

Right Ventricular Lipomatosis: A postmortem study

Mayorathan U^{1*}, Timothy William², Richard C Harruff³

¹Office of the Judicial Medical Officer, Teaching Hospital, Jaffna, Sri Lanka.

²Pierce County Medical Examiner's Office, Tacoma, WA, USA.

³King County Medical Examiner's Office, Seattle, WA, USA.

Abstract


Introduction: The adipose tissue in the right ventricle is frequently found during forensic autopsies. However, the pathological significance of right ventricular lipomatosis was not well studied in the available literature. This study aims to study identify the relationship between right ventricular lipomatosis and sociodemographic factors, BMI, and waist circumference

Methods: Assessment of the fatty infiltration and fibrosis was performed by two pathologists who read all specimens separately. The average of the two values was taken for analysis.

Results: A total of 100 decedents were examined in this study, of which 70 were male, 76 were Caucasians thirteen were black, nine were Asian, and two were Native American. Among the population 76 were older than 30. Seventy-one out of a hundred recorded a BMI of more than 25, and 63 decedents had a normal waist circumference. Fat infiltration of the anterior wall and lateral wall and average fat infiltration of the right ventricle showed significant association with the female sex and the Caucasian population at a 95% confidence interval. Neither cause of death, past medical history, nor fibrosis of the right ventricle walls showed significant association with the fat infiltration of the right ventricle. Yet, age above 30 years and body mass index over 25 showed a significant association in the fat infiltration of the posterior wall (p-value < 0.05). At the same time, higher waist circumference was significantly associated with the average right ventricular fat infiltration (p-value < 0.05).

Conclusion: Right ventricular lipomatosis is significantly associated with BMI and waist circumference in our study. At the same time, it was positively correlated with age, sex, and race.

Keywords: Right ventricular lipomatosis, Body mass index, waist circumference, sociodemographic factors

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Introduction

Right ventricular lipomatosis (RVL) is a regular observation, and we have witnessed this during our day-to-day autopsy practice.[1-3] Right ventricular adiposity is believed to occur only in humans.[4] In the elderly population, more than half of the normal hearts show significant lipomatosis in the right ventricle.[5,6] Fatty infiltration of the right ventricle can occur either with fibrosis or without fibrous tissue.[1,7,8] Intramyocardial lipomatosis is connected with several cardiomyopathies. However, it is difficult to establish the pathological importance of right ventricular fat infiltration. It may be a normal

physiological phenomenon that could not give rise to any functional impairment, or it may be an early stage of arrhythmogenic right ventricular cardiomyopathy (ARVC), which is a heritable and genetically programmed form of the cardiovascular condition where myocytes are replaced by the fat and fibrous tissue and ended up in right ventricular failure, arrhythmias, and sudden cardiac arrest.[9] The estimated prevalence of ARVC/D in the general population ranges from 1:2000 to 1:5000, and men were more affected than women, with an approximate ratio of 3:1.[9] A strong relationship exists between epicardial fat and BMI, especially

with waist circumference.[10] Fat infiltration of the myocardium is also usually associated with obesity[3], but few studies have been done on this. This study aims to evaluate the relationship between right ventricular fat infiltration and the studied population's BMI, waist circumference, and socio-demographic factors.

Methodology

A prospective study was undertaken on men and women aged 18 to 60 who had died either natural or traumatic deaths, including sudden cardiac deaths. Cases of putrefaction, major trauma, or disruption of the heart leading to parenchymal loss and previous heart surgeries were excluded from the study. All autopsies were performed in the King County Medical Examiner's Office (KCMEO) autopsy suite and ethical approval was received from King County health and the Board of Study in Forensic Medicine, Post Graduate Institute of Medicine, University of Colombo.

After carefully selecting the cases, decedents were weighed unclothed and without shoes. The decedents were weighed on a VLC Commercial Duty Floor Scale (Mettler Toledo PTPN, Columbus, Ohio) with a capacity of 5000lb, a resolution of 1lb, and an accuracy of +1 lb. The decedents were measured in anatomical position from heel to cranial apex to the nearest 0.5 inches with 80 inches measuring stick with a resolution of 0.25 inches. To calculate the BMI ($\text{body weight(kg)/length(m)}^2$), body length in inches and weight in pounds were converted to centimeters and kilograms, respectively. Waist circumference was measured by wrapping a measuring tape around the waist at about the level of the umbilicus to the nearest 0.5 inches with 60 inches of measuring tape with a resolution of 0.0625 inches.

The pathologists attached to KCMEO conducted the autopsies, and they performed the autopsies in the same manner. The fatty infiltration and fibrosis of the right ventricular wall were assessed by selecting sections of each from the ventricular septum, anterior wall, lateral wall, and posterior wall. After being marked by the Davidson Marking System color die, these sections were put into a cassette. The anterior wall was colored red, the lateral wall was colored blue, and the posterior wall was colored green. In each case, a 5µm section was stained with Hematoxylin and eosin for microscopic examination. A constant magnification of X 4 was used for all measurements. The percentage of fatty infiltration and fibrosis in each section was evaluated separately. Epicardial fat was not included in the evaluation. Two pathologists read all specimens

separately the average of the two values was taken for analysis.

The intra-reader agreement was excellent (85%). The average free wall fat infiltration (anterior, posterior, and lateral walls) was taken to calculate the overall fat infiltration of the right ventricle.

Results

When considering the socio-demographic factors of the studied population, 70 (70%) were male. While 76 (76%) were Caucasian, thirteen (13%) were black, nine (09%) were Asian, and two (02%) were Native American. The average fat infiltration of males was 15%, and that of females was 26%. The average fat infiltration of the Caucasian population was 20.63%. Seventy-six (76%) samples were from those aged more than 30 years.

Seventy-one (71%) samples were from those who had BMI ≥ 25 , and 63 (63%) had normal waist circumference. In contrast, 37 (37%) had high waist circumference (males ≤ 40 inch/102cm and females ≤ 35 inch/88cm were taken as normal waist circumference). Notably, 19 (19%) deaths were of cardiac origin, and 81 (81%) were due to non-cardiac causes. Seventy-one (71%) people had no history of either diabetes mellitus or hypertension.

The results showed that mean fat infiltration of the anterior wall, lateral wall, posterior wall, and average fat infiltration of the right ventricle was higher in the female population and Caucasian population. But mean fat infiltration of the anterior wall ($p=0.006$), lateral wall ($p=0.002$), and average fat infiltration ($p=0.001$) of the right ventricle was significantly associated with the female population at a 95% confidence interval, and posterior wall lipomatosis also marginally correlate ($p=0.058$) with female cases. Fat infiltration of the anterior wall ($p=0.002$), lateral wall ($p=0.009$), and average fat infiltration ($p=0.003$) were statistically correlated with the white population.

Neither cause of death, past medical history of hypertension/diabetes mellitus, nor fibrosis of the right ventricle walls showed significant association with the fat infiltration of the right ventricle.

Yet, the studied population's age and body mass index showed a significant association in the fat infiltration of the posterior wall ($p=0.016$ and $p=0.023$, respectively). At the same time, waist circumference was significantly associated with the average right ventricular fat infiltration ($p=0.024$) and marginally associated with the anterior wall ($p=0.069$) and lateral wall ($p=0.055$)

lipomatosis. Higher age, body mass index, and waist circumference showed higher fat infiltration percentages. Associations between fat infiltration of the right ventricular free wall and sex, age, race, BMI, waist circumference, cause of death, past medical history, and fibrosis of the right ventricle are indicated in Table 1.

Table 1: Fat infiltration of right ventricular free wall and sex, age, race, BMI, waist circumference, cause of death, past medical history, and fibrosis of the right ventricle

Variable	Number	Fat Infiltration of Right Ventricle					
		Anterior Wall		Lateral Wall		Posterior Wall	
		Mean (%)	p-values	Mean (%)	p-values	Mean (%)	p-values
Sex							
Male	70	19	0.006	19	0.002	07	0.058
Female	30	33		33		12	
Age							
≤30	24	22	0.836	19	0.224	03	0.016
>30	76	23		25		10	
Race							
White	76	27	0.002	26	0.009	09	0.544
Others	24	10		14		07	
BMI							
≤25	29	20	0.373	19	0.249	04	0.023
>25	71	24		25		10	
WC*							
Normal	63	20	0.069	20	0.055	07	0.109
High	37	29		28		11	
COD [†]							
Cardiac	19	20	0.557	23	0.995	10	0.485
Non-Cardiac	81	24		23		08	
PMH [‡]							
HT/DM	24	19	0.319	20	0.468	06	0.393
No HT/DM	76	25		24		09	
Fibrosis of AW [§]							
Yes	36	21	0.599	-	-	-	-
No	64	24		-	-	-	-
Fibrosis of LW [¶]							
Yes	29	-	-	19	0.196	-	-
No	71	-	-	25		-	-
Fibrosis of PW ^α							
Yes	25	-	-	-	-	09	0.684
No	75	-	-	-	-	08	

*=Waist circumference, [†]=Cause of death, [‡]=Past medical history, [§]=Fibrosis of the anterior wall, [¶]=Fibrosis of the lateral wall, ^α=Fibrosis of the posterior wall

Though there is an increasing tendency of t RVL with age, female sex, BMI, and waist circumference, interestingly, the authors found some extreme cases. A 48 years old white male with low BMI and waist circumference showed a significant increase in fat in the right ventricular myocardium shown in Figure 1.

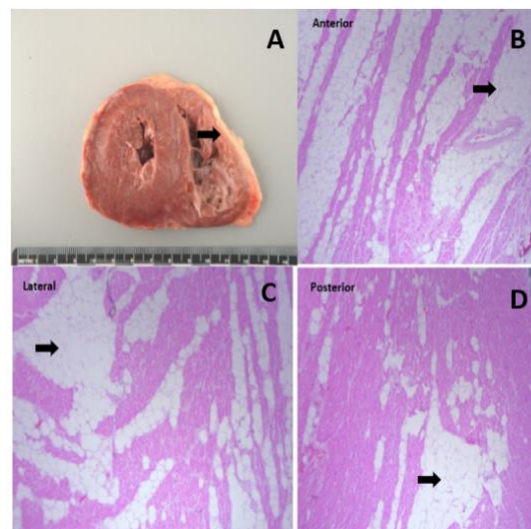


Figure 1: 56-year-old white male with a very low BMI (21kgm-2) and waist circumference(71cm) showed high overall fat infiltration of the right ventricle indicated with black arrows (38%).

- A- Cross section of the heart,
- B- Anterior wall of the right ventricle,
- C- C- Lateral wall of the right ventricle,
- D- D- Posterior wall of the right ventricle (add the type of stain and magnification).

At the same time, 48year old white female with BMI= 28 indicates very high-fat infiltration of the free wall, and a 49-year-old morbidly obese female expressed a negligible amount of fat infiltration in the right ventricle, as shown in Figure 2 and Figure 3, respectively.

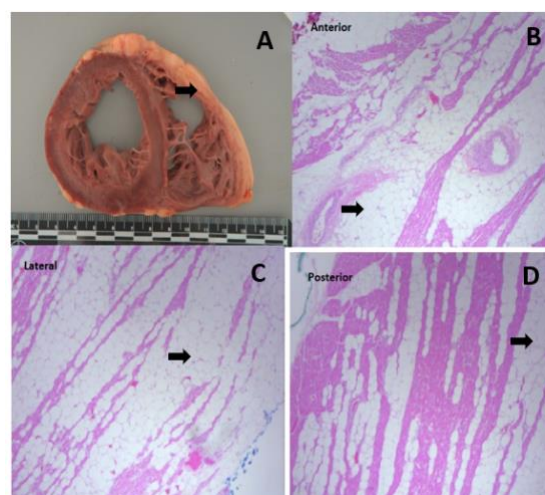


Figure 2: 42-year-old overweight (BMI=29kgm-2) white female with a marginally high waist circumference(99cm) showed extremely high overall fat infiltration of the right ventricle (77%).

- A- Cross section of the heart,

- B- Anterior wall of the right ventricle,
 C- Lateral wall of the right ventricle,
 D- Posterior wall of the right ventricle.

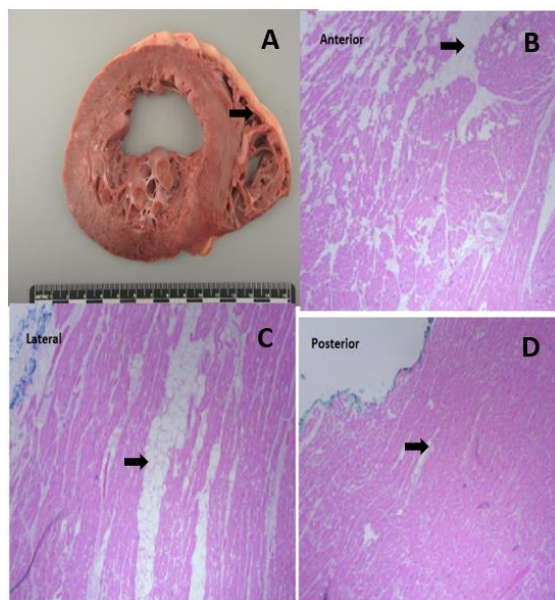


Figure 3: Sixty-two-year-old morbidly obese (BMI=62kgm⁻²) Asian female with a very high waist circumference(173cm) showed extremely minimum overall fat infiltration of the right ventricle (04%).

- A- Cross section of the heart,
 B- Anterior wall of the right ventricle,
 C- Lateral wall of the right ventricle,
 D- Posterior wall of the right ventricle.

Discussion

This study describes the fat infiltration of the right ventricle of hundred decedents of 18 to 60 years who died of natural or traumatic deaths, including cardiac deaths. Results revealed that intramyocardial fat infiltration of the right ventricle is more in the lateral wall, next to the anterior wall, and very low in the posterior wall. Similar observations were made in the epicardial fat distribution of the right ventricle by Tansey et al. in a study of 148 subjects.[11]. Schejbal et al. also reported similar results in a study of 200 hearts, showing that the most significant amount of epicardial fat was present along the ventrolateral edge and the least in the dorsocaudal (diaphragmatic) region. Schejbal et al. also demonstrate a positive correlation between subcutaneous and epicardial fat.[12]

The current study shows that the sex of the subjects is positively correlated with the anterior wall ($p=0.006$), lateral wall ($p=0.002$), Average fat infiltration of the right ventricle ($p=0.001$), and marginally significant with the posterior

wall($p=0.058$). At the same time, posterior wall fat infiltration is positively correlated with the age of the subjects ($p=0.016$). Tansey et al. indicated that a significant association ($p=0.000$) between age in the three different groups (0-19 years, 20-39 years, and ≥ 40 and marginally correlates with anterior($p=0.069$) and lateral($p=0.055$) free wall lipomatosis years), but a positive association between sex and the intramyocardial fat infiltration is noted in over 40 years population ($p=0.000$) and ages between 19-40 show a marginal correlation ($p=0.056$).[11] Fontaine et al. also reinforce that intramyocardial lipomatosis is mainly age-related.[8] Another study by Lorin et al. revealed a positive correlation with age($p=0.0029$) but not with sex ($p=0.4435$).[13] The findings of the Fontaine et al. and Lorin et al. are at odds with our study. In the present study, fat infiltration steadily increases with age in all different parts of the free wall (Anterior, lateral, and posterior walls). Still, it is only statistically significant in the posterior wall. Our study postulates that a positive correlation along with the white population was noted in the anterior wall ($p=0.002$), Lateral wall ($p=0.009$), and average fat infiltration ($p=0.003$). There is no correlation with past medical history (hypertension and diabetes mellitus) in this present study. Still, Yuka Matsuo et al. reported a relationship with hypertension.[14]

The present study postulated that BMI is correlated with posterior free wall fat($p=0.023$). Waist circumference is associated with average fat infiltration ($p=0.024$). In their research, Yuka Matsuo et al. stated that BMI is positively associated with right ventricular lipomatosis.[14] But Lorin et al. deny the association between BMI and right ventricular lipomatosis.[13] Another study indicates there is a strong correlation between obesity and epicardial fat[15], and another study by Holm et al. revealed that association between epicardial fat and visceral fat.[16]

Right ventricular fat infiltration has pathological importance as it frequently confuses the forensic pathologist to differentiate it from the ARVC/D and is often overlooked. ARVC is a genetically determined pathological condition that frequently affects the right ventricle, where the myocardium is getting progressive loss and is replaced by fibrofatty tissue.[11] Initially, it was designated dysplasia because they thought it was a developmental defect of the right ventricular myocardium. Recent developments proved it is an autosomal dominant inherited condition, and the initial name was changed to cardiomyopathy.[17]

Typical ARVC will show diffuse thinning of the right ventricular wall with right ventricular aneurysms in half of the population. Microscopically inflammation and necrosis of the myocytes in an atrophied myocardium are replaced with fibro-fatty tissue. 50% of the left ventricular involvement and 20% of the septal involvement were also observed in ARVC. [11,18] In the present study, none of the 100 hearts fit the macroscopic or microscopic criteria of ARVC. There are cases reported with classical histological findings, but the naked eye seems normal.[19]

Even though ARVC is a well-recognized cause of sudden natural death, the role of lipomatosis alone is still doubtful in its pathological and clinical importance. Increased epicardial fat can interfere the cardiac function as it restricts diastolic relaxation and ventricular filling[20]; increased fat in the heart could have a high risk of rupturing following myocardial infarction.[21] Fat infiltration into the areas where the conduction system is located may cause arrhythmias and cardiac blocks.[6,2]

Basso et al. reported that ARVC has two variances. One is fat infiltration with fibrous tissue called 'Fibro fatty pattern,' and the other is fat infiltration only called 'Fatty pattern.' Further, they diagnosed ARVC, the cases having regional or diffuse transmural fat infiltration or fibro-fatty infiltration of the free wall, which extends onto the endocardium in a patient without known cardiac cause or noncardiac cause of death.[18] Supporting this assumption of a fatty pattern of ARVC, there are reported cases where sudden cardiac deaths occurred with fatty infiltration alone in the free wall of the right ventricle.[23,24]

Fontaine et al. says that myocyte death and repair by scarring following myocarditis is the cause of the transformation of pure lipomatosis into a fibrofatty pattern of the ARVC. So, they considered fatty infiltration alone, and the fibrofatty pattern is two consecutive stages of the pathogenesis of ARVC. Further, they emphasized that intramyocardial fat infiltration alone without fibrosis or inflammation is a pathological condition often overlooked, and they use the term 'fat dissociation syndrome' for this condition.[8]

Burke et al. studied 25 sudden death cases that showed a marked difference between the right ventricle with fatty infiltration alone and the right ventricle with fibrofatty infiltration. They further noticed that fatty infiltration alone was more in older females. Burke concluded that right ventricular

lipomatosis alone is separate and not necessarily connected with sudden cardiac deaths.[7]

Conclusions

This study demonstrates that fat infiltration in the right ventricular myocardium is normal. Obesity, female sex, advanced age, and white people are significantly associated with this condition. It is a challenge for a pathologist to diagnose ARVC during autopsies. Determining ARVC is paramount as it is a well-known cause of sudden cardiac death; simultaneously, diagnosing ARVC with fat alone is controversial. This study and other studies related to RVL are not favoring the identification of ARVC with fat infiltration alone, especially among older adults.

Disclosure statement

Conflicts of Interest: The author(s) declared no potential conflicts of interest concerning the research, authorship, and publication of this article.

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