Association of Left Ventricular Hypertrophy with Hemoglobin Levels in Nonanemic and Anemic Populations

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Keywords

Anemia · Hemoglobin · Echocardiography · Left ventricular hypertrophy

Abstract

Introduction: It is established that anemia leads to adaptive changes in cardiac geometry including left ventricular hypertrophy (LVH). However, published data are still scarce regarding the association of LVH with normal-range hemoglobin levels. **Objective:** To evaluate the association between hemoglobin level and LVH in subjects with or without anemia. **Methods:** The study included 48,034 Korean men and women who received echocardiography during their medical health checkup. They were divided into 4 groups according to their hemoglobin concentration (g/dL) in men (<14, 14–14.9, 15–15.9, and ≥16) and women (<12, 12–12.9, 13–13.9, and ≥15). Multivariate logistic regression analysis was used to calculate adjusted ORs and 95% CI for LVH in each group compared with the group with the lowest hemoglobin. Subgroup analysis was conducted for subjects within

normal hemoglobin levels. **Results:** There was an inverse relationship between hemoglobin levels and LVH, where unadjusted and adjusted ORs and 95% CI for LVH decreased with increasing hemoglobin levels in both men and women. In subgroup analysis, this inverse relationship was also observed in subjects with hemoglobin in the nonanemic range. **Conclusion:** The decrease in hemoglobin was significantly associated with the increased probability of LVH, and this association was found even in nonanemic subjects.

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Introduction

Anemia is a medical condition frequently encountered in the clinical field. The estimated global prevalence of anemia is 24.8% (95% CI 22.9–26.7%), affecting 1.62 billion people (95% CI 1.50–1.74 billion) [1]. Despite the relatively high prevalence of anemia, its clinical implication tends to be underrated in anemic individuals without significant medical problems. However, anemia adverse-

ly affects the cardiovascular system [2], which can be associated with a poor cardiovascular outcome. Anemia is recognized as a potential pathophysiology of cardiac remodeling including left ventricular (LV) hypertrophy (LVH) [3]. Compensatory responses to tissue hypoxemia derived from anemia include increased cardiac output and high blood flow [3]. Previous studies have demonstrated that long-standing flow/volume overload and increased cardiac work result in progressive cardiac enlargement, and LVH in patients with chronic anemia [4–6].

LVH is an abnormal increase in the mass of the LV myocardium caused by a chronically increased workload on the heart [7], predicting cardiovascular morbidity and overall mortality. The prevalence of LVH is 15–21% in the general population and contributes to coronary artery disease, diastolic dysfunction, congestive heart failure, arrhythmia, and sudden cardiac death [8]. Considering the high prevalence of anemia and clinical implication of LVH in the general population, it is worth investigating the association between anemia and LVH with respect to managing potential cardiovascular risk-related LVH. However, most studies have evaluated the anemia-hemoglobin association in clinical patients with chronic kidney disease and overt heart failure [4–6], and only a few data are available for the general population [9]. Moreover, to the best of knowledge, no study has investigated the risk of LVH according to the levels of hemoglobin in individuals without anemia.

In a cohort of apparently healthy Koreans receiving echocardiography and laboratory examinations as part of their health checkup, we investigated the prevalence and association of LVH with different hemoglobin levels. Our subgroup analysis was conducted for subjects with normal hemoglobin level in order to identify the influence of low normal hemoglobin levels on the probability of LVH.

Methods

Study Design and Population

Relevant clinical and echocardiographic data were obtained from the Kangbuk Samsung Health Study (KSHS). Study subjects comprised Korean men and women undergoing a medical health checkup at the Health Promotion Center of the Kangbuk Samsung Hospital. Amongst individuals in the original study, 55,214 had received at least one echocardiogram including tissue Doppler echocardiography between January 2013 and December 2014. Among the 55,214 subjects, 161 had an arrhythmia such as atrial fibrillation, AV block, and tachycardia; 58 had a systolic LV dysfunction (ejection fraction $\leq 50\%$); 1,448 had a history of cancer;

1,017 had a serious medical condition such as cancer or chronic obstructive pulmonary disease; 386 had a history of myocardial infarction or angina; and 4,110 were further excluded for missing values of LV dimension, hemoglobin, and other covariates (e.g., alcohol intake). Finally, the total number of eligible subjects was 48,034.

Clinical and Laboratory Measurements

Study data include medical history assessed by self-administered questionnaire, anthropometric measurements, and laboratory measurements. All study subjects were asked to respond to a health-related behavior questionnaire, which included the topics of alcohol consumption, smoking, and exercise. The degree of physical activity was evaluated by the short form of the validated Korean version of the International Physical Activity Questionnaire (IPAQ). Diabetes mellitus (DM) was defined as fasting serum glucose level of at least 126 mg/dL, serum hemoglobin A_{1c} level of at least 6.5%, or a prior diagnosis of DM [10]. Hypertension was defined as a prior diagnosis of hypertension or having a measured blood pressure (BP) $\geq 140/90$ mm Hg at initial and follow-up examinations. Trained nurses measured BP in the sitting position by automatic device (53000-E2; Welch Allyn, USA). Body mass index (BMI) was calculated by dividing weight (kg) by height squared (m²).

Blood samples were drawn after >12 h of fasting from an antecubital vein. Fasting serum glucose was measured by the hexokinase method. Total cholesterol and triglycerides were measured by enzymatic colorimetric tests. High-density lipoprotein cholesterol (HDL-C) was measured by the homogeneous enzymatic colorimetric test and selective inhibition method, respectively. Hemoglobin and hematocrit were assessed using a flow-cytometric method (XE-2100: automated hematology analyzer; SISMEX, Kobe, Japan). Anemia was defined as a hemoglobin level <13 g/dL in men and <12 g/dL in women [11].

Echocardiographic Data Collection

LV function and structure were evaluated by two-dimensional transthoracic echocardiography with a 4-MHz, sector-type transducer probe (Vivid 7 and E9; GE, Milwaukee, WI, USA) in the study subjects. All echocardiography was performed by trained and registered sonographers following a standardized protocol [12]. Images from standard parasternal long- and short-axis views were digitally stored and reviewed. LV end-diastolic diameter (LVEDD), LV end-systolic diameter (LVESD), interventricular septum thickness (IVST), and posterior LV wall thickness (PWT) were routinely measured in all subjects. LVEDD was indexed by body surface area (BSA); (LVEDD/BSA). LV mass (LVM) (g) was calculated using the following formula: $LVM = 0.8 \times \{1.04 [(LVEDD + IVST + PWT)^3 - (LVEDD)^3]\} + 0.6$ g [12], and indexed for BSA to calculate LVM index (LVMI; g/m²); LV end systolic volume (LVESV), and LV end diastolic volume (LVEDV) were calculated using the following formula: $7.0 / (2.4 + LVESD) \times LVESD^3$ and $7.0 / (2.4 + LVEDD) \times LVEDD^3$. Relative wall thickness (RWT) was calculated by the formula $RWT = (2 \times PWT) / LVEDD$. LVH was defined as LVMI ≥ 115 g/m² in men or ≥ 95 g/m² in women, respectively. RWT >0.42 was determined as abnormal RWT [12]. The morphology of LVH was categorized into eccentric hypertrophy defined by LVH with normal RWT and concentric hypertrophy defined by LVH with abnormal RWT, based on standardized guidelines [12].

Table 1. Main clinical and echocardiographic characteristics of male study participants according to the hemoglobin level

Characteristics	<14 g/dL (n = 1,571)	14–14.9 g/dL (n = 8,119)	15–15.9 g/dL (n = 15,008)	≥16 g/dL (n = 10,344)	p value
Age, years	43.5±8.2	41.3±7.4	40.2±7.2	39.6±7.0	<0.001
Fasting glucose, mg/dL	96.8±13.2	97.0±13.6	97.6±15.4	99.7±19.8	<0.001
HDL-C, mg/dL	54.5±13.8	53.9±12.9	52.5±12.6	51.4±12.8	<0.001
Hemoglobin, g/dL	13.4±0.7	14.6±0.3	15.5±0.3	16.5±0.5	<0.001
Hematocrit, %	40.0±1.9	42.7±1.1	44.9±1.2	47.5±1.6	<0.001
Blood pressure, mm Hg					
Systolic	110.4±11.0	111.7±10.9	113.5±11.1	116.3±11.7	<0.001
Diastolic	71.6±9.0	73.0±9.0	74.7±9.2	77.4±9.8	<0.001
Body mass index, kg/m ²	23.9±2.8	24.3±2.9	24.7±3.0	25.3±3.1	<0.001
Average alcohol use, g/day	16.5±21.8	16.7±22.2	17.5±22.8	19.3±25.2	<0.001
Current smokers, %	24.8	26.5	29.4	34.6	<0.001
High PA, %	16.9	15.8	13.5	12.3	<0.001
Diabetes mellitus, %	8.5	5.8	5.2	6.6	<0.001
Hypertension, %	18.8	16.6	16.8	21.1	<0.001
LVM, g	147.6±30.6	145.5±29.7	144.3±29.3	145.6±30.5	<0.001
LVMI, g/m ²	79.8±15.1	77.7±14.1	76.3±13.7	76.1±14.1	<0.001
LVEDD/BSA, mm/m ²	27.6±2.3	27.1±2.2	26.6±2.2	26.1±2.3	<0.001
RWT	0.325±0.046	0.326±0.047	0.331±0.049	0.339±0.052	<0.001
Left ventricular hypertrophy	36 (2.2)	69 (0.8)	117 (0.8)	100 (1.0)	<0.001
Concentric	4 (11.1)	22 (31.8)	43 (36.7)	51 (51)	
Eccentric	32 (88.8)	47 (68.1)	74 (63.2)	49 (49)	
Ejection fraction	66.8±5.6	66.7±5.6	66.8±5.6	67.0±5.8	0.021

Continuous variables are expressed as means ± SD, and categorical variables as percentages or numbers (%). HDL-C, high-density lipoprotein cholesterol; PA, physical activity; LV, left ventricular; LVEDD/BSA, LV end-diastolic diameter/body surface area; LVM, LV mass; LVMI, LVM index; RWT, relative wall thickness.

Ejection fraction (EF) was calculated using the following formula: $EF = (LVEDV - LVESV) / LVEDV \times 100$. Echocardiographic measurements and subject characteristics were presented in our previously published studies [13, 14].

Statistical Analyses

Study subjects were categorized into 4 groups according to the hemoglobin levels in men (<14, 14–14.9, 15–15.9, and ≥16 g/dL) and women (<12, 12–12.9, 13–13.9, and ≥14 g/dL). In the reference group, hemoglobin level was set to <14 g/dL in men and <12 g/dL in women.

Data are presented as means ± SD for continuous variables and as proportions for categorical variables. Main clinical characteristics and echocardiographic parameters among groups were compared using ANOVA and the χ^2 test for continuous variables and categorical variables, respectively.

The unadjusted and adjusted ORs and 95% CI for LVH were calculated by logistic regression analysis. Covariates with significant differences in their group means or established cardiovascular risk factors (BMI, age, physical activity, alcohol intake, systolic BP, fasting glucose, smoking, and HDL-C) were adjusted for. The subgroup analyses are conducted in subjects within normal hemoglobin level in both men and women.

Linear regression analysis was applied to calculate the rate of LVMI increase (g/m²) per 1 g/dL decrease in hemoglobin.

Generalized additive model analyses were performed to assess the association of the hemoglobin level with the presence of LVH and LVMI as a continuous variable.

All statistical analyses were performed using R 3.5.1 (R Foundation for Statistical Computing, Vienna, Austria), and a value of $p < 0.05$ was considered to be statistically significant.

Results

The clinical and echocardiographic characteristics of the male and female study participants are represented in Tables 1 and 2, respectively. The mean age of the study subjects was 40.4 ± 7.3 years in men and 38.3 ± 8.6 years in women. In males, the group with the highest hemoglobin level (≥16 g/dL) had significantly higher mean values in fasting glucose, systolic and diastolic BP, BMI, and average alcohol consumption (g/day), and were more often

Table 2. Main clinical and echocardiographic characteristics of female study participants according to the hemoglobin level

Characteristics	<12 g/dL (n = 1,570)	12–12.9 g/dL (n = 3,645)	13–13.9 g/dL (n = 5,488)	≥14 g/dL (n = 2,289)	p for trend
Age, years	39.7±7.1	38.1±8.1	38.2±8.9	38.2±9.6	<0.001
Fasting glucose, mg/dL	90.3±12.1	89.9±9.3	91.1±10.4	93.7±17.9	<0.001
HDL-C, mg/dL	65.5±15.5	66.0±14.6	65.4±15.0	65.0±17.0	0.080
Hemoglobin, g/dL	10.9±1.0	12.5±0.3	13.4±0.3	14.4±0.4	<0.001
Hematocrit, %	33.8±2.4	37.6±1.1	39.9±1.1	42.4±1.3	<0.001
Blood pressure, mm Hg					
Systolic	100.7±10.9	99.3±10.2	101.6±11.1	104.5±11.9	<0.001
Diastolic	63.7±8.5	63.4±8.1	65.4±8.5	68.1±9.1	<0.001
Body mass index, kg/m ²	21.9±2.9	21.6±2.9	21.9±3.2	22.3±3.7	<0.001
Average alcohol use, g/day	3.7±9.1	4.4±11.6	4.9±12.5	5.2±11.9	<0.001
Current smokers, %	1.1	1.5	1.8	2.9	<0.001
High PA, %	13.0	12.7	13.2	11.5	0.604
Diabetes mellitus, %	2.0	1.6	2.1	4.2	<0.001
Hypertension, %	4.3	4.1	5.8	8.7	<0.001
Postmenopausal state, %	4.1	8.4	10.7	12.6	<0.001
LVM, g	110.4±23.1	104.3±22.1	104.2±23.3	103.9±25.0	<0.001
LVMI, g/m ²	69.7±12.5	66.2±12.1	65.6±12.6	65.0±13.4	<0.001
LVEDD/BSA, mm/m ²	30.2±2.5	29.8±2.3	29.3±2.4	28.8±2.5	<0.001
RWT	0.301±0.046	0.299±0.046	0.304±0.048	0.314±0.052	<0.001
Left ventricular hypertrophy	56 (3.6)	91 (2.5)	127 (2.3)	67 (2.9)	0.035
Concentric	7 (7.1)	14 (15.3)	24 (18.8)	18 (26.8)	
Eccentric	49 (87.5)	77 (84.6)	103 (81.1)	49 (73.1)	
Ejection fraction	67.7±5.4	67.3±5.3	67.5±5.4	68.0±5.7	<0.001

For further information, see legend to Table 1 or text.

current smokers and hypertensive than the other groups (Table 1). In females, the group with the highest hemoglobin level (≥14 g/dL) had higher mean values of fasting glucose, systolic and diastolic BP, BMI, and average alcohol consumption (g/day), and were more often current smokers, hypertensive, or in menopause, or had DM than other groups (Table 2). With respect to echocardiographic parameters, the group with the lowest hemoglobin level had the highest mean values of LVM (g), LVMI (g/m²), and less often LVH in both men and women, but mean RWT values were lower in the group with the lowest hemoglobin level than in the other groups. Eccentric LVH is the dominant morphology in groups with low hemoglobin.

Multivariate logistic regression analysis indicated an inverse relationship between hemoglobin level and LVH. In men, compared to the group with the lowest hemoglobin level (<14 g/dL: reference), the other groups showed a stepwise decrease in adjusted ORs for LVH according to hemoglobin levels (14–14.9 g/dL: 0.37 [0.24–0.55], 15–15.9 g/dL: 0.34 [0.23–0.49], and ≥16 g/dL: 0.35 [0.23–

0.53]; Table 3). Women showed similar findings at hemoglobin levels ≥13 g/dL (Table 4). These trends were identical even in nonanemic men (13–13.9 g/dL: reference, 14–14.9 g/dL: 0.45 [0.28–0.71], 15–15.9 g/dL: 0.40 [0.26–0.62], and ≥16 g/dL: 0.40 [0.25–0.63]) and nonanemic women (12–12.9 g/dL: reference, 13–13.9 g/dL: 0.66 [0.49–0.89] and ≥14 g/dL: 0.66 [0.46–0.95]). In a linear regression analysis, each 1 g/dL increase in hemoglobin was associated with LVMI decreases of –1.24 g/m² in men and –0.86 g/m² LVMI in women.

Online supplementary Figures 1 and 2 (see www.karger.com/doi/10.1159/000508034) indicate generalized additive model analyses for LVH and LVMI in men and women, respectively.

Discussion

In a Korean study cohort, a lower hemoglobin level was associated with a higher LVM and LVMI, which led to an inverse relationship between hemoglobin and LVH

Table 3. OR and 95% CIs for left ventricular hypertrophy according to the hemoglobin level in men

Characteristics	<14 g/dL	14–14.9 g/dL	15–15.9 g/dL	≥16 g/dL
All participants, <i>n</i>	1,571	8,119	15,008	10,344
Unadjusted OR	1.00 (ref.)	0.37 (0.24–0.55)	0.34 (0.23–0.49)	0.42 (0.28–0.61)
Model 1	1.00 (ref.)	0.32 (0.21–0.48)	0.26 (0.17–0.38)	0.24 (0.16–0.36)
Model 2	1.00 (ref.)	0.31 (0.21–0.48)	0.25 (0.15–0.34)	0.23 (0.15–0.34)
Model 3	1.00 (ref.)	0.39 (0.26–0.60)	0.35 (0.24–0.53)	0.35 (0.23–0.53)
Nonanemic subjects, <i>n</i>	1,401 ¹	8,119	15,008	10,344
Unadjusted OR	1.00 (ref.)	0.44 (0.28–0.68)	0.40 (0.26–0.61)	0.50 (0.32–0.76)
Model 1	1.00 (ref.)	0.38 (0.24–0.59)	0.30 (0.20–0.46)	0.29 (0.18–0.44)
Model 2	1.00 (ref.)	0.37 (0.23–0.58)	0.29 (0.19–0.44)	0.27 (0.17–0.42)
Model 3	1.00 (ref.)	0.45 (0.28–0.71)	0.40 (0.26–0.62)	0.40 (0.25–0.63)

Model 1, unadjusted model + systolic blood pressure; model 2, model 1 + body mass index; model 3, model 2 + age, physical activity, alcohol intake, fasting glucose, smoking, and high density lipoprotein cholesterol.

¹ Hemoglobin 13–13.9 g/dL.

Table 4. OR and 95% CIs for left ventricular hypertrophy according to the hemoglobin level in women

Characteristics	<12 g/dL	12–12.9 g/dL	13–13.9 g/dL	≥14 g/dL
All participants, <i>n</i>	1,570	3,645	5,448	2,289
Unadjusted OR	1.00 (ref.)	0.69 (0.49–0.97)	0.64 (0.47–0.88)	0.82 (0.57–1.17)
Model 1	1.00 (ref.)	0.78 (0.55–1.10)	0.55 (0.40–0.77)	0.54 (0.37–0.79)
Model 2	1.00 (ref.)	0.79 (0.55–1.12)	0.54 (0.39–0.76)	0.52 (0.35–0.76)
Model 3	1.00 (ref.)	0.74 (0.51–1.07)	0.49 (0.34–0.69)	0.49 (0.33–0.73)
Nonanemic subjects, <i>n</i>		3,645	5,448	2,289
Unadjusted OR	–	1.00 (ref.)	0.93 (0.70–1.22)	1.18 (0.86–1.62)
Model 1	–	1.00 (ref.)	0.71 (0.53–0.94)	0.69 (0.49–0.97)
Model 2	–	1.00 (ref.)	0.69 (0.52–0.91)	0.65 (0.46–0.92)
Model 3	–	1.00 (ref.)	0.66 (0.49–0.89)	0.66 (0.46–0.95)

See legend to Table 3 for further information.

in both men and women. The probability of LVH in men with hemoglobin ≥14.9 g/dL and women with hemoglobin ≥13 g/dL was less than half of that in men with hemoglobin <13 g/dL and women with hemoglobin <12 g/dL, respectively. These findings suggest that the decrease in hemoglobin may be associated with an increased risk of LVH. The results of previous studies are in agreement with our results. Adaptive changes in the cardiac geometry frequently occur in chronic anemia [4–6]. Adverse effects of anemia on the LV structure have primarily been studied in patients with chronic illnesses like chronic kidney disease, sickle cell anemia, and underlying cardiovascular diseases [4–6, 15]. Epidemiological studies have indicated a significant association between anemia and LVH even in the general population without known car-

diovascular diseases [9, 16, 17]. These results suggest that anemic levels of hemoglobin are potentially associated with adverse changes in the cardiac geometry. However, data indicating whether this association is still valid in a nonanemic population are still limited. Our analysis shows that subjects with low normal hemoglobin level have a higher probability of LVH than other groups irrespective of gender. This finding suggests that low normal hemoglobin levels are associated with LV remodeling, and consequently LVH.

The presence of LVH in the general population predicts cardiovascular morbidity and mortality [7]. Thus, the high probability of LVH at low normal hemoglobin may be translated into an increased cardiovascular risk in individuals with low normal hemoglobin. Moreover,

considering the mean age of our study subjects (40.4 ± 7.3 in men and 38.3 ± 8.6 years in women), it is inferred that the adverse influence of low normal hemoglobin on cardiac geometry occurs at relatively young age. Earlier presence of LVH may have more adverse effects on the cardiovascular system with the passage of time. Thus, our results may be evidence for the clinical usefulness of hemoglobin measurements to screen individuals at high cardiovascular risk.

In our analysis, subjects with the highest hemoglobin levels (men ≥ 16 g/dL and women ≥ 14 g/dL) had higher mean levels of fasting glucose, BP, BMI, and average alcohol consumption than the groups with the lowest hemoglobin levels (men < 14 g/dL and women < 12 g/dL). These findings seem to be conflicting with previous reports indicating a role of metabolic diseases, including obesity, insulin resistance, and high BP, in the pathogenesis of LVH [18–21]. The metabolic characteristics of our study subjects may be an explanation for these results. In our study subjects, the number of subjects with poor metabolic profiles may be small. In general, our subjects had a favorable metabolic profile with mean fasting glucose, BP, HDL-C, and BMI within normal ranges. Therefore, it is likely that the effect of the metabolic condition on cardiac geometry may be modest in these subjects. Nonetheless, it is of note that women showed more marginal levels in unadjusted and adjusted ORs and 95% CI for LVH than men. This finding suggests that the effect of metabolic conditions on cardiac geometry is more powerful in women than men.

With respect to echocardiographic parameters, while the groups with the lowest hemoglobin level had the highest mean values in LVM and LVMI and the highest prevalence of LVH in both men and women, RWT was lower in the groups with the lowest hemoglobin level than in the groups with the highest hemoglobin. The eccentric pattern of cardiac remodeling is characterized by high LVM and normal RWT [12]. In practice, our analysis showed that the proportion of eccentric hypertrophy increased with the decrease in hemoglobin levels. Previous studies have also found that eccentric LV growth is a common form of cardiac remodeling in anemic patients [4–6, 16, 22]. Hemodynamic compensation for anemia includes the reduction in afterload due to a decrease in systemic vascular resistance, the increase in preload due to an increase in venous return, and increased sympathetic activity and inotropic factors [2]. These adaptive physiological changes may lead to cardiac volume overload, resulting in eccentric LVH. Our results support the notion that volume overload is

a major pathophysiology of LV remodeling in anemic patients. Additionally, it is noted that this cardiac geometry change can begin even in individuals with low normal hemoglobin level.

The merits of this study are the large sample size and reliable clinical data including echocardiography and laboratory examinations. These advantages enabled us to evaluate the association of LVH with hemoglobin levels across anemic and nonanemic ranges.

Nonetheless, several limitations should be acknowledged in the present study.

First, the results from cross-sectional design studies are limited in providing the causative relationship and prognostic implication. In particular, it is not guaranteed that the observed association links to long-term cardiovascular prognosis. Further longitudinal studies should be conducted to investigate whether the association between hemoglobin and LVH results in adverse cardiovascular outcome.

Second, although the hemodynamic status is important in the pathogenesis of LVH, our findings are not representative of the real hemodynamic status in given hemoglobin levels. Additionally, because the lowest hemoglobin level was set as reference, our results could not suggest an influence of high hemoglobin levels on cardiac geometry.

Conclusion

In conclusion, in a large Korean population, a low hemoglobin concentration was significantly associated with the risk of LVH. This association was identically observed in subjects with low normal hemoglobin level. These findings evoke the clinical implication of hemoglobin measurement in assessing cardiovascular risk.

Acknowledgment

This study was based on medical data collected and arranged by the Kangbuk Samsung Cohort Study (KSCS). Therefore, this study could be done by virtue of the labor of all staffs working in KSCS and Total Healthcare Center, Kangbuk Samsung Hospital.

Statement of Ethics

Ethics approval for the study protocol and analysis of the data was obtained from the institutional review board of Kangbuk Samsung Hospital. Informed consent was not required because we only assessed retrospective data without personal identifying information.

Disclosure Statement

The authors have no conflicts of interest.

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Author Contributions

S.K.P. coordinated the study, analyzed the data, and wrote the manuscript as a first author. J.G.K. verified the data on echocardiographic parameters as a cardiologist. H.P.H. participated in conducting the study and manuscript writing. C.-M.O. played a role in data analysis and editing English grammar. J.Y.J. is the guarantor of this work and, as such, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. All authors had access to the data used in this study and participated in writing the manuscript.

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