

# ***CARDIO ROUNDS NEWSLETTER***

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***Dear Doctor,***

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

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## Association Between statin treatment and mortality in dialysis patients with atherosclerotic cardiovascular disorder.

### INTRODUCTION

Cardiovascular (CV) disease, is the major cause of death and is responsible for more than 50% of mortality in dialysis patients. Dialysis patients had much higher rates of atherosclerotic cardiovascular disease (ASCVD) than the general population and more risk factors for ASCVD. In the general population at risk for ASCVD, including patients with non-dialysis-dependent chronic kidney disease (CKD), Statin, a lipid lowering drug, is effective in improving CV outcomes and reducing mortality <sup>(1)</sup>. Major societies' guidelines recommend that patients with



**Cardiovascular Disease**

chronic renal disease and those who are at high risk of atherosclerotic cardiovascular disease adhere to statins at a moderate to high intensity <sup>(2)</sup>. The aim of this study was to assess the effectiveness of statin therapy on long-term mortality in dialysis patients after a first ASCVD.

### METHOD

A retrospective cohort study included a total of 17,242 adult patients with end stage renal disease who experienced their first ASCVD event. Patients were divided into two groups based on whether they received statin therapy after their ASCVD events or not (Statin groups vs, no statin group). Based on the amount of statin usage, patients were further divided into four groups. The cholesterol treatment guideline from the ACC/AHA were used to categorise the statin intensity. The proportion of days covered (PDC) method was employed to calculate the study population's statin adherence rates. All cause and cardiac mortality throughout the follow-up period were the primary endpoints of this study. Health Insurance and review assessment obtained mortality information and causes of death from statistics Korea's death certificate database and compared them to information from medical claim reports. Cox proportional Hazards regression models that were adjusted for demographics and comorbidities were used to assess associations between statin usage and long- term mortality. SAS software V.9.4 was used to conduct the statistical analyses.

### RESULTS

The current study results showed that after a first ASCVD incident, Statins were given for more than half of the dialysis patients (55.7%), with the majority of patients receiving high or moderate intensity statins (76.7% of patients taking moderate-intensity statins and 15.6% of patients taking high intensity statins and 5.1% of patients taking statin-ezetimibe combination). Statin medication independently decreased the risk of all cause death in patients receiving

dialysis for  $32.6 \pm 20.9$  months of follow-up (Table 1). When compared to the no-statin group, the statin group in patients with cerebrovascular accident(CVA) showed a 12% risk reduction in all cause death. Statin treatment had an equivalent trend to lower all-cause mortality in coronary heart disease(CHD) patients, although this trend was not statistically significant. However, Statin therapy did not reduce cardiac mortality in either the general population or any of the ASCVD subgroups. In all the univariable and multivariable Cox regression models, low and moderate- intensity statin treatment or Statin/ezetimibe combination therapy did not significantly associate with cardiac mortality. Statins have a positive impact on all-cause mortality, however this benefit has a greater impact in high-risk dialysis patients, such as those who are diabetic or elderly patients (>65 years old).

|                     | Unadjusted       |         | Adjusted for age and sex |         | Fully adjusted*  |         |
|---------------------|------------------|---------|--------------------------|---------|------------------|---------|
|                     | HR (95% CI)      | p value | HR (95% CI)              | p value | HR (95% CI)      | p value |
| All-cause mortality |                  |         |                          |         |                  |         |
| No statin           | 1 (Reference)    |         | 1 (Reference)            |         | 1 (Reference)    |         |
| Statin              |                  |         |                          |         |                  |         |
| Overall             | 0.98 (0.94–1.03) | 0.454   | 0.96 (0.92–1.01)         | 0.086   | 0.92 (0.88–0.97) | 0.0009  |
| CHD                 | 1.07 (1.01–1.14) | 0.035   | 1.01 (0.95–1.08)         | 0.683   | 0.97 (0.92–1.04) | 0.411   |
| CVA                 | 0.87 (0.78–0.96) | 0.006   | 0.89 (0.81–0.99)         | 0.034   | 0.88 (0.80–0.98) | 0.021   |
| PAD                 | 1.09 (0.98–1.22) | 0.107   | 1.10 (0.98–1.22)         | 0.099   | 1.03 (0.92–1.15) | 0.598   |
| Cardiac mortality   |                  |         |                          |         |                  |         |
| No statin           | 1 (Reference)    |         | 1 (Reference)            |         | 1 (Reference)    |         |
| Statin              |                  |         |                          |         |                  |         |
| Overall             | 1.16 (1.05–1.28) | 0.004   | 1.13 (1.03–1.25)         | 0.014   | 1.12 (1.01–1.23) | 0.031   |
| CHD                 | 1.17 (1.04–1.32) | 0.012   | 1.12 (0.99–1.26)         | 0.078   | 1.09 (0.96–1.23) | 0.170   |
| CVA                 | 1.00 (0.79–1.26) | 0.980   | 1.02 (0.81–1.29)         | 0.847   | 1.05 (0.83–1.33) | 0.693   |
| PAD                 | 1.10 (0.83–1.45) | 0.502   | 1.10 (0.84–1.45)         | 0.499   | 1.09 (0.82–1.44) | 0.565   |

**Table 1-** Statin medication independently decreased the risk of all cause death in patients receiving dialysis for  $32.6 \pm 20.9$  months of follow-up.

Abbreviation-PAD-Peripheral artery disease

## DISCUSSION

The current study showed that after a first ASCVD incident, statin medication independently decreased the risk of all-cause death in individuals undergoing dialysis. According to the study by Lee M et.al showed that particularly among Dialysis patients with CHD or CVA, statin treatment was independently associated with decreased risk of 1- year all-cause death <sup>(3)</sup>. Jung J et.al study also showed that statin medication, preferably in addition with ezetimibe, has been associated with a decreased risk of all cause death in adult patients undergoing maintenance hemodialysis <sup>(2)</sup>.

## CONCLUSION

The current study concludes that “Statin prescription in dialysis patients after a first ASCVD incident is common, accounting for more than half of patients, even though there isn’t any evidence to support this. The majority of patients got moderate or high intensity statins. Patients on dialysis after ASCVD may benefit from statin medication in lowering long-term all-cause mortality”.

Patients on dialysis after atherosclerotic cardiovascular disease may benefit from statin medication in lowering long-term all-cause mortality”.

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## Association between Left Ventricular Remodeling and the Development of Arterial Stiffness

### INTRODUCTION

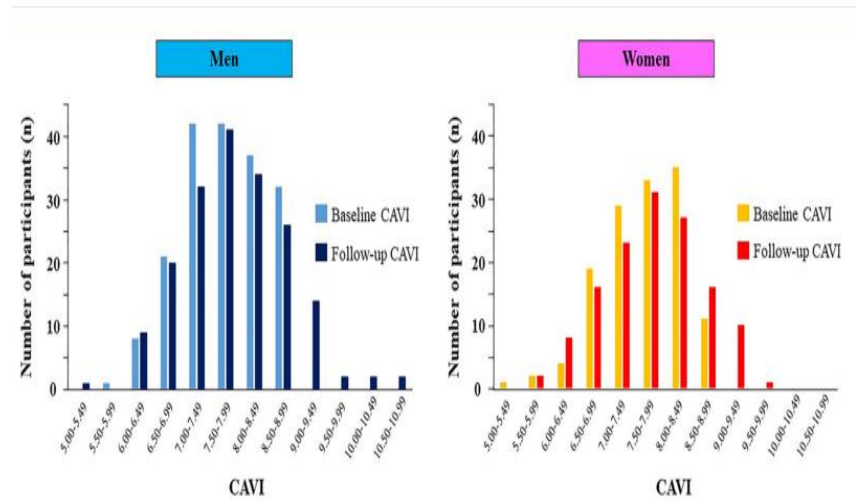
Heart failure (HF) is a serious public health concern with more than 23 million cases exist world-wide <sup>(1)</sup>. The central aorta functions as a blood vessel to carry blood to the body's peripheral organs and as a shock absorber for the heart's pulsatile pressure and flow. Because the aorta is 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 <sup>(2)</sup>. 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 <sup>(1)</sup>.

### 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 1). LVGLS decreased and LV mass index increased considerably (both  $P < 0.001$ ) in the entire population. On the other hand, the LVEF remained unchanged. E/A ratio and e'



**Figure 1- CAVI Values at baseline and follow-up Stratified by sex**

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<sup>(2)</sup>.

## 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.

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**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 <sup>(1)</sup>. For postmenopausal women, metabolic syndrome and psychosocial problems are serious health problems <sup>(2)</sup>. 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 <sup>(1)</sup>.

## 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).

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

**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<sup>(2)</sup>.

## 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.

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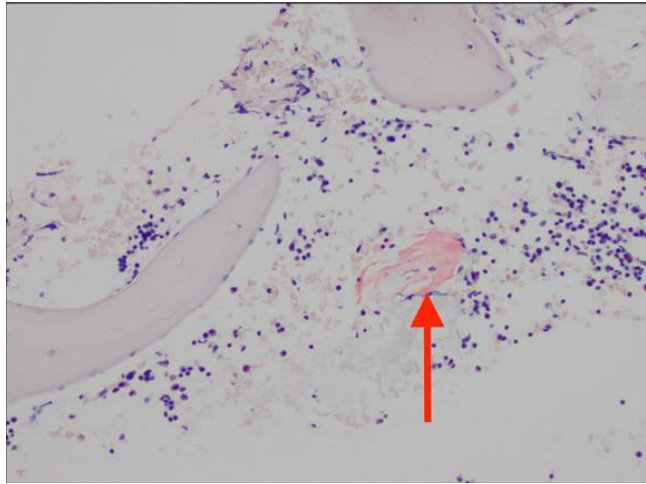
## Refractory Arrhythmias as a Potential Indicator of Underlying Cardiac Amyloidosis – A Case report

## INTRODUCTION

Amyloidosis is categorized as a multisystemic condition that can impair the functionality of a number of organs, including the heart, liver, kidneys, intestines, etc. It is a diagnostic that occurs in 9.7–14.0 cases per million people each year, making it uncommon<sup>(1)</sup>. The clinical and biochemical characteristics of amyloidosis should be taken into consideration while classifying it. As a result, the illness may be systemic (generalized), affecting several organs, or localized, when deposits are restricted to a particular organ, such as the heart. Additionally, primary amyloidosis of the AL (protein A light chains) type is typically defined as a subgroup of systemic amyloidosis<sup>(2)</sup>. The most severe and lethal form of amyloidosis is AL amyloidosis, which is also the most prevalent. Fatigue, unexpected weight loss, and orthostatic hypotension are common nonspecific symptoms of AL amyloidosis in its clinical presentation. The aim of this study was to present a case of a patient who first presented with systemic amyloidosis to demonstrate the potential for additional clinical workup in persistent atrial fibrillation with unsuccessful cardioversion<sup>(1)</sup>.

## CASE PRESENTATION

A 64-year-old woman with end-stage liver disease from probable NASH presented to the hospital for a liver transplant workup. She had a history of hypertension, hyperlipidaemia, heart failure, and presumed nonalcoholic steatohepatitis (NASH). On admission, the electrocardiogram (ECG) showed signs of atrial fibrillation, including low voltage, nonspecific T-wave alterations, and partial right bundle branch blockages. After two unsuccessful amiodarone cardioversions in 2019, the patient's atrial fibrillation still persisted. Her condition began with arrhythmias and advanced to liver problems before she lost a lot of weight.



**Figure 1-Bone marrow biopsy shows positive for Amyloid deposit.**

Physical examination revealed peripheral oedema, ascites, orthostatic hypotension, asterixis in the right hand greater than the left, and periorbital purpura in addition to irregular rate and rhythm. As part of the pre-transplant assessment for likely NASH, the patient underwent gastrointestinal and cardiovascular testing during her most recent hospitalization. Prior to cardioversion, a gastrointestinal evaluation was conducted to look for any potential oesophageal varices. A non-bleeding cratered gastric ulcer and two polyps in the transverse colon and ascending colon were found during endoscopy assessment. The lesions were removed, and then histological testing was conducted on them. The patient underwent synchronized cardioversion twice at 200J after endoscopy, however their atrial fibrillation reappeared right away. For the prevention of stroke, apixaban 5 mg twice per day was maintained. Congo red staining, a sign of amyloidosis, was found in the pathology report of the intestinal tract and gastric mucosa. Further research into amyloidosis was spurred by this discovery in order to determine the severity of the condition of this patient. After performing a transthoracic echocardiogram, it was found that the patient had restrictive cardiomyopathy, as evidenced by bi-atrial enlargement, a dilated inferior vena cava, increased right atrial pressure, pulmonary hypertension, and severe tricuspid insufficiency. These findings are all consistent with cardiac amyloidosis. Atrial fibrillation prevented the patient's diastolic function from being addressed, and the ejection fraction was between 55 and 60%. Right ventricular systolic pressure increased at 40–45 mmHg, and right ventricular systolic function was slightly decreased. The global longitudinal strain (GLS) was demonstrated to be significantly reduced. Magnetic resonance imaging (MRI) showed areas of enhancement within the septum and sub endocardial enhancement at the mid-ventricular and apical segment of the lateral and inferolateral wall, indicating cardiac involvement with amyloidosis. Amyloid infiltration and unusual monoclonal B cell lymphocytosis were found during a bone marrow biopsy (Figure 1). These results demonstrated that the patient's heart and gastrointestinal system were both impacted by multisystemic AL amyloidosis. The patient was given a liver biopsy to check for liver involvement with amyloidosis, but she declined the test. After being informed about the

AL amyloidosis therapy options, the patient stated her desire to be discharged home with in-home hospice care, and all further testing was stopped. The patient visited an oncology clinic the next few days, where cyclophosphamide, bortezomib, and dexamethasone chemotherapy with daratumumab was initiated. A few days after beginning chemotherapy, the patient experienced sepsis and required a readmission to the hospital. She was then taken to the critical care unit where she passed away.

## DISCUSSION

The current study showed that AL amyloidosis is an uncommon disease with an unspecific clinical appearance. The ECG showed signs of atrial fibrillation, including low voltage, nonspecific T-wave alterations, and partial right bundle branch blockages. The patient's heart and gastrointestinal system were both impacted by multisystemic AL amyloidosis. According to the study by Costache I et.al study, Amyloidosis is a well-known but it is a rare disease. The ECG revealed atrial fibrillation with medium ventricular rhythm <sup>(2)</sup>.

## CONCLUSION

The current study concludes that Refractory atrial fibrillation is one of the "red flag" symptoms that should prompt additional investigation into the possibility of AL amyloidosis since later clinical manifestations of the disease can delay treatment, which can have a negative effect on patient outcomes. Chemotherapy is one of the available treatments for AL amyloidosis, however because of the disorder's ambiguous clinical signs and symptoms, treatment is frequently put off, which has a negative impact on patient outcomes. Therefore, early diagnosis is essential for the possibility of good patient outcomes, especially with the start and progress of medicinal therapy for AL amyloidosis.

Early diagnosis is essential for the possibility of good patient outcomes, especially with the start and progress of medicinal therapy for AL amyloidosis.

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