

CARDIOMAG NEWSLETTER

Volume 4| Issue 38| 2023

IN THIS ISSUE

Dear Doctor,

Greetings from Micro Labs Limited. We are happy to bring you “Cardio Mag” which contains latest and interesting news in the field of Cardiology

- **Cardiovascular outcomes and adherence to Antihypertensive medications in cancer patients**
- **Association between Left Ventricular Remodeling and the Development of Arterial Stiffness**
- **The preventive study of association between metabolic syndrome, hypertension, and chronic depression in postmenopausal women.**
- **A Case of multiple lentigines and Noonan syndrome with hypertrophic cardiomyopathy.**

Cardiovascular outcomes and adherence to Antihypertensive medications in cancer patients

INTRODUCTION

Hypertension is a major global risk factor for early mortality and disability. The control rate of hypertension is extremely low ⁽¹⁾. Adherence to medication is essential for hypertensive patients to maintain their health and wellness. Patient's subjective beliefs of their health conditions may have an impact on how well they accept medical advice ⁽²⁾. Non adherence with antihypertensive therapy is one of the factors linked to inadequate control of hypertension. Recent studies have revealed that cancer patients and survivors are more at risk for acquiring hypertension and associated complications. The aim of this study was to evaluate the relationship between antihypertensive medication adherence and clinical outcomes in cancer patients with hypertension ⁽¹⁾.



Cardiovascular disease

METHOD

A Nationwide population based cohort study was conducted in 19246 patients with cancer with concomitant hypertension. The medication possession ratio(MPR), which was measured as the number of days the drug was delivered divided by the refill time, was used to assess medication adherence for antihypertensive therapy. Participants were divided into three groups based on their MPR scores; good ($\text{MPR} \geq 0.8$), moderate ($0.5 \leq \text{MPR} < 0.8$) and poor ($\text{MPR} < 0.5$). They considered an MPR of < 0.8 as nonadherence. Overall and cardiovascular mortality were the primary outcomes and hospitalization for cardiovascular events caused by serious cardiovascular disease was the secondary outcomes. A Cox proportional hazard regression model was used to identify the risk associated with nonadherence to antihypertensive medication. Log-log plots were used to test the proportional hazards hypothesis. Kaplan Meier-curves were produced to show the cumulative incidence of primary outcomes. Log-rank test was used to find differences between groups in the primary outcomes.

RESULTS The current study results showed that 33.6% were in the good adherence group and 66.4% were in the nonadherence (26.3% had moderate adherence and 40.0% had poor adherence). Over a

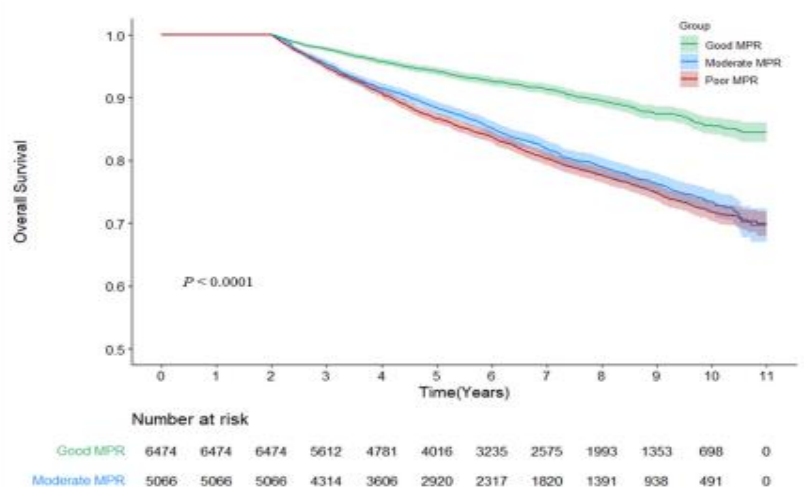


FIGURE-1 Cumulative Kaplan-Meier estimates of overall survival according to Adherence of antihypertensive therapy.

median 8.4-year period of follow up there were 6057 cardiovascular events and 2752 deaths. After adjusting for potential confounders, the moderate and poor adherence groups, as compared to the good adherence group, had a 1.85 fold and 2.19fold greater risk for overall mortality and a 1.72 fold and 1.71 fold elevated risk for cardiovascular mortality respectively. The Kaplan-Meier curve showed lower overall survival in both the moderate and poor adherence groups. In particular, the overlap of the curves of the moderate and poor adherence groups and the separation of the curve between the good adherence and moderate/poor adherence group, with a slightly worse outcome for the poor adherence group occurred (Figure 1). The risk of new-onset cardiovascular events was enhanced by 1.33-fold and 1.34-fold respectively, in the groups with moderate and poor adherence.

DISCUSSION

The current study showed that 66.4% of the cancer patients were nonadherent to their antihypertensive drugs and also showed a significant association between adverse cardiovascular outcomes and nonadherence to antihypersensitive medication. Similar to this study Hershman DL et.al study showed that Nonadherence was associated with an increased risk of experiencing a cardiac event in breast cancer patients ⁽³⁾.

CONCLUSION

The current study concludes that in adult cancer patients with hypertension, nonadherence to antihypertensive treatment was associated to worse all cause and cardiovascular mortality as well as new-onset CVD. To improve cardiovascular outcomes, more attention should be focused on enhancing antihypertensive drug adherence in cancer patients.

To improve cardiovascular outcomes, more attention should be focused on enhancing antihypertensive drug adherence in cancer patients.

References

- 1.Jung MH, Lee SY, Youn JC, Chung WB, Ihm SH, Kang D, Kyoung DS, Jung HO, Chang K, Youn HJ, Lee H. Antihypertensive Medication Adherence and Cardiovascular Outcomes in Patients With Cancer: A Nationwide Population-Based Cohort Study. *Journal of the American Heart Association*. 2023 Jul 8:e029362.
- 2.Patel RP, Taylor SD. Factors affecting medication adherence in hypertensive patients. *Annals of Pharmacotherapy*. 2002 Jan;36(1):40-5.
3. Hershman DL, Accordini MK, Shen S, Buono D, Crew KD, Kalinsky K, Trivedi MS, Hur C, Hu J, Unger JM, Wright JD. Association between nonadherence to cardiovascular risk factor medications after breast cancer diagnosis and incidence of cardiac events. *Cancer*. 2020 Apr 1;126(7):1541-9.

Association between Left Ventricular Remodeling and the Development of Arterial Stiffness

INTRODUCTION

Heart failure (HF) is a serious public health concern with more than 23 million cases exist world-wide ⁽¹⁾. The central aorta functions as a blood vessel to carry blood to the body's peripheral organs and as a shock absorber for the heart's pulsatile pressure and flow. Because the aorta is stiffer, it has less of a pulsatile pressure buffering effect, which increases left ventricular (LV) afterload. As a result, arterial stiffness has been associated to the prevalence of cardiovascular disease ⁽²⁾. A substantial risk factor for heart failure (HF) found by the Framingham Heart Study is increased arterial stiffness as measured by pulse wave velocity (PWV). The aim of this study was to evaluate the association between left ventricular Remodeling and the progression of Arterial stiffness ⁽¹⁾.

METHOD

A Retrospective community based cohort study was conducted in 317 participants who had baseline-normal cardio-ankle vascular index (CAVI) and were free of cardiovascular disease. All individuals had their fasting serum levels of glucose, cholesterol, creatinine, and BNP (B-type natriuretic peptide) tested. Transthoracic echocardiography was used to measure the size, mass, and function of the Left Ventricle (LV). To measure early (E) and late (A) peak velocities, pulsed-wave Doppler analysis of the mitral input was done. To determine the mean early diastolic velocity, tissue Doppler mitral annular early diastolic velocity (e') of the septal and lateral sides were measured and averaged. LV global longitudinal strain (LVGLS) was assessed by speckle-tracking. The Chi-square test was used to compare categorical variables, and the appropriate t-test or Wilcoxon rank sum test was used to analyse continuous variables. JMP 14 (SAS Institute) statistical software was used for all statistical analyses.

RESULTS

The current study results showed that Women were older and more likely to have hyperlipidaemia than men, who also had significantly higher BMIs, higher rates of diabetes and current smoking (all $P < 0.05$). Men and women did not have different baseline CAVI value (figure 2). LVGLS decreased and LV mass index increased considerably (both $P < 0.001$) in the entire population. On the other hand, the LVEF remained

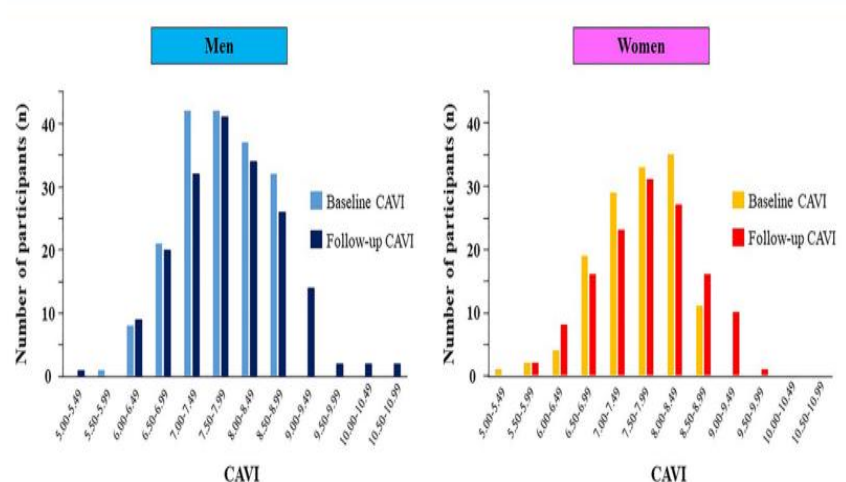


Figure 2- CAVI Values at baseline and follow-up Stratified by sex

unchanged. E/A ratio and e' velocity, two LV diastolic metrics, decreased (both $P < 0.05$) throughout follow-up, although E/e' ratio remained stable. Men were found to have larger LV sizes, higher LV mass indexes, and worse LVGLS than women, while women were found to have considerably higher E/e' ratios (all $P < 0.05$). After adjusting for demographics and baseline cardiovascular variables, generalized estimating equation analyses revealed that longitudinal increases in CAVI were not associated with changes in LV mass index or e' velocity, rather they were associated with impaired LVGLS (estimate 0.46, 95% CI: 0.11-0.82; $P = 0.010$). CAVI progression remained linked with change in LVGLS even after adjusting for longitudinal change in variables (estimate 0.50, 95% CI: 0.16-0.85; $P = 0.004$). Only women in the sex-specific analysis showed a significant relationship between CAVI advancement and LVGLS decline (estimate 0.92, 95% CI: 0.27-1.58; $P = 0.006$).

DISCUSSION

The current study showed the relationship between changes in LV structure and function and longitudinal changes in arterial stiffness in a community based population without significant cardiovascular disease. Even at an early, subclinical stage before LVEF decreases, the larger trend in arterial stiffness was significantly associated with adverse LV remodelling. Similar to this study Ohyama Y et.al study showed the positive correlation between higher LV mass index and LV mass volume ratio (LVMVR) shows that increased aortic arch stiffness is related to greater LV concentric Remodeling ⁽²⁾.

CONCLUSION

The current study concludes that LVGLS worsening in individuals without cardiovascular disease is independently associated with an increase in arterial stiffness and this study also demonstrated the crucial part that vascular ventricular coupling plays in the progressive deterioration of ventricular function. Increased arterial stiffness prevention measures may help to avoid Clinical HF and a decline in LV function.

Left ventricular global longitudinal strain worsening in individuals without cardiovascular disease is independently associated with an increase in arterial stiffness.

REFERENCES

1. Yoshida Y, Nakanishi K, Jin Z, Daimon M, Ishiwata J, Sawada N, Hirokawa M, Kaneko H, Nakao T, Mizuno Y, Morita H. Association Between Progression of Arterial Stiffness and Left Ventricular Remodeling in a Community-Based Cohort. *JACC: Advances*. 2023 Jul 5:100409.
2. Ohyama Y, Ambale-Venkatesh B, Noda C, Chugh AR, Teixido-Tura G, Kim JY, Donekal S, Yoneyama K, Gjesdal O, Redheuil A, Liu CY. Association of aortic stiffness with left ventricular remodelling and reduced left ventricular function measured by magnetic resonance imaging: the multi-ethnic study of atherosclerosis. *Circulation: Cardiovascular Imaging*. 2016 Jul;9(7): e004426.

The preventive study of association between metabolic syndrome, hypertension, and chronic depression in postmenopausal women.

INTRODUCTION

The risk of cardiovascular events is increased by a group of risk factors known as the metabolic syndrome (MetS), which includes central obesity, hypertension, hyperglycaemia, hypertriglyceridemia, and low high-density lipoprotein (HDL) cholesterol. The most prevalent psychiatric condition worldwide and in primary healthcare settings is chronic depression (CD). Cardiovascular patients are significantly more likely to have CD, with prevalence rates ranging from 20% to 45% than the general population. In clinical practice, a difficult issue is the early diagnosis of CD ⁽¹⁾. For postmenopausal women, metabolic syndrome and psychosocial problems are serious health problems ⁽²⁾. It's essential to treat CD when it's diagnosed in postmenopausal women with MetS in order to enhance their quality of life. The aim of this study was to determine the prevalence of CD in postmenopausal women with MetS and/or hypertension ⁽¹⁾.

METHODS

A total of 500 postmenopausal women with hypertension between the ages of 48 and 68 and 100 consecutive postmenopausal women with MetS were included in this study. A total of 500 consecutive normotensive women without MetS, aged 48 to 68, were included in the control group. Along with anthropometric data such as body weight, height, BMI, and waist and hip circumference measurements, a thorough personal history of metabolic and CVD was also obtained. The individuals' BP values were determined by averaging their three blood pressure readings. The Adult Treatment Panel III of the National Cholesterol Education Program was used to diagnose MetS. According to the National Institute for Health and Care Excellence (NICE) 2009 Guidelines, CD recognition and assessment were done for all women receiving therapy together with anti-depressive medication and cognitive behavioural therapy. After 10 minutes of rest, the patient had transthoracic echocardiography while lying in the left lateral decubitus position on a 30°-raised exam table. A multifrequency transducer-equipped Echo-Doppler device called the Philips Epiq 7 Ultrasound device for Cardiology, Healthcare, Viale Sarca 235, Milan (Italy), was employed. A diagnosis of cardiomyopathy was made using well established criteria.

RESULTS

The current study results showed that when compared to the control group, postmenopausal women with MetS had a significantly greater rate of CD [$P < 0.007$]. Women with MetS and hypertension had a significantly greater CD rate ($P < 0.0000$) [Table 1]. Women with MetS and women with hypertension both had similar CD rates, and also women with metabolic cardiomyopathy and women with hypertensive cardiomyopathy ($P < 0.44$ and $P < 0.65$, respectively). Women with metabolic cardiomyopathy and women with hypertensive

cardiomyopathy both had significantly higher CD rates than controls ($P<0.0000$ and $P<0.0000$, respectively).

	HYPERTENSION	CONTROL	ODDS RATIO	P-VALUE
All Women	500	500		
Women with CD	107(27%)	45(8%)	2.7	<0.000
Women with CD and Metabolic cardiomyopathy	43(8%)	0	2.9	<0.00

Table-1 Comparison of women with hypertension and controls for the prevalence of CD.

DISCUSSION

The current study showed that in postmenopausal females with MetS, CD is relatively common. Women with MetS had a two-fold higher risk than the general population of developing CD, while hypertensive women had an approximately three-fold higher risk. Similar to this study, Kwon E et.al study showed that in postmenopausal women, it was found that trait anxiety and depression were associated with the prevalence of metabolic syndrome (2).

CONCLUSION

The current study concludes that there is an association between MetS and CD in postmenopausal women that is significantly greater in the presence of hypertension. The association, however, was similar among women who had hypertensive or metabolic cardiomyopathy. An intervention is required to improve CD diagnosis in postmenopausal women, especially in those with MetS and/or hypertension because undiagnosed and untreated CD is linked to poor cardiovascular outcomes.

An association between Metabolic syndrome and Chronic depression in postmenopausal women that is significantly greater in the presence of hypertension. The association, however, was similar among women who had hypertensive or metabolic cardiomyopathy.

REFERENCES

- 1.Palmiero P, Maiello M, Amati F, Ciccone MM, Paul T. Association between metabolic syndrome, hypertension, and chronic depression: a postmenopausal women prevention study. Italian Journal of Medicine. 2023 Jul 11;17(1).
- 2.Kwon E, Nah EH, Kim H, Joe SH, Cho HI. Association between metabolic syndrome and psychological characteristics in Korean postmenopausal women. Korean Journal of Health Promotion. 2016 Jun 1;16(2):119-26.

A Case of multiple lentigines and Noonan syndrome with hypertrophic cardiomyopathy.

INTRODUCTION

A pathogenic variation (PV) in the PTPN11 gene, which codes for a protein tyrosine phosphatase nonreceptor type 11 protein, causes Noonan syndrome with multiple lentigines (NSML), previously referred to as LEOPARD syndrome. Hypertrophic cardiomyopathy (HCM) is the most frequent cardiac condition resulted from NSML in 70%–80% of the cases ⁽¹⁾. A frequent genetically transmitted condition known as hypertrophic cardiomyopathy is characterized clinically by unexplained left ventricular enlargement. The condition has a variable clinical course and result; whereas some individuals have severe exercise limitations and recurrent arrhythmias, others have few or no noticeable cardiovascular symptoms ⁽²⁾. This case report presented a case of multiple lentigines and Noonan Syndrome with hypertrophic cardiomyopathy.

CASE PRESENTATION

A 54-year-old Mexican male was born from an uncomplicated pregnancy to healthy nonconsanguineous parents. Strabismus was noticed and surgically repaired at the age of two. Multiple flat brown macules appeared during childhood, primarily on the face and trunk. The development of the psychomotor system was normal. An electrocardiogram (ECG) with T-wave inversion in leads 1, V1-V6, and increased voltage in precordial leads was discovered in a 50-year-old patient during perioperative studies for surgical correction of bilateral and umbilical hernias. This was confirmed by a transthoracic echocardiogram, which also revealed apical HCM with a ventricular cavity that had the shape of an ace of spades and increased septal thickness up to 21mm. Additionally, a 24-hour Holter revealed 15 occurrences of non-sustained ventricular tachycardia with a right bundle branch block morphology and ventricular extra systoles in 5.8% of the beats. With a left ventricular ejection fraction of 55%, a cardiac magnetic resonance was performed, which was compatible with apical HCM (Figure 1). Late enhancement was discovered in 16.6 g, which is equivalent to fibrosis in 19.6% of the mass. He was considered a candidate for implanted cardioverter defibrillator installation based on the American Heart Association's 5-year sudden death calculation (6.25% risk), which was successfully completed at age 53. He was referred to a genetics consultation for the purpose of diagnosing HCM as a result of these findings. Physical examination findings included a 163 cm (height potential: 171.5 cm) short stature, a high anterior hairline, down slanted palpebral fissures, hypertelorism, long depressed philtrum, prominent nasolabial folds, low-set ears, winged neck, pectus excavatum, wide-spaced nipples, and multiple lentigines. After performing next-generation sequencing on a panel of genes linked to RASopathies in response to a suspicion of NSML, the heterozygous pathogenic mutation c.836A>G (p. Tyr279Cys) in PTPN11 was discovered and verified by Sanger sequencing. Extension experiments on siblings and parents were conducted, and they all came out negative, proving that the mutation is de

novo. The patient is childless. A spinal X-ray that showed enhanced lordosis and an audiometry that indicated no hearing impairment were both used in the examination of comorbidities.

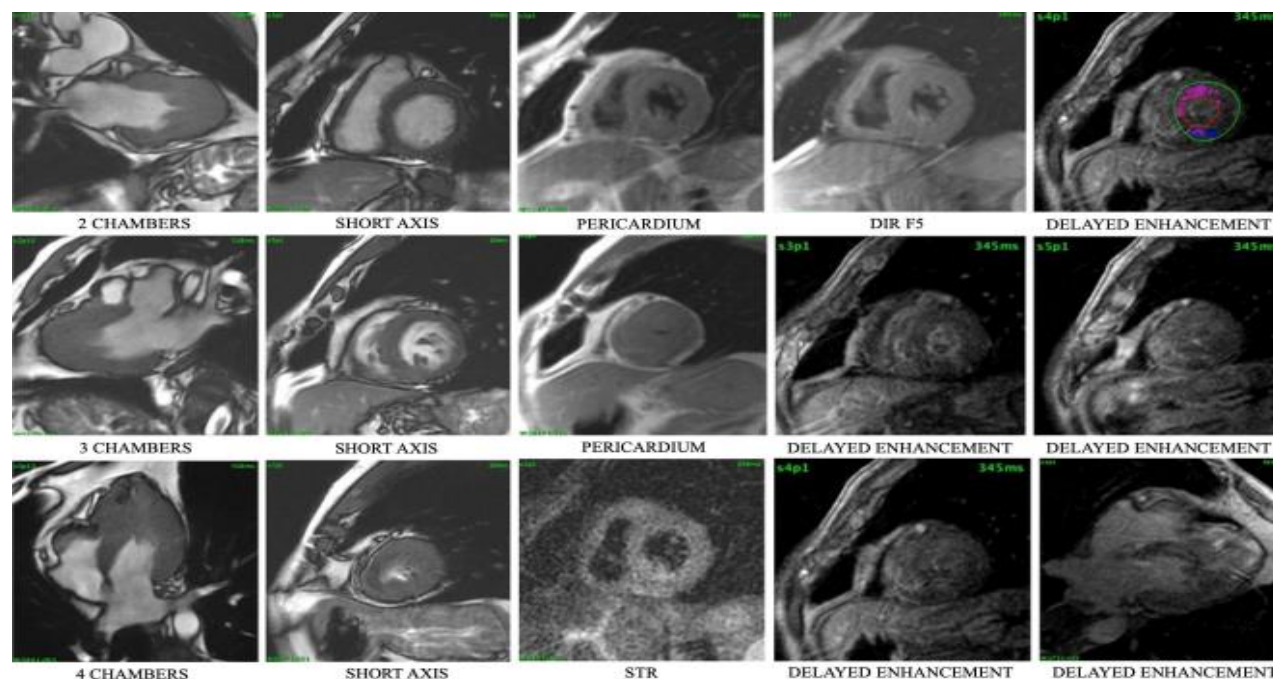


Figure-1 Cardiac MRI scanning of patient with Noonan syndrome with multiple lentigines

DISCUSSION

In this case study, a male patient developed an apical hypertrophic cardiomyopathy was diagnosed with NSML because of his short stature, multiple lentigines, winged neck, pectus excavatum and a heterozygous PV in PTPN11 c.836A>G. Similar to this study, Khan F et.al study presented a case of Noonan syndrome because of his short stature, ear and eye abnormalities, low posterior hair line, cubitus valgus and webbed neck. Pulmonary valvular stenosis and hypertrophic cardiomyopathy were the major cardiovascular abnormalities ⁽³⁾

CONCLUSION

The current case report highlights the significance of suspecting NSML in cases that present with lentigines, short stature, and HCM. Due to the overlapping symptoms of several RASopathies, the molecular test can help in the diagnosis of these conditions.

This case report highlights the significance of suspecting Noon syndrome with multiple lentigines in cases that present with lentigines, short stature, and Hypertrophic cardiomyopathy. Due to the overlapping symptoms of several RASopathies, the molecular test can help in the diagnosis of these conditions.

REFERENCES

- 1.Rivero-García P, del Carmen Campuzano-Estrada I, Hernandez-Felix JH. Hypertrophic cardiomyopathy in an adult patient with Noonan syndrome with multiple lentigines. Clinical Case Reports. 2023 Jun;11(6).
- 2.Elliott P, McKenna WJ. Hypertrophic cardiomyopathy. The Lancet. 2004 Jun 5;363(9424):1881-91.
- 3.Khan F, Waqar S, Jamal NU, Saleem A. Noonan syndrome: a case report. Annals of Health Research. 2018 Jun 17;4(1):82-7.



This scientific input is prepared from the Department of Medical Services, an initiative of M/s Micro Labs Limited under the aegis of Micro Knowledge Academy. The information contained herein is for education purpose only. The content is developed by compiling information from various authentic and published literatures. Although great care has been taken to assure the accuracy of the publication, M/s Micro Labs Limited shall not be responsible or in any way liable for any inaccuracy, errors, or omissions resulting from negligence or otherwise howsoever or any consequences arising there from. In spite of best efforts, the information in this publication may become outdated over time. M/s Micro Labs Limited shall not be responsible in any manner whatsoever, for any action taken, opinions expressed, advice rendered or accepted, any direct, incidental, special or consequential loss and damage caused on the basis of any material or information presented in this publication / update.