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The Significance of Ventricular Volume in the Evaluation of Secondary Cardiomyopathy at Autopsy

Joo Young Na[1] · Byung Woo Min[1]
Yeong Hui Kim[2] · Seung Hyun Chung[1]
Young Jik Lee[1,3] · Hyung Seok Kim[1,4]
Jong Tae Park[1,5]

Departments of [1]Forensic Medicine and [2]Pathology, Chonnam National University Medical School, Gwangju; [3]Department of Pathology, St. Carollo Hospital, Suncheon; [4]Center for Biomedical Human Resources at Chonnam National University; [5]Law School, Chonnam National University, Gwangju, Korea

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Corresponding Author
Jong Tae Park, M.D.
Department of Forensic Medicine, Chonnam National University Medical School, 5 Hak-dong, Dong-gu, Gwangju 501-746, Korea
Tel: +82-61-220-4090
Fax: +82-61-223-4250
E-mail: jtpark@jnu.ac.kr

Background: The weight, shape and consistency of the heart, and the thickness of the ventricular wall are used as parameters for evaluating postmortem heart and diagnosing cardiomyopathy at autopsy. **Methods:** The weight and volume of the ventricles and the thickness of the left ventricular wall of 58 hearts were measured and analyzed. **Results:** In the group of dilated hearts, the ventricular weight, ventricular volume, ventricular volume/ventricular weight, and left ventricular volume/right ventricular volume increased, whereas ventricular wall thickness decreased. In the group of hypertrophied hearts, the ventricular weight, ventricular volume, and thickness of the ventricular wall increased but ventricular volume/ventricular weight and left ventricular volume/right ventricular volume did not change significantly. In the group of undetermined hearts, it was later found that four of the cases should have been included in the dilated heart group and another two cases in the hypertrophied heart group. **Conclusions:** In addition to conventional methods, the measuring ventricular volume is useful for evaluating a postmortem heart and may suggest postmortem differential diagnoses of dilated or hypertrophied forms of secondary cardiomyopathies.

Key Words: Autopsy; Cardiac remodeling; Cardiomyopathies; Postmortem heart; Ventricular volume

A normal heart maintains its structure by being very well adapted to its role of supplying blood to the pulmonary and the systemic circulation. In various conditions such as ischemic heart disease, valvular disease, congenital abnormalities, and cardiac arrhythmia, the heart goes through a remodeling process resulting in reduced cardiac contractility and ultimately cardiac failure. During this process, hemodynamic and morphological changes occur concurrently. The morphological changes can be clinically categorized into cardiac hypertrophy and cardiac dilatation.[1]

Clinically, remodeling of the heart can be functionally evaluated using cardiac ultrasonography in addition to measuring other clinical symptoms. However, a functional test is not possible at autopsy. The postmortem heart is evaluated by measuring heart weight, ventricular wall thickness, and other histopathological findings. Nearly 60-70% of the forensic autopsy cases are unnatural deaths and the remaining 30-40% are natural deaths in Korea.[2-4] An accurate evaluation of the heart during autopsy is critical because among the natural death cases, more than 50-60% are sudden cardiogenic deaths.[2-4] A precise evaluation is also important for unnatural death cases that have trauma coinciding with cardiac disease, because the degree of contribution from each cause must be assessed. In particular, ischemic heart disease, cardiomyopathy, and myocarditis are important causes of sudden cardiogenic death. Most autopsy cases lack clinical information. Conventional cardiac evaluation tools aid in diagnosing ischemic heart disease and myocarditis, but such methods have limitations for cardiomyopathy. Restrictive cardiomyopathy was excluded from this study because it is rarely involved with sudden death on forensic autopsy.[5] However, it is important to diagnose and distinguish between dilated and hypertrophic cardiomyopathy. Both are related to cardiac arrhythmia and can lead to sudden death.[5,6] The macroscopic appearance of dilated cardiomyopathy and hypertrophic cardiomyopathy both include increased weight, and interstitial fibrosis and hypertrophy of cardiomyocytes can be found microscopically.[5,6] There are cases in which the characteristics of the two diseases either exist simultaneously or separately develop from two different diseases.[7-9] In such circumstances, diagnoses from autopsies using the conventional cardiac evaluation method without any clinical information may lead to highly subjective outcomes. Furthermore, but it is also difficult to provide a differential diagnosis.

Therefore, we measured ventricular volume as an additional parameter to evaluate postmortem heart and improve the objectivity for distinguishing between dilated cardiomyopathy and hypertrophic cardiomyopathy when secondary cardiomyopathy is suspected. We also investigated whether or not measuring ventricular volume can be used as a valid and objective indicator when analyzing the progress of cardiac remodeling, such as secondary dilated and hypertrophic cardiomyopathy.

MATERIALS AND METHODS

Autopsy cases in the Department of Forensic Medicine at Chonnam National University Medical School were used in this study. Decomposing hearts and direct damage such as a stab wound were excluded. We used Hughes' diagnostic approach recommendations as a reference using conventional methods in the following order.[10] 1) The removed heart's overall weight was measured with the ventricles, atria, and great vessels intact and any existing coronary artery disease was identified. 2) The weight of right and left ventricles was measured, after both right and left atria along with the great vessels were removed. 3) The volume of right and left ventricles was measured by subtracting the weight measured in step 2) from the weight of ventricles filled with water poured in through the tricuspid and mitral valve, respectively (Fig. 1). Volume was measured five times and the measurements were averaged. 4) The heart was fixed using 10% neutral buffered formalin and serial 1 cm wide sections were made perpendicular to the long axis of the heart. Then, the thickness of the left ventricular free wall and the interventricular septum was measured, excluding the papillary muscle portion and the trabeculae. 5) The valves were examined to identify valvular diseases. 6) A histological examination of the heart was conducted.

Each value obtained from the above measurements was analyzed separately, and the ratio of the values was calculated; ventricular volume/ventricular weight, left ventricular volume/ventricular weight, right ventricular volume/ventricular weight, left ventricular volume/ventricular volume, right ventricular volume/ventricular volume, and left ventricular volume/right ventricular volume. We also obtained the ratio of the interventricular septum thickness to left ventricular free wall thickness to examine hypertrophic changes in cardiac muscle.

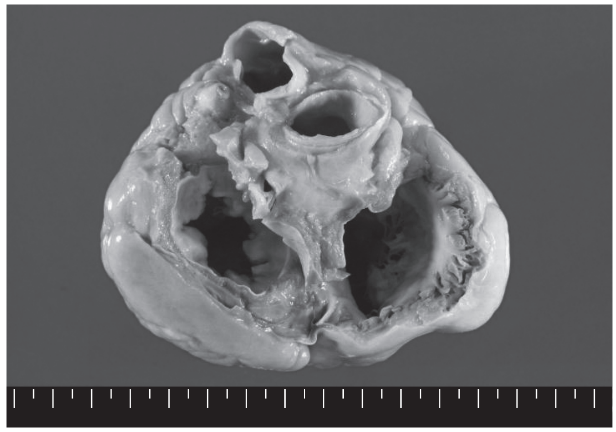

Fig. 1. For measuring ventricular volume, both atria and great vessels are eliminated.

Cases in the control group were death cases caused by trauma not involving cardiogenic death and cases without a history of cardiac disease such as hypertension or ischemic heart disease. Cases in the dilated heart group were identified based on dilated cardiomyopathy diagnostic methods with reference to forensic pathology. They showed macroscopic findings such as reduced elasticity of cardiac muscle, a globular appearance (Fig. 2A), thickness of the cardiac muscle <1.5 cm (Fig. 2B) and histologically showed interstitial fibrosis. In contrast, the hypertrophied heart group retained the elasticity of cardiac muscle and showed a hypertrophic external appearance (Fig. 2D). With reference to the report of Hitosugi *et al.*[11] on predicting normal heart weight, the cases categorized into the hypertrophied heart group were hearts that had their ventricular wall thickened by >1.5 cm (Fig. 2E), and histologically showed hypertrophy and disarray of cardiomyocytes, as well as interstitial fibrosis (Fig. 2F). The undetermined heart group included cases with heart diseases such as ischemic heart disease and hypertension but without sufficient morphological changes to be included in the dilated heart or hypertrophied heart group using the aforementioned classification methods.

The subjects of this study were 58 hearts from autopsy cases. The cases were categorized into four groups: 13 cases in the control group, 14 cases in the dilated heart group, nine cases in the hypertrophied heart group, and 22 cases in the undetermined heart group. Primary cardiomyopathy is disease predominantly confined to the heart muscle, whereas secondary cardiomyopathy has myocardial involvement as a component of a systemic

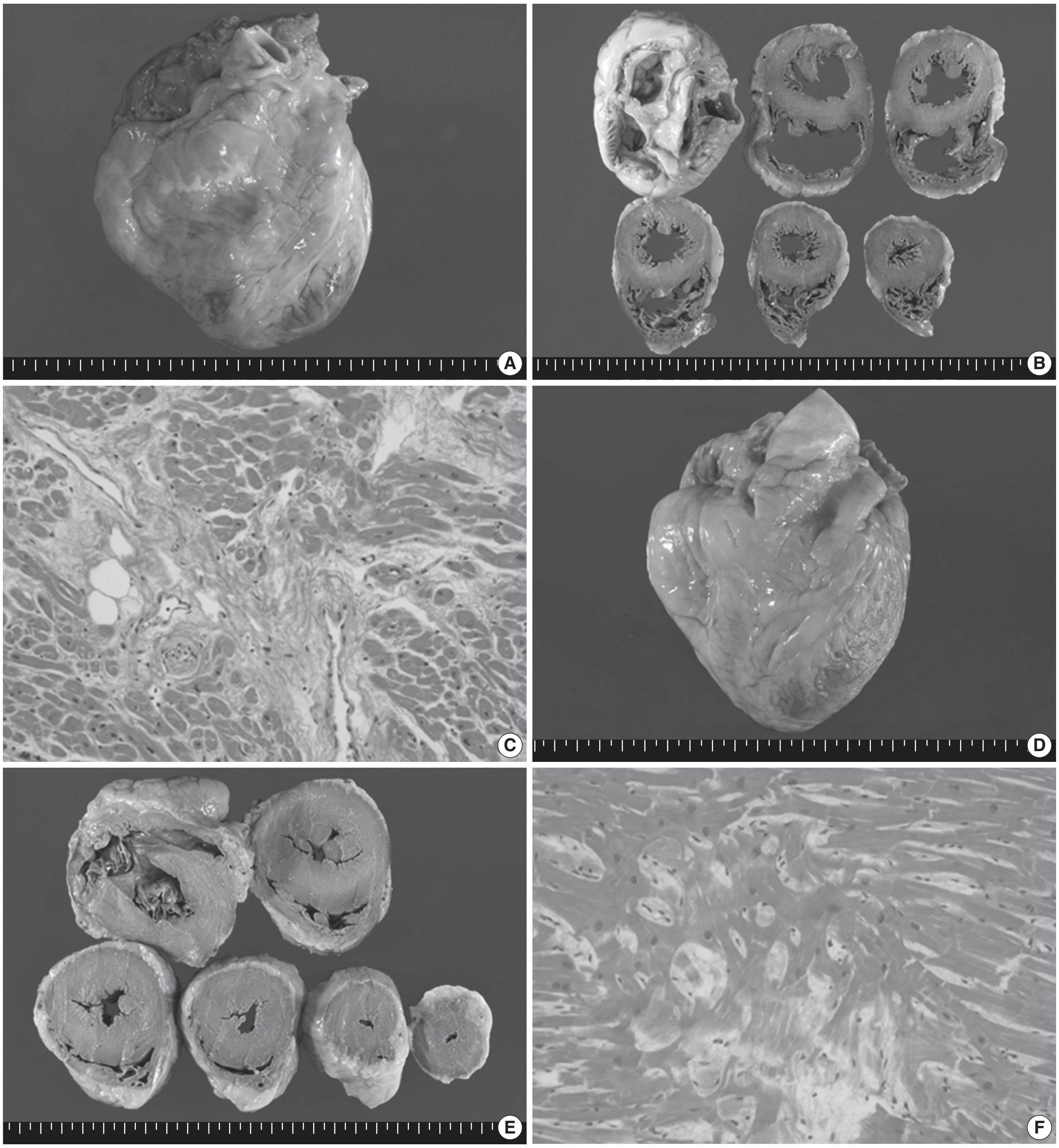

Fig. 2. (A) The heart of case 5 in the dilated heart group shows a globular and flabby appearance. (B) The thicknesses of the left ventricular wall and interventricular septum are not hypertrophied in this transverse section. (C) This figure shows cardiomyocytes of various sizes with interstitial fibrosis. (D) The heart of case 5 in the hypertrophied heart group has a hypertrophic appearance. (E) The thicknesses of the left ventricular wall and interventricular septum are hypertrophied in this transverse section. (F) This figure shows disarray, hypertrophy, and characteristic branching of cardiomyoctyes as well as the interstitial fibrosis characteristic of hypertrophic cardiomyopathy.

or multiorgan disorder.[6] We did not distinguish between primary and secondary cardiomyopathy, because the purpose of this study was not to evaluate primary cardiomyopathy but to examine and evaluate dilated and hypertrophied hearts based on gross measurements and the macroscopic appearance found at autopsy.

Statistical significance was analyzed using the Mann-Whitney U test (SPSS ver. 13.0, SPSS Inc., Chicago, IL, USA). Gross findings and the ventricular measurement results were compared to determine whether measuring ventricular volume was meaningful to help provide a differential diagnosis between the dilated heart and hypertrophied heart groups. Remodeling appearance such as cardiac dilation and hypertrophy of the hearts in each group, was evaluated based on ventricular weight and volume.

RESULTS

This study focused on 58 cases of 40 males (69.0%) and 18 females (31.0%). Their ages ranged from 20 to 80 years (mean, 49.8±12.6 years). The dilated heart group had 14 cases, the hypertrophied heart group nine cases, the undetermined heart group 22 cases, and the control group 13 cases.

Control group

Of the 13 cases in the control group, six were males (46.2%) and seven were females (53.8%). Their age ranged from 20 to 60 years (average, 39.5±12.1 years for males and 40.9±12.8 years for females). Weights of male and female hearts were 329.2±30.2 g and 277.9±30.7 g, respectively. Ventricular weights were 271.5±34.4 g and 219.3±23.9 g, respectively. Left ventricular volume for males was 25.8±9.7 mL and 15.7±8.2 mL for females. Right ventricular volumes were 34.3±13.2 mL and 35.6±9.0 mL for males and females, respectively. Total ventricular volume for males and females was 60.2±20.4 mL, and 51.3±15.7 mL, respectively (Tables 1, 2).

Table 1. Volume, weight, and thickness of ventricle in control group

Case No.	Sex	Age (yr)	Total heart Wt. (g)	Vent. Wt. (g)	Vent. Vol. (mL)	LV Vol. (mL)	RV Vol. (mL)	LV free wall thickness (cm)	IVS thickness (cm)
1	M	45	325	240	95	35	60	1.3	1.1
2	M	33	355	300	55	22	33	1.3	1.0
3	M	55	320	270	73	38	35	1.3	1.5
4	M	20	300	255	50	25	25	1.4	1.7
5	M	38	375	325	49	24	25	1.5	1.3
6	M	46	300	240	39	11	28	1.5	1.3
7	F	32	295	245	31	5	26	1.3	1.6
8	F	49	280	215	41	11	30	1.3	1.1
9	F	25	250	190	80	30	50	1.0	0.8
10	F	41	280	235	45	20	25	1.2	1.2
11	F	50	310	225	54	15	39	1.3	1.5
12	F	60	305	240	60	19	41	1.5	1.5
13	F	29	225	185	48	10	38	1.3	1.1

Wt., weight; Vent., ventricle; Vol., volume; LV, left ventricle; RV, right ventricle; IVS, interventricular septum; M, male; F, female.

Table 2. Comparison of ratio of each parameter in control group

Case No.	Vent. Vol./Vent. Wt. (%)	LV Vol./Vent. Wt. (%)	RV Vol./Vent. Wt. (%)	LV Vol./Vent. Vol. (%)	RV Vol./Vent. Vol. (%)	LV Vol./RV Vol. (%)	IVS/LV free wall
1	39.6	14.6	15.4	36.8	63.2	58.3	0.8
2	18.3	7.3	13.3	40.0	60.0	66.7	0.8
3	27.0	14.1	19.3	52.1	47.9	108.6	1.2
4	19.6	9.8	19.6	50.0	50.0	100.0	1.2
5	15.1	7.4	15.1	49.0	51.0	96.0	0.9
6	16.3	4.6	11.8	28.2	71.8	39.3	0.9
7	12.7	2.0	6.5	16.1	83.9	19.2	1.2
8	19.1	5.1	12.4	26.8	73.2	36.7	1.0
9	42.1	15.8	19.8	37.5	62.5	60.0	0.8
10	19.1	8.5	18.9	44.4	55.6	80.0	1.0
11	24.0	6.7	12.4	27.8	72.2	38.5	1.2
12	25.0	7.9	13.2	31.7	68.3	46.3	1.0
13	25.9	5.4	11.3	20.8	79.2	26.3	0.8

Vent., ventricle; Vol., volume; Wt., weight; LV, left ventricle; RV, right ventricle; IVS, interventricular septum.

The ventricular volume to weight ratio was 22.7±9.3% for males and 24.0±9.2% for females. The ratios of left ventricular volume to ventricular weight and right ventricular volume to ventricular weight were 9.6±4.0% and 15.8±3.1% for males and 7.3±4.3% and 13.5±4.6% for females. The ratios of left and right ventricular volumes to ventricular volume for males and females were 42.7±9.3%, 57.3±9.3% and 29.3±9.6%, 70.7±9.6%, respectively. Left ventricular volume to right ventricular volume ratios for males and females were 78.2±27.4% and 43.9±20.7%, respectively.

The thickness of the left ventricular free wall for males and females was 1.4±0.1 cm and 1.3±0.1 cm, respectively, whereas the interventricular septum was 1.3±0.3 cm for both males and females. The ratio of interventricular septum thickness to left ventricular free wall thickness was 1.0±0.2 cm in both males and females.

Dilated heart group

The dilated heart group had 14 cases with 11 males (78.6%) and three females (21.4%). Their ages ranged from 38 to 80 years (average, 57.3±12.2 years for males and average 52.7±12.7 for females). There were seven cases of cardiogenic sudden death, two cases of suffocation, two cases of chest trauma, and one case each of alcohol intoxication, pneumonia, and subdural hemorrhage (Tables 3, 4).

Weights of male and female hearts were 429.5±61.0 g, 337.0±63.9 g, respectively, and ventricular weights were 347.3±45.3

Table 3. Volume, weight, and thickness of ventricle in dilated heart group

Case No.	Sex	Age (yr)	Total heart Wt. (g)	Vent. Wt. (g)	Vent. Vol. (mL)	LV Vol. (mL)	RV Vol. (mL)	LV free wall thickness (cm)	IVS thickness (cm)	COD
1	M	60	355	300	134	66	68	1.2	1.5	IHD
2	M	59	380	295	197	90	107	0.8	1.0	DCMP
3	M	44	420	330	215	108	107	1.2	1.5	Asphyxia
4	M	52	395	310	225	110	115	1.0	1.0	IHD
5	M	77	570	425	211	96	115	1.4	1.4	Chest trauma
6	M	56	400	305	201	98	103	1.0	1.2	Pneumonia
7	M	80	425	340	190	93	97	1.3	1.4	DCMP
8	M	50	500	410	179	79	100	1.2	1.2	SDH
9	M	45	400	355	230	110	120	1.1	1.0	Chest trauma
10	M	62	465	390	306	143	163	1.0	1.0	DCMP
11	M	45	415	360	197	89	108	1.2	1.2	DCMP
12	F	38	266	210	136	67	69	1.2	1.3	Alcoholic DI
13	F	61	355	290	170	84	86	1.1	1.1	DCMP
14	F	59	390	305	187	107	80	1.2	1.2	Smothering

Wt., weight; Vent., ventricle; Vol., volume; LV, left ventricle; RV, right ventricle; IVS, interventricular septum; COD, cause of death; M, male; F, female; IHD, ischemic heart disease; DCMP, dilated cardiomyopathy; SDH, subdural hemorrhage; DI, drug intoxication.

Table 4. Comparison of ratio of each parameter in dilated heart group

Case No.	Vent. Vol./Vent. Wt. (%)	LV Vol./Vent. Wt. (%)	RV Vol./Vent. Wt. (%)	LV Vol./Vent. Vol. (%)	RV Vol./Vent. Vol. (%)	LV Vol./RV Vol. (%)	IVS/LV free wall
1	44.7	22.0	22.7	49.3	50.7	97.1	1.3
2	66.8	30.5	36.3	45.7	54.3	84.1	1.3
3	65.2	32.7	32.4	50.2	49.8	100.9	1.3
4	72.6	35.5	37.1	48.9	51.1	95.7	1.0
5	49.6	22.6	27.1	45.5	54.5	83.5	1.0
6	65.9	32.1	33.8	48.8	51.2	95.1	1.2
7	55.9	27.4	28.5	48.9	51.1	95.9	1.1
8	43.7	19.3	24.4	44.1	55.9	79.0	1.0
9	64.8	31.0	33.8	47.8	52.2	91.7	0.9
10	78.5	36.7	41.8	46.7	53.3	87.7	1.0
11	54.7	24.7	30.0	45.2	54.8	82.4	1.0
12	64.8	31.9	32.9	49.3	50.7	97.1	1.1
13	58.6	29.0	29.7	49.4	50.6	97.7	1.0
14	61.3	35.1	26.2	57.2	42.8	133.8	1.0

Vent., ventricle; Vol., volume; Wt., weight; LV, left ventricle; RV, right ventricle; IVS, interventricular septum.

g and 268.3±51.1 g, respectively. Left ventricular volume and right ventricular volume were 98.4±19.9 mL and 109.4±22.5 mL for males and 86.0±20.1 mL and 78.3±8.6 mL for females. Total ventricular volumes for males and females were 207.7±41.7 mL and 164.3±26.0 mL, respectively.

The ventricular volume to weight ratio was 60.2±11.3% for males and 61.6±3.1% for females. The ratios of left ventricular volume to ventricular weight and right ventricular volume to ventricular weight were 28.6±5.8% and 31.6±5.7% for males and 32.0±3.1% and 29.6±3.4% for females. The ratios of left and right ventricular volumes to ventricular volume for males and females were 47.4±2.0%, 52.6±2.0% and 52.0±4.5%, 48.0±4.5%, respectively. Left ventricular volume to right ventricular volume ratios for males and females were 90.3±7.3% and 109.5±21.0%, respectively. Overall, we found that ventricular weight increased compared to that in the control group and that although both left and right ventricular volume increased, it was more obvious in the left ventricle.

The thickness of the left ventricular free wall and interventricular septum in males was 1.1±0.2 cm and 1.2±0.2 cm, and it was 1.2±0.1 cm and 1.2±0.1 cm for females. The ratio of interventricular septum thickness to left ventricular free wall thickness for males and females were 1.1±0.1 and 1.0±0.1, respectively.

Hypertrophied heart group

The hypertrophied heart group had nine cases. Eight were males (88.9%) and one was a female (11.1%). Ages ranged from 28 to 69 years, (average age 52.0±12.4 for males; and the one female was aged 48). Seven cases of cardiogenic sudden death and two cases of head trauma were observed (Tables 5, 6).

We could not calculate and compare the mean values because there was only one female case in the hypertrophied heart group. The average weight of eight cases of male hearts categorized in the hypertrophied heart group was 513.8±79.9 g, and the ventricular weight was 422.9±66.0 g. Left ventricular volume and right ventricular volume were 39.3±22.1 mL and 63.6±30.0 mL, respectively, and the entire ventricular volume was 102.9±47.9 mL.

The ventricular volume to weight ratio was 24.1±9.5%. The ratios of left ventricular volume to ventricular weight and right

Table 5. Volume, weight, and thickness of ventricle in hypertrophied heart group

Case No.	Sex	Age (yr)	Total heart Wt. (g)	Vent. Wt. (g)	Vent. Vol. (mL)	LV Vol. (mL)	RV Vol. (mL)	LV free wall thickness (cm)	IVS thickness (cm)	COD
1	M	28	500	410	147	38	109	1.5	1.8	HCMP
2	M	57	605	510	95	45	50	2.0	1.8	IHD
3	M	49	635	498	200	90	110	1.8	1.5	HCMP
4	M	48	445	375	67	19	48	2.0	1.8	IHD
5	M	69	560	460	67	28	39	1.8	1.7	IHD
6	M	57	415	345	96	29	67	1.3	2.0	Head trauma
7	M	62	445	340	60	27	33	1.5	1.8	Head trauma
8	M	46	505	445	91	38	53	1.9	1.5	IHD
9	F	48	425	330	36	15	21	1.5	1.8	HCMP

Wt., weight; Vent., ventricle; Vol., volume; LV, left ventricle; RV, right ventricle; IVS, interventricular septum; COD, cause of death; M, male; F, female; HCMP, hypertrophic cardiomyopathy; IHD, ischemic heart disease.

Table 6. Comparison of ratio of each parameter in hypertrophied heart group

Case No.	Vent. Vol./Vent. Wt. (%)	LV Vol./Vent. Wt. (%)	RV Vol./Vent. Wt. (%)	LV Vol./Vent. Vol. (%)	RV Vol./Vent. Vol. (%)	LV Vol./ RV Vol. (%)	IVS/LV free wall
1	35.9	9.3	26.6	25.9	74.1	34.9	1.2
2	18.6	8.8	9.8	47.4	52.6	90.0	0.9
3	40.2	18.1	22.1	45.0	55.0	81.8	0.8
4	17.9	5.1	12.8	28.4	71.6	39.6	0.9
5	14.6	6.1	8.5	41.8	58.2	71.8	0.9
6	27.8	8.4	19.4	30.2	69.8	43.3	1.5
7	17.6	7.9	9.7	45.0	55.0	81.8	1.2
8	20.4	8.5	11.9	41.8	58.2	71.7	0.8
9	10.9	4.5	6.4	41.7	58.3	71.4	1.2

Vent., ventricle; Vol., volume; Wt., weight; LV, left ventricle; RV, right ventricle; IVS, interventricular septum.

ventricular volume to ventricular weight were 9.0±3.9% and 15.1±6.7%. The left and right ventricular volume to ventricular volume ratios were 38.2±8.6% and 61.8±8.6%, whereas the left ventricular volume to right ventricular volume ratio was 64.4±21.7%. In general, a noticeable increase was observed in the ventricular weight compared to that in the male control group.

The thickness of the left ventricular free wall and the interventricular septum of the eight male heart cases were 1.7±0.3 cm and 1.7±0.2 cm, respectively. The ratio of interventricular septum thickness to left ventricular free wall thickness was 1.0 ±0.2.

Undetermined heart group

The undetermined heart group had 22 cases (15 males [68.2%] and seven females [31.8%]). Their age ranged from 34 to 78 years, (average age 49.7±10.2 years for males; 52.6±13.1 years for females). The cause of death was sudden cardiogenic death in seven cases; two cases each of a stab wound on body parts other than the heart; diabetes mellitus; fire; hypothermia; and one case each of variceal bleeding, chest trauma, abdominal trauma, alcohol intoxication, carbon monoxide intoxication, drowning, and suffocation (Tables 7, 8).

Heart weights for male and female were 373.3±43.5 g and 347.1±33.8 g, respectively. The ventricular weights were 305.3 ±35.0 g and 277.9±27.8 g for males and females, respectively. Left ventricular volume and right ventricular volume for male were 23.9±9.8 mL and 46.1±15.1 mL, and they were 36.1± 15.1 mL and 51.9±13.9 mL for females. Total ventricular volumes for males and females were 70.1±23.3 mL and 79.4±19.8 mL, respectively.

The ventricular volume to weight ratio was 23.1±8.1% for males and 31.6±7.2% for females. The ratios of left ventricular volume to ventricular weights and right ventricular volume to ventricular weight were 7.9±3.4% and 15.2±5.1% for males, and 12.9±4.9% and 18.6±5.0% for females. The left and right ventricular volume to ventricular volume ratios for males and females were 33.9±6.2% and 66.1±6.2% and 40.7±11.9% and 59.3±11.9%, respectively. Left ventricular volume to right ventricular volume ratios for males and females were 52.7± 15.1% and 75.2±38.5%, respectively. Compared with the control group, ventricular weight and volume increased, whereas the ventricular volume to weight ratio and the ratio of left and right ventricular volume remained relatively similar.

The thickness of the left ventricular free wall in males and fe-

Table 7. Volume, weight, and thickness of ventricle in undetermined group

Case No.	Sex	Age (yr)	Total heart Wt. (g)	Vent. Wt. (g)	Vent. Vol. (mL)	LV Vol. (mL)	RV Vol. (mL)	LV free wall thickness (cm)	IVS thickness (cm)	COD
1	M	46	320	260	40	10	30	1.8	1.5	IHD
2	M	36	310	265	91	35	56	1.3	1.2	IHD
3	M	48	315	265	94	34	60	1.3	1.3	IHD
4	M	59	360	295	44	14	30	1.9	1.8	IHD
5	M	51	375	295	90	40	50	1.5	1.5	CO intoxication
6	M	49	345	275	35	16	19	1.7	1.3	Chest trauma
7	M	49	350	300	34	12	22	1.5	1.5	Hemoperitoneum
8	M	44	350	285	63	18	45	1.6	1.5	Varix bleeding
9	M	64	360	295	95	25	70	1.4	1.3	Hypothermia
10	M	43	445	370	76	22	54	1.8	1.8	IHD
11	M	63	395	300	88	30	58	1.5	1.4	IHD
12	M	69	425	340	61	20	41	1.5	1.3	Fire
13	M	50	425	350	100	40	60	1.5	1.8	IHD
14	M	34	415	345	75	23	52	1.5	1.2	Asphyxia
15	M	40	410	340	65	20	45	1.5	1.4	Stab
16	F	50	380	310	81	24	57	1.5	1.3	DM
17	F	58	350	290	103	51	52	1.5	1.5	Stab
18	F	51	305	245	62	19	43	1.3	1.0	Alcoholic DI
19	F	52	345	285	86	25	61	1.3	1.5	Hypothermia
20	F	41	335	250	105	39	66	1.2	1.3	Drowning
21	F	38	315	255	60	35	25	1.5	1.3	DM
22	F	78	400	310	59	60	59	1.3	1.3	Fire

Wt., weight; Vent., ventricle; Vol., volume; LV, left ventricle; RV, right ventricle; IVS, interventricular septum; COD, cause of death; M, male; F, female; IHD, ischemic heart disease; CO, carbon monoxide; DM, diabetes mellitus; DI, drug intoxication.

Table 8. Comparison of ratio of each parameter in undetermined group

Case No.	Vent. Vol./Vent. Wt. (%)	LV Vol./ Vent. Wt. (%)	RV Vol./ Vent. Wt. (%)	LV Vol./ Vent. Vol. (%)	RV Vol./ Vent. Vol. (%)	LV Vol./RV Vol. (%)	IVS/LV free wall
1	15.4	3.8	11.5	25.0	75.0	33.3	0.8
2	34.3	13.2	21.1	38.5	61.5	62.5	0.9
3	35.5	12.8	22.6	36.2	63.8	56.7	1.0
4	14.9	4.7	10.2	31.8	68.2	46.7	0.9
5	30.5	13.6	16.9	44.4	55.6	80.0	1.0
6	12.7	5.8	6.9	45.7	54.3	84.2	0.8
7	11.3	4.0	7.3	35.3	64.7	54.5	1.0
8	22.1	6.3	15.8	28.6	71.4	40.0	0.9
9	32.2	8.5	23.7	26.3	73.7	35.7	0.9
10	20.5	5.9	14.6	28.9	71.1	40.7	1.0
11	29.3	10.0	19.3	34.1	65.9	51.7	0.9
12	17.9	5.9	12.1	32.8	67.2	48.8	0.9
13	28.6	11.4	17.1	40.0	60.0	66.7	1.2
14	21.7	6.7	15.1	30.7	69.3	44.2	0.8
15	19.1	5.9	13.2	30.8	69.2	44.4	0.9
16	26.1	7.7	18.4	29.6	70.4	42.1	0.9
17	35.5	17.6	17.9	49.5	50.5	98.1	1.0
18	25.3	7.8	17.6	30.6	69.4	44.2	0.8
19	30.2	8.8	21.4	29.1	70.9	41.0	1.2
20	42.0	15.6	26.4	37.1	62.9	59.1	1.1
21	23.5	13.7	9.8	58.3	41.7	140.0	0.9
22	38.4	19.4	19.0	50.4	49.6	101.7	1.0

Vent., ventricle; Vol., volume; Wt., weight; LV, left ventricle; RV, right ventricle; IVS, interventricular septum.

males were 1.6±0.2 cm and 1.4±0.1 cm, respectively, and the interventricular septum was 1.5±0.2 cm for males and 1.3±0.2 cm for females. The ratio of interventricular septum thickness to left ventricular free wall thickness for male and female were 0.9±0.1 and 1.0±0.1, respectively.

Cardiac remodeling

Fig. 3 shows analysis of the morphological changes in the heart due to cardiac remodeling such as cardiac dilation and hypertrophy in relation to ventricular weight and volume for each heart group. The ventricular weight and volume of the control group was about 300 g and 100 mL, respectively. The undetermined heart group's ventricular volume showed only a slight increase, but the ventricular weight increased by approximately 400 g. In the hypertrophied heart group, the ventricular volume remained similar to that of the undetermined heart group but showed a larger change in ventricular weight, with more than a 500 g increase. In the dilated heart group, both the ventricular weight and volume increased by more than 400 g and 300 mL, respectively. We were able to categorize the 58 cases into three groups. In undetermined group, two cases that showed a more significant increase in ventricular volume than weight were classified as the dilated heart group, whereas the four cases with a more evident rise in ventricular weight than in volume were classified into the hypertrophied heart group. Overall, the undetermined heart group lay in between the two groups (Table 9).

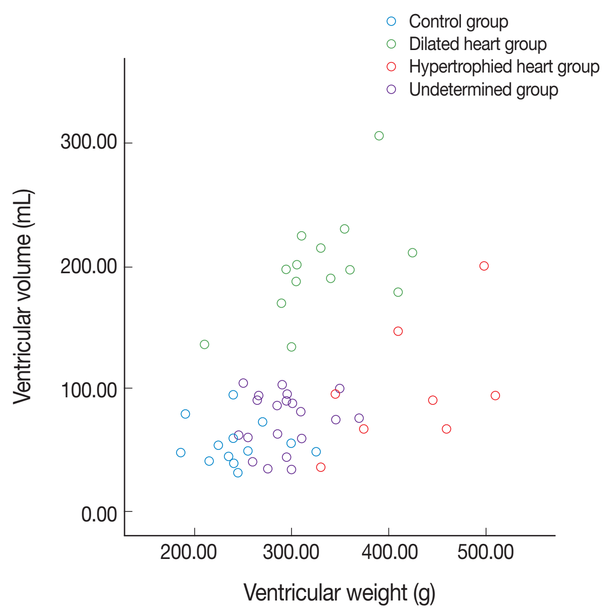

Fig. 3. This graph shows the distributions of the 58 hearts according to ventricular weight and ventricular volume.

Table 9. Comparison of mean between control group and other groups

	Control		Dilated heart group		Hypertrophied heart group		Undetermined group	
	M=6	F=7	M=11	F=3	M=8	F=1	M=15	F=7
Age (yr)	39.5±12.1	40.9±12.8	57.3±12.2 (0.020)	52.7±12.7 (0.267)	52.0±12.4 (0.043)	NA	49.7±10.2 (0.095)	52.6±13.1 (0.128)
Total heart Wt. (g)	329.2±30.2	277.9±30.7	429.5±61.0 (< 0.001)	337.0±63.9 (0.267)	513.8±79.9 (0.001)	NA	373.3±43.5 (0.055)	347.1±33.8 (0.001)
Vent. Wt. (g)	271.7±34.4	219.3±23.9	347.3±45.3 (0.003)	268.3±51.1 (0.267)	422.9±66.0 (0.001)	NA	305.3±35.0 (0.080)	277.9±27.8 (0.001)
LV Vol. (mL)	25.8±9.7	15.7±8.2	98.4±19.9 (<0.001)	86.0±20.1 (0.017)	39.3±22.1 (0.142)	NA	23.9±9.8 (0.569)	36.1±15.1 (0.007)
RV Vol. (mL)	34.3±13.2	35.6±9.0	109.4±22.5 (<0.001)	78.3±8.6 (0.017)	63.6±30.0 (0.020)	NA	46.1±15.1 (0.178)	51.9±13.9 (0.026)
Vent. Vol. (mL)	60.2±20.4	51.3±15.7	207.7±41.7 (0.001)	164.3±26.0 (0.017)	102.9±47.9 (0.001)	NA	70.1±23.3 (0.424)	79.4±19.8 (0.007)
Vent. Vol./Vent. Wt. (%)	22.7±9.3	24.0±9.2	60.2±11.3 (<0.001)	61.6±3.1 (0.017)	24.1±9.5 (0.755)	NA	23.1±8.1 (0.850)	31.6±7.2 (0.097)
LV Vol./Vent. Wt. (%)	9.6±4.0	7.3±4.3	28.6±5.8 (<0.001)	32.0±3.1 (0.017)	9.0±3.9 (0.950)	NA	7.9±3.4 (0.267)	12.9±4.9 (0.053)
LV Vol./Vent. Vol. (%)	42.7±9.3	29.3±9.6	47.4±2.0 (0.808)	52.0±4.5 (0.017)	38.2±8.6 (0.414)	NA	33.9±6.2 (0.045)	40.7±11.9 (0.097)
RV Vol./Vent. Wt. (%)	15.8±3.1	13.5±4.6	31.6±5.7 (<0.001)	29.6±3.4 (0.017)	15.1±6.7 (0.573)	NA	15.2±5.1 (0.791)	18.6±5.0 (0.165)
RV Vol./Vent. Vol. (%)	57.3±9.3	70.7±9.6	52.6±2.0 (0.808)	48.0±4.5 (0.017)	61.8±8.6 (0.414)	NA	66.1±6.2 (0.045)	59.3±11.9 (0.097)
LV Vol./RV Vol. (%)	78.2±27.4	43.9±20.7	90.3±7.3 (0.808)	109.5±21.0 (0.017)	64.4±21.7 (0.414)	NA	52.7±15.1 (0.045)	75.2±38.5 (0.097)
LV free wall thickness (cm)	1.4±0.1	1.3±0.1	1.1±0.2 (0.003)	1.2±0.1 (0.183)	1.7±0.3 (0.020)	NA	1.6±0.2 (0.035)	1.4±0.1 (0.318)
IVS thickness (cm)	1.3±0.3	1.3±0.3	1.2±0.2 (0.462)	1.2±0.1 (0.833)	1.7±0.2 (0.005)	NA	1.5±0.2 (0.267)	1.3±0.2 (0.805)
IVS/LV free wall thickness	1.0±0.2	1.0±0.2	1.1±0.1 (0.098)	1.0±0.1 (0.833)	1.0±0.2 (0.755)	NA	0.9±0.1 (1.000)	1.0±0.1 (0.902)

Values are presented mean±standard deviation (p-value[a]).
[a]Mann-Whitney U test.
M, male; F, female; NA, not applicable; Wt, weight; Vent., ventricle; LV, left ventricle; Vol., volume; RV, right ventricle; IVS, interventricular septum.

DISCUSSION

A conventional evaluation of the heart at autopsy includes several components: observation of the external and internal gross appearance, measurement of the heart's entire weight and thickness of the ventricular wall, serial sectioning of the coronary artery, and histological testing. This study used the normal heart weight prediction method suggested by Hitosugi *et al.*[11] which considers gender, height, and body weight, as well as the conventional evaluation method mentioned above to compare and analyze the 58 cases. We categorized the hearts into a control group, a dilated heart group, a hypertrophied heart group, and an undetermined heart group. The types of heart disease and the cause and manner of death did not considered because focus of this study was to evaluate secondary cardiomyopathy. In particular, we measured ventricular weight rather than the entire weight of the heart. We also measured the left and right ventricular volume separately in addition to the weight for a comparative analysis.

The weights of male and female hearts in the control group were 329.2±30.2 g and 277.9±30.7 g, respectively, and the ventricular weights were 271.5±34.4 g and 219.3±23.9 g. Left ventricular and right ventricular volumes for male were 25.8±9.7 mL and 34.3±13.2 mL; and they were 15.7±8.2 mL and 35.6±9.0 mL for females. The thickness of the left ventricular free wall in males and females were 1.4±0.1 cm and 1.3±0.1 cm, respectively and for the interventricular septum they were 1.3±0.3 cm for both males and females. Although the number of cases in the control group was small, we consider our results to be basic data that can be used as a standard for hearts in the Korean population because such results of ventricular weight, volume, and thickness have not been reported previously in a domestic study.

It is imperative to evaluate the postmortem heart to determine the cause of death because it is impossible to provide a functional evaluation of the heart at autopsy, and it is difficult to obtain clinical records with a precise history even in autopsy cases in which there are sudden cardiogenic deaths. Therefore, several methods have been suggested to evaluate the heart at autopsy including measuring cardiac volumes.[11-13] Hutchins and Anaya[12] measured atria, ventricular, and cardiac wall thickness in 456 hearts and found that the weight of a normal heart is 319 g, the mean left ventricular volume is 43 mL, and the mean right ventricular volume is 70 mL. Although the volume of the left and right ventricles of the control group in this study was less than what Hutchins and Anaya[12] reported, the left and right ventricle ratios were similar. We assume that a smaller ventricular volume was attributed to the difference in measuring methods or racial differences. It is difficult to make a simple comparison because there have been no studies that have reported ventricular volume measurements in normal hearts from the Korean population. There could be a debate about our results as to whether each heart was in the systolic or the diastolic phase at the time of death. When alive, the ventricular volume is affected by cardiac contraction and dilation. However, most cases of sudden cardiogenic death go through ventricular arrhythmia and ventricular tachycardia.[14] Furthermore, it is unreasonable to compare with clinical volume measurements obtained by cardiac ultrasonography because a postmortem heart dose not have the ability to contract and dilate, and the measuring methods are different. The results of this study can only be used for postmortem evaluation of the heart. Nevertheless, as this study is the first attempt to study Koreans and provided only 13 cases in the control group, more data from additional cases are required.

The group with dilated hearts showed increases in both ventricular weight and volume compared to the control group, with a more notable rise in ventricular volume. That group had ventricular volume to weight ratios of 60.2±11.3% for males and 61.6±3.1% for females.

In the clinical data of their comparative study, Wissler *et al.*[15] reported that cases with a left ventricular volume of more than 60 mL at autopsy are related to cardiac failure or cardiogenic shock, and that a large left ventricular volume is clinically associated with a reduction in stroke volume and cardiogenic shock. None of the cases in the control group of our study had a left ventricular volume exceeding 60 mL. All 14 cases in the dilated heart group, one of nine cases (11.1%) in the hypertrophied heart group, and one of 22 cases (4.5%) in the undetermined heart group had left ventricular volumes >60 mL. Such results suggest that measuring left and right ventricular volume separately when diagnosing the cause of death at autopsy could be a useful indicator for determining and differentiating cardiogenic deaths. The thickness of the left ventricular free wall and the interventricular septum of the dilated heart group were 1.1±0.2 cm and 1.2±0.2 cm for males and 1.2±0.1 cm and 1.2±0.1 cm for females. The thickness in the dilated heart group was smaller than those of the other three groups.

The hypertrophied heart group showed several characteristics. First, there was a significant increase in overall heart weight and ventricular weight. This is a large difference compared to the control, dilated heart and undetermined heart groups. Ventricular weight was measured separately along with conventionally measured overall heart weight. We consider the ventricular weight alone to be a more objective indicator for evaluating the heart at autopsy than the weight of the entire heart. This is because overall heart weight includes the weight of the atria and great vessels which are irrelevant to myocardial hypertrophy. There also may be differences in atrial and great vessel weight depending on autopsy skills.

Second, the hypertrophied heart group showed increases in volume, but to a lesser degree than those in the dilated heart group. We determined that ventricular volume was significant enough to be used to distinguish between a hypertrophied heart and a dilated heart. Notably, the ventricular volume to weight ratio for male in the hypertrophied heart group (24.1±9.5%) was similar to that in the control (22.7±9.3%) and the undetermined heart group (23.1±8.1%) but was far different from the dilated heart group (60.2±11.3%). Moreover, the left ventricle to right ventricle volume ratio for male in hypertrophied heart group was 64.4±21.7%, which was smaller than the control group (78.2±27.4%) and the ratio for the dilated heart group (90.3±7.3%). Such a result is the consequence of ventricular hypertrophy exceeding ventricular dilation in the hypertrophied heart group. The increase in ventricular volume was thought to be mostly due to the increase in right ventricular volume. Such characteristics of a hypertrophied heart are important distinguishing factors for identifying dilated hearts in which the ventricular volume has increased much more than the ventricular weight and when the left ventricular volume is more than the right ventricular volume.

Third, ventricular wall hypertrophy was observed. In general, primary hypertrophic cardiomyopathy usually results in hypertrophy of the interventricular septum, although the degree of hypertrophy can vary from slight (>1.3 cm) to severe (3.0-5.0 cm).[16] In this study, the hypertrophied heart group showed mostly slight hypertrophy of the interventricular septum, ranging from 1.5 to 2.0 cm. The degree of cardiac hypertrophy or obstruction of outflow in the left ventricle was unrelated to sudden death. However, extreme hypertrophy of the ventricular wall increases the risk of sudden death.[17-19] There is minimal risk of sudden death for ventricular hypertrophy < 1.9 cm, whereas this risk increases to approximately 40% at more than 3.0 cm of ventricular hypertrophy.[20] Of the nine cases in the hypertrophied heart group, seven cases led to sudden cardiogenic death, yet showed only slight hypertrophy. In other words, many cases seem to be connected to sudden death even when there was no severe thickening. There was one case of asymmetrical hypertrophy in which the left ventricular free wall to interventricular septum ratio was more than 1.3. The remaining eight cases were concentric hypertrophies. Most instances of primary hypertrophic cardiomyopathy involve asymmetrical hypertrophy, and in the majority of these, the thickened site is the interventricular septum.[21] Concentric hypertrophy is usually found in compensatory hypertrophic cardiomyopathy.[22] Thus, most cases in the hypertrophied heart group in this study were similar to compensatory secondary cardiac hypertrophy resulting from cardiac loading or other cardiac diseases. Nevertheless, one needs to consider the possibility that an observation could be subjective, as ventricular wall measurements could change depending on which part of the cardiac wall is measured, the direction of the cross section, and the exclusion or inclusion of the papillary muscle or trabeculae.

The undetermined heart group was similar to the hypertrophied heart group in that the ventricular volume to ventricular weight ratio was conserved when both ventricular weight and volume increased. Unlike the dilated heart group, which had an excess increase in volume compared to weight, the value in the undetermined heart group resembled that in the hypertrophied group. An analysis of the morphological change in hearts due to cardiac muscle remodeling based on ventricular weight and volume is shown in Fig. 3.

Cases similar to the dilated and hypertrophied heart group were found in the undetermined group. Cases 10, 13, 14, 17, 19, and 22 had increased ventricular weights compared to those in the control group (271.7±34.4 g for male, 219.3±23.9 g for female). The most evident morphological characteristics that distinguish hypertrophied hearts from dilated hearts was a more obvious increase in ventricular weight than volume, and in right ventricular volume than left in the hypertrophied heart. It was the opposite for the dilated heart group; a more marked increase in ventricular volume than ventricular weight was observed, particularly for left ventricular volume. Such characteristics were revealed using ventricular volume to weight ratios and left ventricular volume to right ventricular volume ratios. We determine that cases 10, 13, 14, and 19 were closely related to the hypertrophied heart group and that cases 17 and 22 were closer to the dilated heart group.

The heart of case 3 in the hypertrophied heart group showed features of both the hypertrophied and dilated heart groups, i.e., increased ventricular weight, ventricular free wall thickness, and ventricular volume, particularly left ventricular volume. But, the ventricular volume to weight ratio had increased mildly compare to that in the dilated heart group. Similarly, the hearts of cases 1 and 8 in the dilated heart group had increased ventricular weight, volume, and a mildly increased ventricular volume to weight ratio. These findings indicate that the heart of case 3 in the hypertrophied heart group and of cases 1 and 8 in the dilated heart group were between hypertrophied heart group and dilated heart group.

After reviewing the results, we conclude that analyzing ventricular weight and volume measurements is beneficial for identifying the spectral change of secondary cardiomyopathy in sudden cardiogenic death autopsy cases. Furthermore, measuring the ventricular weight and volume of hearts with secondary cardiac changes at autopsy is a useful indicator to determine the degree of change in gross appearance of the heart resulting from cardiac muscle remodeling. But, it is difficult to know whether secondary myocardial changes in the undetermined heart group would have progressed to a dilated heart through cardiac hypertrophy, because the progression of cardiac remodeling ceased at autopsy.

Several limitations should be noted. First, this study analyzed a limited number of cases because it was a forensic autopsy study. Second a molecular diagnosis of cardiomyopathy was not made. We were unable to analyze the results distinguishing primary from secondary cardiomyopathy. Third, contraction due to rigor mortis should be considered when a postmortem heart is evaluated. In our study, the standard deviations of ventricular volume in each group were large. We think that this was due to the small number of cases, rigor mortis of postmortem heart, and/or phase of cardiac contraction. Last, this study did not have any clinical information on the hearts obtained at autopsy. It would have been possible to do a comparative analysis between clinical results and the cardiac evaluation data measured at autopsy, if clinical data had been submitted.

Despite the limitations mentioned above, the results are significant. It is the first study in Korea to actually measure left and right ventricular volumes, which provide a standard for evaluating the gross appearance of the heart. Furthermore, we suggests a method and means for measuring ventricular weight and volume as an objective parameter that can aid in distinguishing between dilated cardiomyopathy and hypertrophic cardiomyopathy and two types of secondary cardiomyopathy. This ability was previously limited by conventional autopsy skills. Last, the results provide an objective indicator for evaluating the degree of change in secondary cardiac remodeling by measuring ventricular weight and volume. In conclusion, measuring the ventricular volume could be a new indicator that can complement the limitations of classical evaluation methods.

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