patients is presented in Table 3. Echocardiographic was examined one month after the procedure. Left ventricular (LV) end-diastolic diameter (38.8 ± 4.9 to 40.2 ± 4.6, $P = 0.005$) and LV end-systolic diameter (22.6 ± 4.2 to 24.3 ± 3.3, $P = 0.03$) were significantly increased in women after the procedure; however, there was no difference in LV diameters in men after the procedure ($P > 0.05$ for all). IVS diameter (20.9 ± 2.8 to 20.4 ± 3.5, $P = 0.11$ for women and 22.8 ± 3.6 to 21.3 ± 3.4, $P = 0.01$ for men) was only reduced in men; however, resting LVOT gradient [100 (69-132) to 32 (18-70), $P < 0.001$ for women and 77 (58-103) to 30 (21-75), $P < 0.001$ for men] was significantly reduced in both genders. The percentage of SAM was also significantly reduced in both women and men after the procedure ($P = 0.02$ for both).

**Table 1: The baseline characteristics of all patients and the difference in demographics between genders**

| | All patients (*n*=53) | Women (*n*=29) | Men (*n*=24) | *P*-value |
|---|---|---|---|---|
| Age at the time of ablation* (years) | 56.4±12.1 | 59.5±12.3 | 52.7±10.8 | 0.04 |
| NYHA functional class, *n* (%) | | | | 0.03 |
| Class II | 8 (15.1) | 0 (0) | 8 (33.3) | - |
| Class III | 41 (77.4) | 26 (89.7) | 15 (62.5) | - |
| Class IV | 4 (7.5) | 3 (10.3) | 1 (4.2) | - |
| Angina, *n* (%) | 21 (39.6) | 12 (41.4) | 9 (37.5) | 0.7 |
| Syncope, *n* (%) | 18 (34) | 8 (27.6) | 10 (41.7) | 0.3 |
| The family history of SCD, *n* (%) | 20 (37.7) | 8 (27.6) | 12 (50) | 0.09 |
| Preoperative non-sustained VT, *n* (%) | 16 (30.2) | 9 (31) | 7 (29.2) | 0.8 |
| **ECG, *n* (%)** | | | | |
| Sinus rhythms | 47 (88.7) | 25 (86.2) | 22 (91.7) | 0.5 |
| AF | 6 (11.3) | 4 (13.8) | 2 (8.3) | NA |
| LBBB | 2 (3.8) | 1 (3.4) | 1 (4.2) | NA |
| RBBB | 1 (1.9) | 1 (3.4) | 0 (0) | NA |
| Hypertension, *n* (%) | 20 (37.7) | 14 (48.3) | 6 (25) | 0.08 |
| Diabetes mellitus, *n* (%) | 8 (15.1) | 6 (20.7) | 2 (8.3) | NA |
| Hyperlipidemia, *n* (%) | 13 (24.5) | 7 (24.1) | 6 (25) | 0.9 |
| Prior coronary revascularization, *n* (%) | 4 (7.5) | 1 (3.4) | 3 (12.5) | NA |
| Prior stroke, *n* (%) | 2 (3.8) | 0 (0) | 2 (8.3) | NA |
| ICD, *n* (%) | 2 (3.8) | 1 (3.4) | 1 (4.2) | 0.9 |
| The permanent pacemaker, *n* (%) | 1 (1.9) | 1 (3.4) | 0 (0) | NA |
| **Medications, *n* (%)** | | | | |
| Beta blocker | 47 (88.7) | 25 (86.2) | 22 (91.7) | 0.5 |
| Calcium channel blocker | 8 (15.1) | 6 (20.7) | 2 (8.3) | NA |
| ACEI/ARB | 10 (18.9) | 6 (20.7) | 4 (16.7) | 0.7 |
| Furosemid | 8 (15.1) | 7 (24.1) | 1 (4.2) | 0.04 |
| Spironolacton | 2 (3.8) | 2 (6.9) | 0 (0) | NA |
| Amiodarone | 11 (20.8) | 4 (13.8) | 7 (29.2) | 0.17 |

*Mean ± standard deviation. NHYA: New York Heart Association, SCD: Sudden cardiac death, ECG: Electrocardiography, AF: Atrial fibrillation, LBBB: Left bundle branch block, RBBB: Right bundle branch block, ICD: Internal cardioverter defibrillator, ACEI: Angiotensin-converting enzyme inhibitors, ARB: Angiotensin receptor blockers, VT: Ventricular tachycardia, NA: Non-applicable

Accordingly, mitral regurgitation severity was also decreased after the procedure for both genders ($P$ = 0.004 for women, and $P$ < 0.001 for men) (Table 3).

## Clinical outcomes

The mean follow-up period was 12.7 ± 3.3 years. There was no repeated ASA procedure in the overall cohort. Three (5.4%) patients required surgical myectomy, and among these patients, 2 of them also required mitral valve replacement. ICD implantation after discharge was noted in 4 (7.5%) patients. The mean NYHA functional class decreased from 2.7 0.5 to 1.9 0.6 in men ($P$ < 0.001) and 3.1 0.3 to 2.0 0.6 in women ($P$ < 0.001) after the procedure. Seven (13.2%, 4 female and 3 male) patients died after hospital discharge. Three of 7 deaths were due to CV causes. A detailed description of the causes of death is outlined in Table 4. MACE was observed in 13 (24.5%) patients. The overall survival rates after the ASA procedure at 1, 5 and

**Table 2: Procedural and post-procedural characteristics of all patients and comparison between genders**

| | All patients (*n*=53) | Women (*n*=29) | Men (*n*=24) | *P*-value |
|---|---|---|---|---|
| **Procedural characteristics** | | | | |
| Pre-procedural gradient† (mmHg) | 85 (70-109) | 83 (70-115) | 85 (66-100) | 0.7 |
| Post-procedural gradient† (mmHg) | 20 (10-40) | 20 (10-40) | 20 (15-40) | 0.48 |
| The volume of ethanol† (mL) | 1.6 (1.1-2.0) | 1.5 (1.0-2.0) | 2.0 (1.5-2.0) | 0.03 |
| Intraprocedural CHB, *n* (%) | 18 (34) | 11 (37.9) | 7 (29.2) | 0.15 |
| Intraprocedural VT/VF, *n* (%) | 1 (1.9) | 1 (3.4) | 0 (0) | NA |
| **Post-procedural characteristics** | | | | |
| Persistent/recurrent CHB, *n* (%) | 10 (18.9) | 8 (27.6) | 2 (8.3) | 0.07 |
| Pericardial effusion, *n* (%) | 3 (5.7) | 3 (10.3) | 0 (0) | NA |
| Hematoma, *n* (%) | 4 (7.5) | 4 (13.8) | 0 (0) | NA |
| The administration of ES, *n* (%) | 3 (5.7) | 2 (6.9) | 1 (4.2) | 0.67 |
| LBBB, *n* (%) | 3 (5.7) | 2 (6.9) | 1 (4.2) | 0.67 |
| RBBB, *n* (%) | 16 (30.2) | 9 (31) | 7 (29.2) | 0.8 |
| LAFB, *n* (%) | 8 (15.1) | 4 (13.8) | 4 (16.7) | 0.7 |
| Peak troponin I† (ng/mLx1000) | 24.7 (12.1-31.9) | 20 (10.3-28.3) | 26.2 (14.3-45) | 0.22 |
| ICU stay† (hours) | 59 (48-96) | 72 (50-120) | 48 (40-72) | 0.02 |
| Hospital stay† (days) | 7 (6-8) | 7 (6-8.5) | 7 (4-8) | 0.8 |
| ICD before discharge, *n* (%) | 6 (11.3) | 4 (13.8) | 2 (8.3) | 0.5 |

†Median (interquartile range). CHB: Complete heart block, VT: Ventricular tachycardia, VF: Ventricular fibrillation, LBBB: Left bundle branch block, RBBB: Right bundle branch block, LAFB: Left anterior fascicular block, ICU: Intensive care unit, ICD: Intracardiac cardioverter defibrillator, NA: Non-applicable

**Table 3: Comparison of pre- and postprocedural echocardiographic data of male and female patients**

| | Women (*n*=29) | | | Men (*n*=24) | | |
|---|---|---|---|---|---|---|
| | Pre-procedural | Post-procedural | *P*-value | Pre-procedural | Post-procedural | *P*-value |
| LVEDD* (mm) | 38.8±4.9 | 40.2±4.6 | 0.005 | 39.5±4.5 | 41.6±5.5 | 0.35 |
| LVESD * (mm) | 22.6±4.2 | 24.3±3.3 | 0.03 | 22.1±2.9 | 25.3±4.9 | 0.6 |
| LA* (mm) | 45.1±5.5 | 43.8±4.9 | 0.2 | 44.9±5.4 | 45.5±5.6 | 0.28 |
| LVEF† (%) | 64 (60-66) | 60 (60-65) | 0.08 | 65 (60-68) | 60 (60-65) | 0.07 |
| IVS* (mm) | 20.9±2.8 | 20.4±3.5 | 0.11 | 22.8±3.6 | 21.3±3.4 | 0.01 |
| Resting LVOT gradient† (mmHg) | 100 (69-132) | 32 (18-70) | <0.001 | 77 (58-103) | 30 (21-75) | <0.001 |
| SAM, *n* (%) | 27 (93.1) | 16 (55.2) | 0.02 | 20 (83.3) | 13 (54.2) | 0.02 |
| MR, *n* (%) | | | 0.004 | | | <0.001 |
| Mild | 9 (31) | 18 (62.1) | | 13 (54.2) | 17 (70.8) | |
| Moderate | 11 (37.9) | 7 (24.1) | | 6 (25) | 3 (12.5) | |
| Severe | 9 (31) | 4 (13.8) | | 5 (20.8) | 4 (16.7) | |

*Mean ± standard deviation, †Median (interquartile range). LVEDD: Left ventricular end-diastolic diameter, LVESD: Left ventricular end-systolic diameter, LA: Left atrium, LVEF: Left ventricular ejection fraction, IVS: Interventricular septum, LVOT: Left ventricular outflow tract, SAM: Systolic anterior motion, MR: Mitral regurgitation

12 years were 96%, 87%, 76%, and 76%, respectively (Figure 3). There was no difference in the overall survival rates between male and female patients (log-rank $P = 0.4$) (Figure 3). However, the cumulative incidence of MACE in women was significantly higher than in male patients (log-rank $P = 0.03$) (Figure 4).

## DISCUSSION

Our results demonstrated that age at the time of ablation was higher and the presentation NYHA functional class was worse in female patients. The volume of ethanol usage was higher in male patients, whereas the duration of ICU stay after ASA was higher in female patients. Post-procedural increases in LV diameters were more prominent in female patients, however, the decrease in IVS thickness was more prominent in male patients. Our results also demonstrated that the overall survival rates after the ASA procedure at 1, 5, 10, and 12 years were 96%, 87%, 76%, and 76%, respectively. There was no difference in overall survival rates between male and female patients, however, the cumulative incidence of MACE in women patients was significantly higher than in male patients.

Our results are consistent with preexisting reports in terms of late presentation and worse clinical profiles in female patients.[5] This was partially explained by the protective effects of estrogens in women's hearts. Various animal models have shown that the female heart has a greater hypertrophic reserve and the transition to HF was quicker in male hearts in pressure-overloaded rat models.[8] Additionally, it is obvious that all CV diseases are underdiagnosed, under-treated, and under-recognized in female patients globally.[9] The women's access

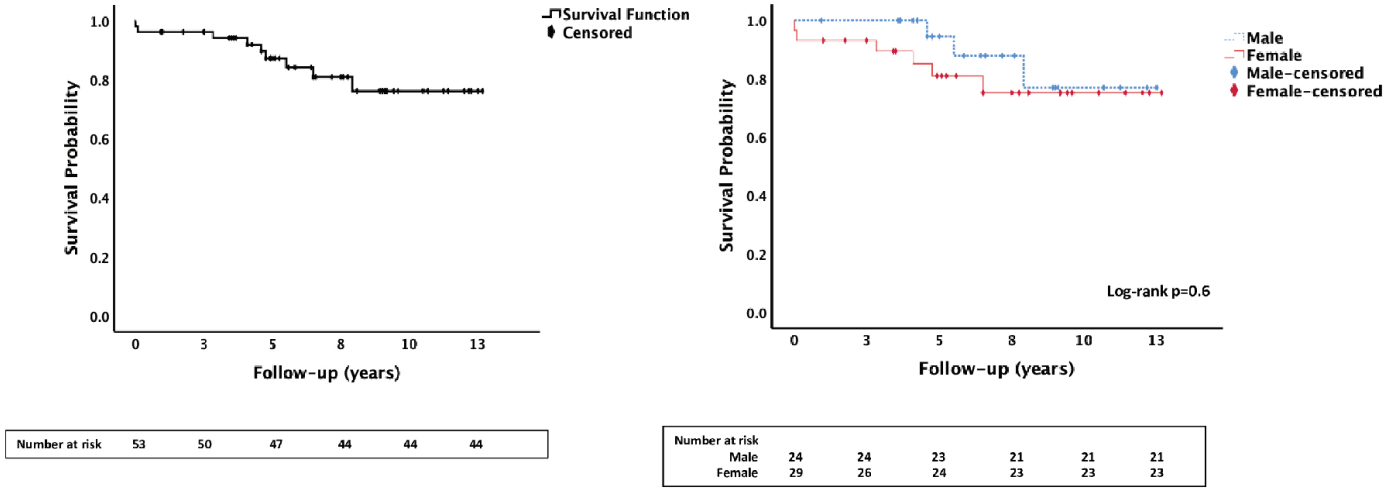


**Figure 3:** Kaplan-Meier survival curves for all-cause mortality in all patients and difference between female and male patients

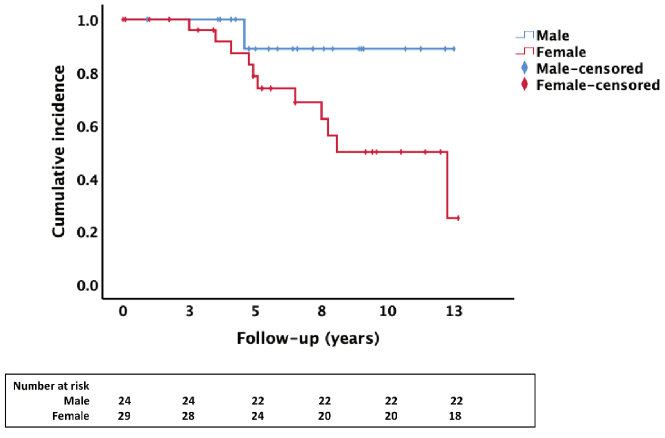


**Figure 4:** Kaplan-Meier cumulative incidence curves for MACE in female and male patients

*MACE: Major adverse cardiovascular events*

**Table 4: A detailed description of causes of death after hospital discharge**

| Age (years) | Gender | Cause of death |
|---|---|---|
| 51 | Female | Acute respiratory distress syndrome secondary to SARS-CoV-2 |
| 56 | Female | Sudden cardiac death secondary to ventricular fibrillation |
| 69 | Male | Heart failure |
| 65 | Male | Acute respiratory distress syndrome secondary to SARS-CoV2 |
| 72 | Female | Heart failure |
| 74 | Female | Septic shock |
| 59 | Male | Respiratory failure secondary to amyotrophic lateral sclerosis |

SARS-CoV2: Severe acute respiratory syndrome coronavirus-2

to optimal health care was limited because of socioeconomic and sociocultural factors, resulting in late presentation and treatment in female patients.

We showed that the increase in LV diameters after the ASA procedure was statistically significant in women, however, we were unable to show this effect in men patients. Contrary to our findings, Chen et al.[10] demonstrated that reverse remodeling after ASA was greater in men than in women. They have also shown that the main predictor of LV reverse remodeling was a change in the LVOT gradient. In our study, the magnitude of change in the LVOT gradient was higher in women [100 (69-132) to 32 (18-70) vs 77 (58-103) to 30 (21-75)] than in men, which might have resulted in a more prominent increase in LV diameters in female patients. We also showed that the decrease in IVS thickness was more prominent in male patients. The greater volume of ethanol usage in male patients might have resulted in this observation as higher doses of ethanol have resulted in more decrease in IVS diameter.[11]

Several single-center and national ASA registries establish the short- and long-term results of the ASA procedure in the literature.[12-16] Our results were comparable with large registries including the EURO-ASA registry which demonstrated a 10-year survival rate of 77%[15] and the North American ASA registry which demonstrated a 9-year survival rate of 74%.[12] Contrary to our findings, the largest single-center study from our country showed a 10-year survival rate of 85%.[16] The main difference between these two studies from Turkey was the higher pre-discharge median LVOT gradient after the ASA procedure in our study [32 (18-70) in women and 30 (21-75) in men vs 21 (10-33) in women and 21 (11-32) in men]. EURO-ASA registry demonstrated that each mmHg elevation in LVOT gradient after the procedure resulted in ~1% increase in overall mortality.[15] The higher mean residual LVOT gradient in our study might have resulted in this discrepant result.

The overall survival rates after ASA treatment was similar between genders in our cohort. Our results were comparable with the large Euro-ASA registry[7], which demonstrated similar outcomes between male and female patients. We also showed that the cumulative incidence of MACE in women was significantly higher than in male patients. Similar to our findings, female sex was found to be the only significant predictor of MACE related to HCMP.[17] This may be explained by several reasons. First, the smaller LV cavity and higher residual LVOT gradient in female patients might have resulted in a higher incidence of HF hospitalizations.[18,19] Second, women had a poor diastolic reserve and higher LV filling pressures, which might have resulted in a higher incidence of HF with preserved ejection fraction in women.[20] Finally, NYHA functional class was found to be a significant predictor of AF in HCMP.[21] The worse NYHA functional class in female patients might have resulted in more frequent AF in our study.

### Study limitations

The major limitation of our study was the small size of the cohort. Additionally, it has limitations specific to retrospective analyzes the lack of assessment of CV mortality is another important limitation. We could not assess whether there was a difference in CV mortality after the ASA procedure between genders. The fact that the medical treatments received by the patients after the procedure were not evaluated may have affected the results regarding MACE.

## CONCLUSION

Women presented at a later age and had a worse NYHA functional capacity before the ASA procedure. There was no difference in all-cause mortality between genders, but the cumulative incidence of MACE was higher in women after the procedure. Earlier evaluation of female patients with HCMP for ASA procedure might have resulted in fewer MACEs during follow-up.

### Ethics

**Ethics Committee Approval:** The study protocol was approved by the Dokuz Eylül University Non-invasive Research Ethics Committee (approval number: 2022/33-08, date: 19.10.2022).

**Informed Consent:** Informed consent was obtained from all subjects before the procedure.

**Peer-review:** Externally peer-reviewed.

### Authorship Contributions

Surgical and Medical Practices: H.D., B.A., N.B., Ö.B., Ö.G., Concept: A.Ç., Design: A.Ç., E.Ö., Data Collection or Processing: A.A.B., Z.K., Analysis or Interpretation: A.Ç., E.Ö., Literature Search: A.Ç., Z.K., Writing: A.Ç.

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RESEARCH ARTICLE

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# Evaluation of Cardiovascular Risks and Dyslipidemia in HIV-positive Patients

Banu Karaca[1], Fahrettin Tuğrul Çitekçi[2], Beyza Erol[1], Bahar Örmen[1], Nurbanu Sezak[1], Figen Kaptan[1], Tuncay Kırış[2]

[1]İzmir Katip Çelebi University, Atatürk Training and Research Hospital, Clinic of Infectious Diseases, İzmir, Turkey
[2]İzmir Katip Çelebi University, Atatürk Training and Research Hospital, Clinic of Cardiology, İzmir, Turkey

## Abstract

**Background and Aim:** Cardiovascular diseases are the leading cause of death worldwide. We evaluated dyslipidemia and cardiovascular risks in human immunodeficiency virus (HIV)-positive patients.

**Materials and Methods:** We enrolled patients in this study between January 1, 2018, and December 31, 2022, at the infectious diseases outpatient clinic. A total of 189 HIV-positive cases and 199 cases with normal examination findings within the same timeframe were compared in terms of cardiovascular risk factors.

**Results:** The study included 388 individuals, of whom 189 were HIV-positive patients and 199 were in the control group. The mean age of the HIV-positive group was 47.8 ± 11.5; 64.9% were men. Framingham's risk score was found to be statistically higher in the HIV-positive patient group ($P = 0.001$). Total cholesterol, low-density lipoprotein, and triglyceride levels were higher in the HIV-positive group ($P < 0.001$, $P < 0.001$, and $P = 0.023$). A higher proportion of patients in the moderate- and high-risk categories were HIV positive.

**Conclusion:** In HIV-positive patients on antiretroviral therapy, an increase in lipid profiles was observed in those categorized as moderate and high cardiovascular risk groups compared with the control group.

**Keywords:** HIV, dyslipidemia, cardiovascular risk

## INTRODUCTION

Cardiovascular disease (CVD) is the leading cause of death worldwide.[1] Elevated blood lipid levels, particularly low-density lipoprotein (LDL) cholesterol, are the most important risk factor for coronary artery disease. In addition, high levels of triglycerides are considered a significant risk factor in this regard. A sedentary lifestyle, smoking, advanced age, hypertension, and the presence of diabetes mellitus constitute major risk factors for coronary artery diseases.[2,3] Human immunodeficiency virus (HIV)-positive individuals experience suppression of viral replication through antiretroviral therapy (ART), which prolongs their lives. However, chronic inflammation and continuous use of antiviral treatments can increase long-term cardiovascular risks in these patients.[4] The presence of comorbidities such as diabetes, dyslipidemia, and other metabolic disorders particularly complicates the management of these individuals.[5] Identifying risk factors and their management is the primary goal in reducing cardiovascular mortality. As per the risk scoring recommended by the American Heart Association, individuals are categorized into low-, moderate-, and high-risk classes.[6] Identifying high-risk patients and administering appropriate treatments is crucial in reducing cardiovascular mortality. This study compared HIV-positive individuals with an HIV-negative control group regarding dyslipidemia and cardiovascular risk factors.

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**Address for Correspondence:** Banu Karaca, İzmir Katip Çelebi University, Atatürk Training and Research Hospital, Clinic of Infectious Diseases, İzmir, Turkey
**E-mail:** banukaraca@yahoo.com
**ORCID ID:** orcid.org/0000-0003-1470-356X

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## MATERIALS AND METHODS

A single-center retrospective study was conducted using data extracted from hospital records. The study encompassed the period from January 1, 2018, to December 31, 2022, at our tertiary care hospital's infectious diseases outpatient clinic. A total of 189 HIV-positive cases and 199 cases with normal examination findings within the same timeframe were compared in terms of cardiovascular risk factors. We excluded patients with a history of coronary artery disease. The American Heart Association's Framingham risk score assessment considered gender, age, total cholesterol, high-density lipoprotein (HDL) cholesterol levels, systolic blood pressure, smoking status, and the presence of diabetes. Total cholesterol more than 200 mg/dL, LDL >100 mg/dL, HDL <55 mg/dL, and triglyceride >135 mg/dL were accepted as high. Framingham risk score values >20% were categorized as high risk, values <10% were considered low risk, and values in between were classified as moderate risk. The İzmir Katip Çelebi University Non-Invasive Clinical Research Ethics Committee approved the study (decision no: 0383, date: 19.08.2023).

### Statistical analysis

Statistical tests were performed using SPSS version 19 (SPSS Inc., Chicago, IL, USA). Continuous variables are presented as mean ± standard deviation, and categorical variables are shown as the number of subjects, with the percentage of the total numbers. Either Student's t-test or the Mann-Whitney U test was used to compare parametric values between the two groups, as appropriate. The chi-squared test was used to compare categorical variables. Two-sided *P* values <0.05 were considered statistically significant.

## RESULTS

The study included 388 individuals, of whom 189 were HIV-positive patients and 199 were in the control group. The mean age of the HIV-positive group was 47.8 ± 11.5; 64.9% were men. Sociodemographic characteristics of the patient and control groups are given in Table 1. The number of females was higher in the control group. There was no statistically significant difference between the mean ages of the patients and control groups (47.7 ± 13.6 vs. 47.9 ± 9.2, $P = 0.862$, respectively). In addition, we obtained no significant difference in the means of the frequency of hypertension and diabetes mellitus, body mass index, smoking, marital status, alcohol use, or systolic blood pressure between the two groups. The mean total cholesterol level of the HIV-positive group was 234.3 ± 36.9 mg/dL, LDL 159.2 ± 22.6 mg/dL, HDL 42.7±11.3 mg/dL, and triglyceride 160 mg/dL. Total cholesterol, LDL, and triglyceride levels were statistically higher in the HIV-positive group ($P < 0.001$, $P < 0.001$, and $P = 0.023$ respectively, Table 2). Framingham's risk score was found to be statistically higher in the HIV-positive patient group ($P = 0.001$). When comparing HIV-positive patients with the control group, it was observed that in both groups, most patients were in the low cardiovascular risk category. However, a higher proportion of patients in the moderate- and high-risk categories were HIV positive (Figure 1, Table 1, $P < 0.031$). There was no significant difference in terms of HDL levels in the HIV-positive group.

**Table 1: Baseline characteristics of the study population**

| Variables | HIV (+) (*n*=189) | Control (*n*=199) | *P*-value |
|---|---|---|---|
| Age, years | 47.7±13.6 | 47.9±9.2 | 0.862 |
| BMI (kg/m$^2$) | 28.1±3.9 | 27.5±4.2 | 0.129 |
| Female gender (%) | 36 (19) | 100 (50) | <0.001 |
| Hypertension, *n* (%) | 74 (39) | 89 (45) | 0.267 |
| Diabetes mellitus, *n* (%) | 56 (30) | 55 (28) | 0.664 |
| Smoking, *n* (%) | 49 (26) | 65 (33) | 0.145 |
| Marital status, *n* (%) | 25 (5) | 11 (5) | 0.573 |
| Married, *n* (%) | 107 (57) | 107 (54) | |
| Single/divorce *n* (%) | 82 (43) | 92 (46) | |
| Alcohol usage, *n* (%) | 49 (26) | 57 (29) | 0.428 |
| Systolic blood pressure (mmHg) | 119±13 | 120±19 | 0.835 |
| Framingham risk points | 6 (4-9) | 5 (3-6) | 0.001 |
| Framingham risk | | | 0.031 |
| Low-risk *n* (%) | 178 (94) | 197 (99) | |
| Moderate risk *n* (%) | 6 (3) | 1 (1) | |
| High-risk *n* (%) | 5 (3) | 1 (1) | |

BMI: Body mass index, HIV: Human immunodeficiency virus

Of the patients, 5.07 were using 2 nucleoside reverse transcriptase inhibitor (NRTIs) + integrase inhibitor (INSTI), 22.2% one NRTI+ INSTI, 4.7% 2NRTIs + protease inhibitor (PI)/ritonavir (RTV) or PI/cobicistat (COBI), 7.9% 2NRTIs + INSTI + booster and as ART. 90% of the patients receiving regimens containing protease inhibitors, 66.1% of the patients receiving 2NRTIs + INSTI, 90.2% of the patients receiving one NRTI + INSTI, and 80 percent of the patients receiving 2NRTIs + INSTI + booster had abnormalities in at least one lipid parameter.

## DISCUSSION

In this study, it was observed that lipid levels were higher in HIV-positive patients receiving ART than in the control group, and it was determined that this condition could increase the risk of CVDs in the future. During chronic diseases, the inclusion of CVDs in the clinical situation alters the prognosis. Effective ART treatment has ensured viral suppression in HIV-positive patients, leading to increased lifespans for these individuals. As a result, advanced age-related conditions such as atherosclerosis are more frequently observed among this population. Elevation of cardiovascular risk factors alongside chronic inflammation causes clinical issues. In our study conducted between January 1, 2018, and December 31, 2022, HIV-positive patients under follow-up at the Infectious Diseases Outpatient Clinic were compared with a control group without chronic illnesses in terms of cardiovascular risks. The majority of HIV-positive patients (178, 94%) were in the low-risk category. The group categorized as moderate and high risk included a higher proportion of HIV-positive cases (11,6%, Table 1). The prevalence of low cardiovascular risk in both the patient and control groups was attributed to their relatively low mean ages (mean age: 47.8 ± 11.5). In our society, sedentary lifestyles, smoking, and poor dietary habits resulting in disrupted lipid metabolism contribute to a high cardiovascular-related mortality rate.[7] HIV infection leads to chronic inflammation, and previous studies have demonstrated that antiretroviral agents administered to manage the infection can also result in changes in lipid metabolism, leading to dyslipidemia, premature atherosclerosis, and the development of coronary artery disease.[8,9] In the literature, antiretroviral agents exhibit various effects on lipid metabolism, notably causing an increase in triglyceride levels and a decrease in HDL cholesterol levels, thereby contributing to elevated coronary risk factors.[10] Certain antiretrovirals have also been reported to induce alterations in triglyceride and LDL cholesterol levels.[11] For adult individuals with chronic HIV infection, the initiation of ART is recommended regardless of the CD4 T lymphocyte count. In individuals who have not previously received ART, the ART regimen typically consists of a backbone of two NRTI drugs supplemented with one of the drugs from the INSTI or NNRTI class or a pharmacokinetically boosted PI drug such as COBI or RTV. The recommended NRTI backbone comprises ABC/3TC or a combination of tenofovir (tenofovir disoproxil fumarate or tenofovir alafenamide) and emtricitabine.[12]

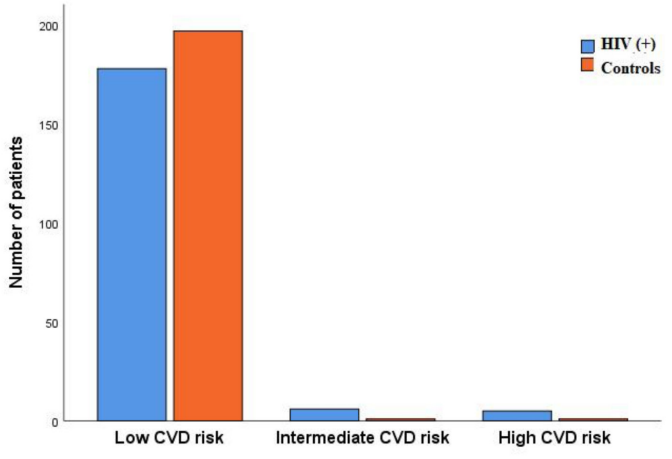


**Figure 1:** Cardiovascular risk assessment of HIV-positive and control groups according to the Framingham scoring system

*HIV: Human immunodeficiency virus, CVD: Cardiovascular disease*

In patients receiving combination therapy with protease inhibitors, there is an increase in cardiovascular event risk alongside the deterioration of the lipid profile.[13] In our study, similar to the literature, when looking at the HDL, LDL, triglyceride, and total cholesterol cut-off values in patients receiving a combination containing a protease inhibitor, the patient ratio with at least one high value was calculated as 90%. Dyslipidemia was observed in patients receiving other treatment regimens as well. However, in the low-risk group, which constituted most patients, there was no significant

**Table 2: Laboratory findings of patients**

| Variable | HIV (+) (n=189) | Control (n=199) | *P*-value |
|---|---|---|---|
| Total cholesterol (mg/dL) | 234.3±36.9 | 205.5±13.1 | <0.001 |
| LDL-C (mg/dL) | 159.2±22.6 | 130.1±17.4 | <0.001 |
| HDL-C (mg/dL) | 42.7±11.3 | 41.8±4.3 | 0.294 |
| Triglyceride (mg/dL) | 160 (115-246) | 147 (109-194) | 0.023 |

LDL-C: Low-density lipoprotein cholesterol, HDL-C: High-density lipoprotein cholesterol, HIV: Human immunodeficiency virus

difference in terms of cardiovascular risk compared with the control group. Current anti-lipidemic treatment guidelines emphasize that treatment should be determined not only based on lipid values but also on the presence of additional cardiovascular risk factors in patients.

### Study limitations

The limitations of our study are its retrospective nature and single-center nature, and the relatively small number of cases. In this age group, the Framingham cardiovascular risk scoring system is less sensitive than that in older age groups. There is a need for large-scale, prospective, multicenter studies to demonstrate the association between hyperlipidemia caused by ART and increased cardiovascular mortality.

## CONCLUSION

In HIV-positive patients followed at the Infectious Diseases Outpatient Clinic who had received ART, an increase in lipid profiles was observed in those categorized as moderate and high cardiovascular risk groups compared with the control group. The long-term impact of this issue on CVDs should be further investigated in large-scale studies in the future.

### Ethics

**Ethics Committee Approval:** The İzmir Katip Çelebi University Non-Invasive Clinical Research Ethics Committee approved the study (decision no: 0383, date: 19.08.2023).

**Informed Consent:** Retrospective study.

**Peer-review:** Externally peer-reviewed.

### Authorship Contributions

Concept: B.K., Design: B.K., T.K., Data Collection or Processing: F.T.Ç., B.E., Analysis or Interpretation: B.Ö., N.S., F.K., T.K., Literature Search: B.K., N.S., Writing: B.K., T.K.

**Conflict of Interest:** No conflict of interest was declared by the authors.

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CASE REPORT

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# Reversible Pulmonary Hypertension Associated with Myasthenia Gravis

**Ahmet Taha Şahin, Yakup Alsancak, Öznur Keskin, Mehmet Akif Düzenli**

Necmettin Erbakan University, Meram Faculty of Medicine, Department of Cardiology, Konya, Turkey

## Abstract

Myasthenia gravis (MG) is an autoimmune disease that causes localized and generalized muscle weakness caused by antibodies targeting various components of the postsynaptic membrane. Respiratory muscle involvement as a feared complication of this disease can be life-threatening and cause respiratory failure requiring intubation and mechanical ventilation. The relationship between MG and pulmonary hypertension (PH) has been rarely seen in the literature, and here we present a case who presented with respiratory failure and started treatment with the diagnosis of PH and was diagnosed with MG in the follow-up.

**Keywords:** Myasthenia gravis, neuromuscular disease, pulmonary hypertension

## INTRODUCTION

Myasthenia gravis (MG) is a chronic autoimmune disease in which weakness in the skeletal muscles is created by immune system antibodies that affect different components of the postsynaptic membrane and impair neuromuscular transmission.[1] Acetylcholine receptor antibodies are found in approximately 80% of patients with MG. Although this disease is more common among women under 40 years of age than in men of the same age group, it is predominant in male patients over 50 years of age.[2] Respiratory failure is a life-threatening complication of MG. However, its relationship with pulmonary hypertension (PH) remains unclear.[3] This report presents the case of a 35-year-old patient diagnosed with PH after presenting with chronic respiratory failure. The patient had been intubated during treatment for coronavirus disease-2019 (COVID-19) and received no significant benefits from pulmonary arterial hypertension (PAH)-specific treatment. The patient's symptoms were relieved after the treatment for MG.

## CASE REPORT

A 35-year-old male patient with no comorbidities presented to our clinic with exertional dyspnea and fatigue. The patient's history revealed that he had experienced respiratory arrest 10 months prior to the diagnosis. This was followed by a two-week intubation period and subsequent inhaler treatments. No accompanying autoimmune comorbidities were observed. On physical examination, the respiratory component (P2) of the second heart sound was dominant with a 2/6 systolic murmur on the right parasternal border. The electrocardiogram was in sinus rhythm (Figure 1). The patient had never received cardiac therapy, and a chest X-ray was evaluated as normal (Figure 2). The patient's N-terminal pro-brain-type natriuretic peptide level was 221 pg/mL.

Transthoracic echocardiography (TTE) showed normal left ventricular function, enlarged right ventricular (RV) end-diastolic chamber sizes [RV: 39 mm, right atrial (RA): 36×47 mm], moderate to severe tricuspid regurgitation (peak systolic tricuspid regurgitation velocity: 3.8 mm), and borderline RV function

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**Address for Correspondence:** MD Ahmet Taha Şahin, Necmettin Erbakan University, Meram Faculty of Medicine, Department of Cardiology, Konya, Turkey
**E-mail:** tahasahin94@gmail.com
**ORCID ID:** orcid.org/0000-0002-2928-1059

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(tricuspid annular plane systolic excursion: 18 mm and RV Sm: 12 cm/s). Using TTE, the diameter of the inferior vena cava was measured as 1.9 cm with a collapsibility of over 50%. Color flow Doppler imaging showed no suspicion of a left-to-right shunt. The patient's estimated systolic pulmonary artery pressure (PAP) (63 mmHg) was high. Transesophageal echocardiography confirmed the absence of a left-to-right shunt.

In examinations performed in the chest diseases clinic, computed tomography (CT) revealed the patient's thorax to be normal (Figure 3). Subsequent ventilation perfusion scintigraphy showed that the patient was at low risk of embolism (Figure 4). No uptake was observed in high-resolution CT (HRCT) imaging because of the persistence of dyspnea, and CT angiography did not detect pulmonary embolism (Figure 5). Pulmonary function tests revealed an FEV1/FVC of 81% and normal DLCO levels. In a 6-minute walking test, the patient was measured as moving 300 meters. His $O_2$ saturation was 92% before the

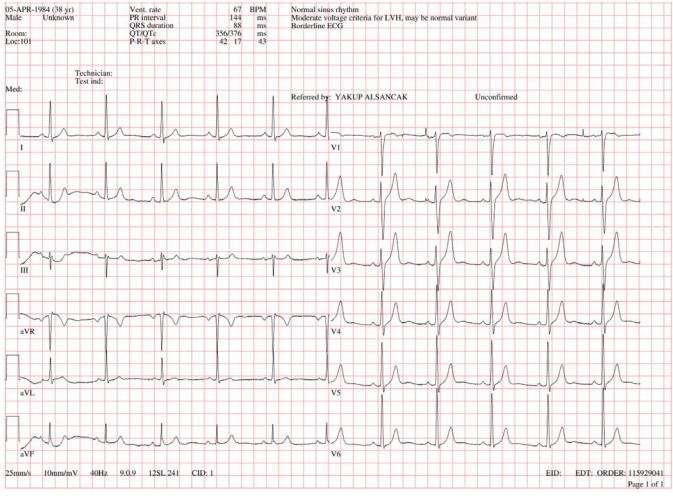


**Figure 1:** Electrocardiogram does not demonstrate any obvious pathology

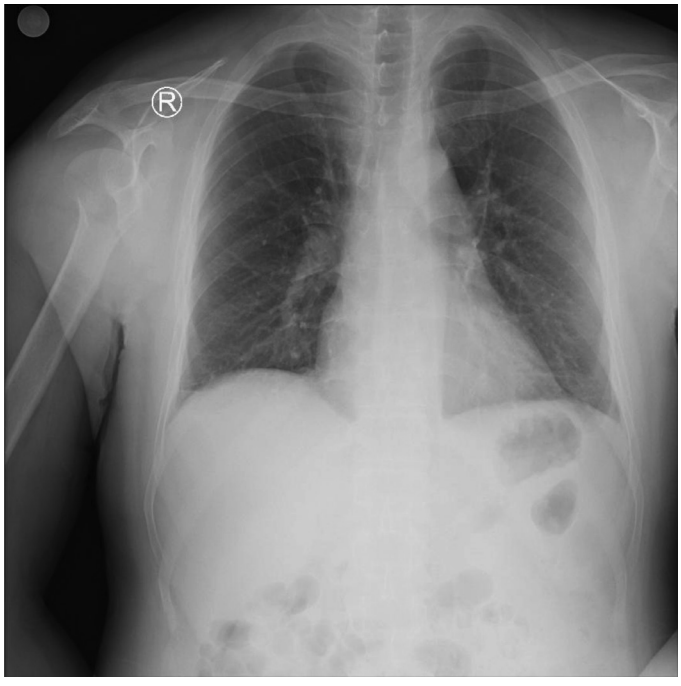


**Figure 2:** Chest X-ray was evaluated as normal

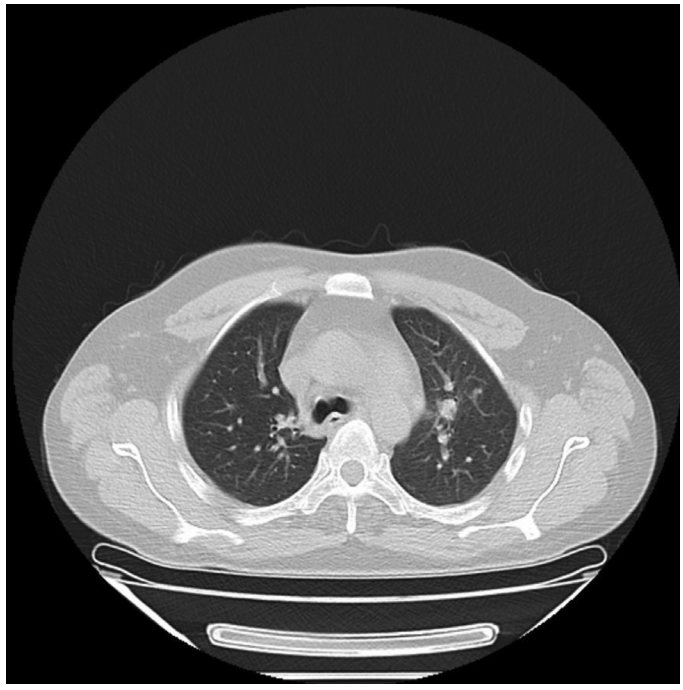

**Figure 3:** There was no significant pathological change in computed tomography

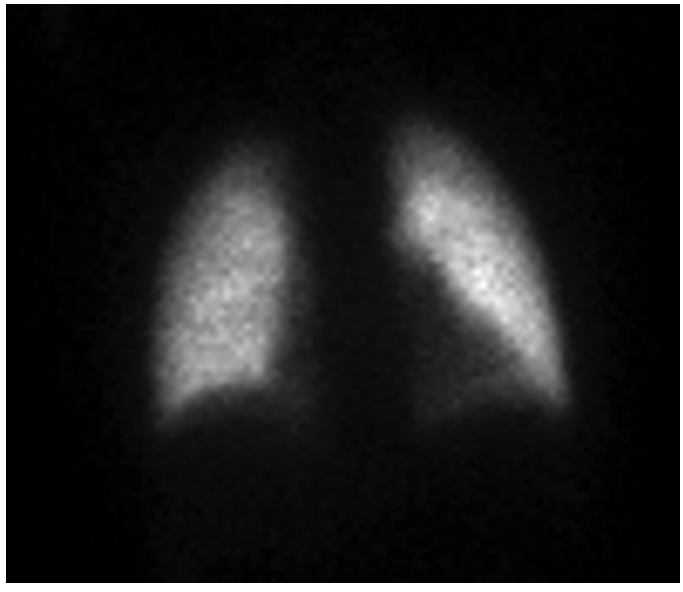

**Figure 4:** The scintigraphy shows a normal pulmonary perfusion

walking test and 86% after. During right heart catheterization, the patient's pulmonary vascular resistance was 3.7 wood units, RA pressure was 5 mmHg, cardiac output was 5.9 L/min, and pulmonary capillary wedge pressure was 9 mmHg. In repeated measurements, his average PAP was 47, 26, and 33 mmHg. The vasoreactivity test was negative. The left ventricular end diastolic pressure was 11 mmHg. A fluid loading test was also performed. The patient was found to be in the intermediate-risk group for primary PH and was treated with macitentan 10 mg 1*1. In a follow-up visit, clinical findings included persistence of a New York Heart Association Functional Capacity (NYHA FC) of 2-3, drooping eyelids, development of chronic fatigue, decremental response observed in a sequential nerve stimulation test performed in consultation with the neurology department, and detection of anti-acetylcholine receptors (0.71 nmol/L). A diagnosis of MG was made. It was noted that no MG crisis was observed while the patient was infected with COVID-19. Macitentan treatment was interrupted, and IV immunoglobulin and pyridostigmine were administered. In a follow-up one month later, his complaints had lessened and he had a NYHA FC of 1. The estimated sPAP value in the patient 's control TTE was 30 mmHg. Informed consent was obtained from the patient.

## DISCUSSION

Awareness of primary PH has increased in recent years. PH has various causes and can manifest with complaints including dyspnea, exercise intolerance, and chest pain. It is observed in approximately 1% of the population; this rate is slightly higher in patients over 65 years of age. The prognosis is worse in patients with severe RV dysfunction.[4]

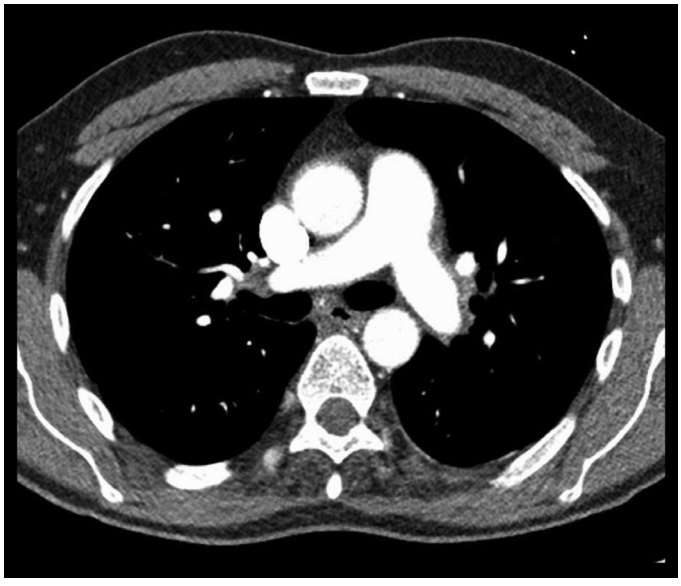

**Figure 5:** CT angiography did not detect pulmonary embolism

*CT: Computed tomography*

Chronic neuromuscular diseases, such as MG, polymyelitis, and Guillain-Barré syndrome, can lead to respiratory failure by causing neuromuscular paralysis in the acute or chronic phase.[5] Specifically, MG can cause a restrictive pattern of respiratory failure with diaphragmatic involvement, notably in the later stages of the disease.[6] However, although MG is known to cause right heart failure and PH, it is not frequently encountered.[7]

MG can cause PH by affecting the thoracic muscles and diaphragm, leading to deterioration in lung compliance. It is possible that an intense immune response to COVID-19 activates MG. For these reasons, MG is among the causes of group 3 or group 5 PH. However, this also means that there is no specific treatment recommendation for PAH.

The patient in the case presented here arrived at our clinic with complaints of chronic dyspnea and exercise intolerance after COVID-19 infection. After detecting elevated PAP in the initial examination, transoesophageal echocardiography, spirometry measurements, HRCT, and ventilation-perfusion scintigraphy were used to exclude other possible causes. Performing these examinations is important to eliminate congenital heart diseases that may be involved in the etiology of PH, pulmonary fibrosis, and lung parenchymal diseases that can occur after pneumonia.

Treatment of PH did not relieve the patient's symptoms, and MG was diagnosed after the onset of additional findings. A diagnosis of MG is often made late because the symptoms of the disease can be non-specific. To treat MG, the patient was administered IV immunoglobulin and pyridostigmine, and his symptoms regressed; PAP values were also observed to decrease in follow-up appointments. This case is similar to that published by Oguzhan et al.[8] in which reversible PH was detected after MG treatment. because of the relaxation of the lung muscles after immunoglobulin and pyridostigmine, the patient's PAP decreased and the need for PH treatment was eliminated.

Reversible PH can also be seen, especially in autoimmune thyroid diseases.[9] Therefore, close follow-up of PAP values is important, although it is rarely associated with autoimmune diseases. The increase in MG findings after the initiation of macitentan as a PAH-specific treatment in our patient also suggested an MG attack secondary to the drug. In these patients, the use of the soluble guanylate cyclase stimulator riociguat instead of endothelin receptor antagonists may be a more appropriate option. It was thought that it may have a nitric oxide- mediated benefit. There is not enough evidence for this. Further studies are required.

In our case, we presented our patient who started PAH-specific treatment with the diagnosis of PH, but was diagnosed with MG after the symptoms did not resolve and there were

additional findings. In our patient, PAP values regressed after IV immunoglobulin and pridostigmine treatment, giving us the opportunity to see a rare case in the literature for reversible PH, also suggesting that there may be an increase in MG findings due to macitentan.

## Ethics

**Informed Consent:** Informed consent was obtained from the patient.

**Peer-review:** Internally peer-reviewed.

## Authorship Contributions

Surgical and Medical Practices: Y.A., Concept: A.T.Ş., Design: A.T.Ş., Data Collection or Processing: Ö.K., Analysis or Interpretation: A.T.Ş., Y.A., M.A.D., Literature Search: A.T.Ş., Y.A., Ö.K., Writing: A.T.Ş.

**Conflict of Interest:** No conflict of interest was declared by the authors.

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