SYSTEMATIC REVIEW

Prognosis associated with geometric patterns of left ventricular remodeling: systematic review and network meta-analysis [version 1; peer review: 1 approved with reservations, 1 not approved]

Qishi Zheng^{1,2*}, Germaine Loo^{3*}, Thu-Thao Le^{4,5}, Luming Shi^{1,2,6}, Edwin Shih-Yen Chan^{1,2,6}, Calvin W. L. Chin^{ 4,5}

¹Department of Epidemiology, Singapore Clinical Research Institute, Singapore, Singapore

²Cochrane Singapore, Singapore, Singapore

³Department of Internal Medicine, Singapore General Hospital, Singapore, Singapore

⁴Department of Cardiology, National Heart Center Singapore, Singapore, Singapore

⁵Cardiovascular Sciences ACP, Duke NUS Graduate Medical School, Singapore, Singapore

⁶Centre for Quantitative Medicine, Duke NUS Graduate Medical School, Singapore, Singapore

* Equal contributors

V1 First published: 19 Jul 2019, 8:1130
<https://doi.org/10.12688/f1000research.19907.1>

Latest published: 19 Jul 2019, 8:1130
<https://doi.org/10.12688/f1000research.19907.1>

Abstract

Background: There are four geometric patterns (normal geometry, concentric remodeling, concentric and eccentric hypertrophy) used to describe cardiac remodeling. Although left ventricular hypertrophy (LVH) is associated with adverse prognosis, the incremental prognostic value of geometric patterns is less certain. We examined characteristics and prognosis associated with the four conventional patterns of left ventricle (LV) remodeling.

Methods: A comprehensive literature search was performed on MEDLINE/PubMed, Embase and the Cochrane Library until January 2019. Network meta-analysis was used to pool data from direct and indirect prognostic comparisons of the four geometric patterns. All-cause mortality was defined as the study outcome.

Results: A total of 22 echocardiographic studies (76,142 individuals; 50.1% males; 64.4±7.9 years) of diverse cardiovascular diseases were included. Concentric LVH was associated with the highest prevalence of cardiovascular risk factors and diseases; and eccentric hypertrophy was associated with a high prevalence of atrial fibrillation and low LV ejection fraction. Compared to normal geometry, the risk of all-cause mortality was increased in concentric hypertrophy (risk ratio 1.97 [95% confidence interval 1.63-2.39]) but similar to eccentric hypertrophy (risk ratio 1.15 [95% confidence interval 0.97-1.36]).

Conclusions: The study populations examined in the meta-analysis

Open Peer Review

Approval Status

	1	2
version 1
19 Jul 2019	view	view

1. **Bruno Trimarco**, University of Naples
 Federico II, Naples, Italy

2. **Tee Joo Yeo** , National University Heart
 Centre Singapore, National University Health
 System, Singapore, Singapore

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were heterogeneous. Concentric LVH conferred the highest risk of all-cause mortality that overlapped with eccentric hypertrophy. Strategies to improve LVH risk stratification should be examined in future research.

Keywords

Left ventricular hypertrophy, geometric patterns of left ventricular remodeling, concentric remodeling, concentric hypertrophy, eccentric hypertrophy

Corresponding author: Calvin W. L. Chin (cchin03m@gmail.com)

Author roles: **Zheng Q:** Data Curation, Formal Analysis, Methodology, Writing – Original Draft Preparation, Writing – Review & Editing; **Loo G:** Data Curation, Formal Analysis, Methodology, Writing – Original Draft Preparation; **Le TT:** Data Curation, Writing – Review & Editing; **Shi L:** Formal Analysis, Methodology, Writing – Review & Editing; **Chan ESY:** Formal Analysis, Methodology, Writing – Review & Editing; **Chin CWL:** Conceptualization, Project Administration, Supervision, Writing – Original Draft Preparation, Writing – Review & Editing

Competing interests: No competing interests were disclosed.

Grant information: The author(s) declared that no grants were involved in supporting this work.

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How to cite this article: Zheng Q, Loo G, Le TT *et al.* **Prognosis associated with geometric patterns of left ventricular remodeling: systematic review and network meta-analysis [version 1; peer review: 1 approved with reservations, 1 not approved]** F1000Research 2019, 8:1130 <https://doi.org/10.12688/f1000research.19907.1>

First published: 19 Jul 2019, 8:1130 <https://doi.org/10.12688/f1000research.19907.1>

Introduction

The left ventricle (LV) remodels as a response to cardiovascular disease and myocardial injury. Characterized by an increase in LV myocardial mass, left ventricular hypertrophy (LVH) is an established predictor of poorer cardiovascular outcomes¹.

Four classical geometric patterns of LV remodeling have been defined based on LV mass and relative wall thickness: normal, concentric remodeling, concentric and eccentric hypertrophy². This convenient approach of characterizing LV remodeling has been studied across various patient populations, including patients with coronary artery disease, aortic stenosis, hypertensive heart disease and community-based general populations^{3–6}. Whilst some studies demonstrated prognostic associations with these patterns of LV remodeling, others have not. Knowledge of remodeling patterns (concentric and eccentric hypertrophy) provided particularly limited incremental prognostic information beyond LVH^{1,7–10}.

In this study, we aim to conduct a comprehensive systematic review and network meta-analysis to examine the characteristics and prognosis associated with the four conventional geometric patterns of LV remodeling.

Methods

Literature search and eligibility criteria

A comprehensive literature search was performed on MEDLINE/PubMed (1946 onwards), Embase (1974 onwards) and the Cochrane Library (1996 onwards) until January 2019. Full text publications evaluating the four conventional LV geometry patterns (normal geometry, concentric remodeling, concentric and eccentric hypertrophy) and prognosis were included. The basic search protocol and specific terms used in the search strategy are available as *Extended data*¹¹. We conducted the literature search using Medical Subject Headings or Emtree, and free text terms. There were no restrictions on language.

Two investigators (Q.Z. and G.L.) independently searched for eligible studies based on the pre-defined eligibility criteria. Full-text studies that compared the prognosis of the four conventional LV geometry patterns (i.e. normal geometry, concentric remodeling, concentric and eccentric hypertrophy) were included. We excluded publications in non-adult populations, case reports, commentaries, abstracts, letters-to-editors and review articles. The bibliography in the identified publications and review articles were also reviewed.

Data extraction and quality assessment

The following data were extracted in duplicates by the two investigators (Q.Z. and G.L.) from the included studies: (1) study characteristics (publication year and patient population); (2) baseline characteristics (mean age, sex distribution, and proportion of patients with hypertension, coronary artery disease, diabetes and other significant risk factors); (3) the four LV remodeling patterns; and (4) adverse prognosis defined as all-cause mortality. Eligible studies that did not report all-cause mortality as an end-point were still included to examine

clinical characteristics associated with geometric patterns of LV remodeling. Any disagreements were resolved by discussion with a third investigator (C.W.L.C.). In publications with survival curves, the cumulative survival rates were estimated by digitizing the plots (WebPlotDigitizer version 3.9, Austin, Texas, USA).

Two investigators (C.W.L.C. and Z.Q.) independently appraised the quality of each study using the Quality In Prognosis Studies tool¹². Six domains (study participation, study attrition, prognostic factor measurement, outcome measurement, study confounding; and statistical analysis and reporting) were evaluated to assess the risk of bias in the prognostic studies. In each of the six domains, the risk of bias was classified as “low”, “moderate” or “high”.

Statistical analysis

A network geometry of the four LV remodeling patterns was constructed. Each node represented a remodeling pattern and its size was weighted by the number of individuals in that group. The connecting line between two nodes denoted direct comparison and its thickness reflected the number of studies included.

The random-effects meta-regression models were used to measure the impact of baseline characteristics on the effect size of the outcome. The risk ratio (RR) of each LV remodeling group was estimated and reported in the study. To rank the prognosis of all the geometric patterns, we used surface under the cumulative ranking (SUCRA) values¹³. Rank probabilities of all the groups were first estimated, then followed by a step function to summarize the cumulative ranking for estimating the SUCRA values of each group, ranging from 0 to 100%. Larger SUCRA values indicated better prognosis.

Both node-splitting and inconsistency modeling were used to test the consistency assumption. The former method involved fitting a series of node-splitting models, one model for each group pair in which there was direct and indirect comparisons. In the latter method, an inconsistency model was fitted and the global Wald test would determine if significant inconsistency was present¹⁴. Statistical analyses were performed using Stata/MP Version 13 (StataCorp., College Station, Texas, USA), with the network and network graphs package.

Results

Studies and participants

From an initial 257 publications, 22 echocardiographic studies of diverse cardiovascular diseases satisfied inclusion/exclusion criteria and were included in this study (Figure 1)^{6–10,15–31}. The thresholds used to define LVH and increased concentricity were heterogeneous across the studies (Table 1).

Of the 76,142 individuals pooled from the 22 studies (50.1% males; 64.4±7.9 years), 49.7% had normal geometry; and 31.1%, 10.5% and 8.7% had concentric remodeling, concentric and eccentric hypertrophy, respectively. The proportion of females with concentric and eccentric hypertrophy was high (40–45%). Compared to the other geometric patterns, concentric

Figure 1. PRISMA flow chart. The systematic review and network meta-analysis was conducted according to the guidelines recommended by PRISMA.

hypertrophy was associated with the highest prevalence of cardio-metabolic risk factors and cardiovascular diseases. Eccentric hypertrophy was associated with a high prevalence of atrial fibrillation and low LV ejection fraction (Table 2).

Adverse prognosis associated with geometric patterns of left ventricular remodeling

Most of the studies demonstrated low risk of bias in the six domains examined (Table 3). The network geometry of LV remodeling patterns was constructed in Figure 2. Concentric remodeling was associated with higher all-cause mortality compared to normal geometry (RR 1.56 [95% confidence interval (CI): 1.31 to 1.85]), and a lower mortality risk compared to concentric hypertrophy (RR 0.79 [95% CI 0.67 to 0.93]). The mortality risk of concentric remodeling was similar compared to eccentric hypertrophy (RR 0.91 [95% CI 0.76 to 1.09]) (Table 4).

Compared to normal geometry, concentric hypertrophy was associated with highest risk of all-cause mortality (RR 1.97 [95% CI 1.63 to 2.39]; Table 4). The confidence limits overlapped

with eccentric hypertrophy (RR 1.71 [95% CI 1.43 to 2.04]). Moreover, the mortality risk of concentric hypertrophy was not significantly increased compared to eccentric LVH (RR 1.15 [95% CI 0.97 to 1.36]). Based on the SUCRA values, the geometric patterns ranked from best to worst prognosis were: normal geometry, concentric remodeling, eccentric hypertrophy and concentric hypertrophy (Figure 3).

Results from both node-splitting method and inconsistency model showed no evidence on the violation of consistency assumption between direct and indirect comparisons. Specifically, the pooled estimates between models of consistency (red diamonds) and inconsistency (green diamonds) were identical because all the studies included the four remodeling patterns (Figure 4).

Discussion

In this systematic review and network meta-analysis of 22 echocardiographic publications (n=76,133 individuals), we report the characteristics and prognosis associated with the

Table 1. Baseline characteristics of included studies.

Reference	Population	Patients (n)	Females (n)	Age (years)	Definition of left ventricular hypertrophy		Definition of increased concentricity	Follow-up duration (years)
					Males (g/m ²)	Females (g/m ²)		
Beger 2011	Coronary artery disease	973	251	66.8	102	88	Posterior Wall thickness; 11mm	4.9
Verma 2008	Coronary artery disease	603	192	65.6	115	95	RWT; 0.42	2.1
Ghali 1998*	Coronary artery disease	446	201	56.9	131	100	RWT; 0.45	9.0
Shigematsu 1998	Hypertension	77	25	57.0	125	125	RWT; 0.44	Not stated
Gerdtz 2008	Hypertension	937	388	65.5	116	104	RWT; 0.43	4.8
Fabiani 2017	Hypertension	749	325	62.0	115	95	RWT; 0.42	3.7
Verdecchia 1996	Hypertension	274	37	53.0	125	125	RWT; 0.45	3.2
Kohara 1999	Hypertension	150	78	58.3	118	108	RWT; 0.41	Not stated
Krumholz 1995	General Population	3209	1813	57.0	143	102	RWT; 0.45	7.7
Lieb 2014	General Population	4492	216	53.3	207g	170g	RWT; Males: 0.419; Females: 0.435	4.0
Gardin 2001	General Population (>65 years old)	2506	1622	-	>95th percentile	>95th percentile	RWT; 0.48	6.0
Milani 2006	Patients EF>50%	35, 602	18, 869	60.0	116	104	RWT; 0.43	3.2
Lavie 2006	Patients EF>50% (>70 years old)	9771	5569	77.5	116	104	RWT; 0.43	3.1
Lavie 2009	Patients EF>50% (>70 years old)	8088	4564	77.0	116	104	RWT; 0.43	3.1
Ghali 1998*	Patients EF>45%	542	347	54.0	131	100	RWT; 0.45	9.0
Katz 2013	HFpEF	402	251	62.8	48g/m ^{2.7}	44g/m ^{2.7}	RWT; 0.42	1.0
Apostolakis 2014	Atrial fibrillation	2433	1058	69.0	115	95	RWT; 0.42	3.5
Shah 2014	Atrial Fibrillation	1088	496	69.1	115	95	RWT; 0.42	6
Debry 2017	Aortic stenosis	331	150	73.0	115	95	RWT; 0.42	3.1
Capoulade 2017	Aortic stenosis	747	426	69.0	49g/m ^{2.7}	47g/m ^{2.7}	RWT; 0.42	6.4
Rymuza 2017	Aortic stenosis (TAVI)	208	107	79.4	115	95	RWT; 0.42	1.5
Paoletti 2016	Chronic kidney disease	445	222	64.0	131	100	RWT; 0.45	5.9
Park 2018	Ischemic strokes	2069	787	65.5	115	95	RWT; 0.42	3.1

* Two populations were studied in the same publication.

RWT regional wall thickness; HFpEF heart failure preserved ejection fraction; EF ejection fraction; TAVI transcatheter aortic valve implantation

Table 2. Clinical characteristics associated with geometric patterns of left ventricular remodeling.

	Normal Geometry	Concentric Remodeling	Concentric Hypertrophy	Eccentric Hypertrophy
Age, years	61.7	65.3	65.4	64.1
Females, %	15.8	25.1	45.6	42.2
Systolic blood pressure, mmHg	134.6	136.7	147.1	141.5
Diabetes mellitus, %	9.4	16.7	24.4	17.5
Hypertension, %	27.6	44.0	67.1	58.1
Coronary artery disease, %	6.9	12.8	22.1	9.7
Strokes, %	3.5	5.5	7.1	4.4
Atrial fibrillation, %	11.2	21.3	23.9	22.3
Left ventricular mass index, g/m ²	83.9	84.8	133.3	127.2
Regional wall thickness	0.95	1.13	1.29	1.08
Ejection fraction, %	59.2	60.9	58.9	53.3

Table 3. Assessing quality of prognostic studies in systematic reviews.

Reference	Study participation	Study attrition	Prognostic factor measurement	Outcome measurement	Study confounding	Statistical analysis and reporting
Krumholz 1995	Low	Low	Low	Low	Low	Low
Verma 2008	Low	Low	Low	Low	Low	Low
Lieb 2014	Low	Low	Low	Low	Low	Low
Gardin 2001	Low	Low	Low	Low	Low	Low
Milani 2006	Low	Low	Moderate	Moderate	Low	Low
Lavie 2006	Low	Low	Moderate	Moderate	Low	Low
Beger 2011	Low	Low	Low	Low	Low	Low
Katz 2013	Low	Moderate	Low	Low	Low	Low
Verdecchia 1996	Low	Low	Low	Low	Low	Low
Kohara 1999	Low	Low	Low	Low	Low	Moderate
Apostolaskis 2014	Low	Low	Low	Low	Low	Low
Ghali 1998	Low	Low	Low	Low	Low	Low
Debry 2017	Low	Low	Low	Low	Low	Low
Paoletti 2016	Low	Low	Low	Low	Low	Low
Shigematsu 1998	Low	Low	Low	Low	Low	Low
Gerdts 2008	Low	Low	Low	Low	Low	Low
Fabiani 2017	Low	Low	Low	Low	Low	Low
Park 2018	Low	Low	Low	Low	Low	Low
Lavie 2009	Low	Low	Moderate	Moderate	Low	Low
Capoulade 2017	Low	Low	Low	Low	Low	Low
Rymuza 2017	Low	Moderate	Low	Low	Low	Low
Shah 2014	Low	Low	Low	Low	Low	Low

Figure 2. Network constructed for the different left ventricular remodeling patterns. The numbers on the connecting lines denote the studies included for direct comparison.

Table 4. Prognosis associated with geometric patterns of left ventricular remodeling. Results presented in risk ratio and corresponding 95% confidence interval.

	Reference group			
	Normal Geometry	Concentric Remodeling	Concentric Hypertrophy	Eccentric hypertrophy
Normal Geometry	1.00	0.64 [0.54, 0.76]*	0.51 [0.43, 0.60]*	0.59 [0.49, 0.70]*
Concentric Remodeling	1.56 [1.31, 1.85]*	1.00	0.79 [0.67, 0.93]*	0.91 [0.76, 1.09]
Concentric Hypertrophy	1.97 [1.63, 2.39]*	1.27 [1.08, 1.49]*	1.00	1.15 [0.97, 1.36]
Eccentric Hypertrophy	1.71 [1.43, 2.04]*	1.10 [0.92, 1.31]	0.87 [0.73, 1.03]	1.00

*p-value < 0.05

Test of consistency: $\chi^2(1)=2.72$, $P=0.099$

Figure 3. Forest plot of direct comparisons with pooled results from network meta-analysis. A, normal geometry; B, concentric remodeling; C, concentric hypertrophy; D, eccentric hypertrophy.

different patterns of LV remodeling. The study populations were heterogeneous and, importantly, the definitions used to classify the geometric patterns were not uniform. Concentric hypertrophy is associated with the highest prevalence of cardiometabolic risk factors and diseases. Eccentric hypertrophy is associated with a high prevalence of atrial fibrillation and the lowest LV ejection fraction. Although concentric hypertrophy is associated

with the highest risk of all-cause mortality, the risks overlapped with eccentric hypertrophy. Eccentric hypertrophy has a similar mortality risk compared to concentric remodeling.

The pathophysiology of LVH has been well described and studied for the past 50 years^{32,33}. Cardiac hypertrophy is initially an adaptive response to the wall stress according to the Law

Figure 4. (a) Rank probabilities of effectiveness and SUCRA scores; and (b) prognosis of the four geometric patterns of left ventricular hypertrophy.

of LaPlace. Ultimately, cardiac decompensation occurs as a consequence of myocyte death and myocardial fibrosis^{34,35}. Whilst geometric patterns of LV remodeling are clinically meaningful to describe the hypertrophic response due to mechanical stress from either pressure (concentric hypertrophy) or volume overload (eccentric hypertrophy), it may not adequately identify the transition point where adaptive hypertrophy decompensates (Figure 5). This transition point before cardiac decompensation occurs is an important potential risk marker to target more intensive management and closer surveillance. In this study, we have demonstrated that both concentric and eccentric hypertrophy were associated with similar risks of increased all-cause mortality. These observations may suggest that the risk of adverse prognosis is increased once LVH develops, regardless of geometric patterns. It may also suggest that some patients with concentric or eccentric LVH may be in the compensated phase and begets the question of whether there are other strategies to identify high-risk LVH phenotypes.

To address the complex interaction between LV dilatation and myocardial thickening in the pathophysiology of LVH, several studies have recently examined an expanded four-group LVH classification: dilated/non-dilated concentric hypertrophy and dilated/non-dilated eccentric hypertrophy^{36–40}. In this proposed four-group LVH classification, dilated concentric hypertrophy was associated with the worst prognosis and non-dilated eccentric hypertrophy had the most favourable profile^{36–39}. However, more guidance is needed before this complex classification can be integrated into routine clinical practice. Recently, we have developed the remodeling index (RI), based on a biophysical model of Laplace's Law. The RI integrates LV volume and myocardial thickening into a single measurement⁴¹. We further demonstrated that hypertensive LVH patients with abnormally low RI (suggestive of excessive myocardial

thickening relative to LV dilatation) had increased myocardial fibrosis, elevated circulating markers of myocardial injury and wall stress; and in a small number of patients with dilated cardiomyopathy, an abnormally high RI (suggestive of excessive LV dilatation relative to myocardial thickening) was associated with adverse cardiovascular events⁴¹. The prognostic value and clinical utility of this index are currently being examined in a large cohort of hypertensive patients (ClinicalTrials.gov identifier: [NCT02670031](#)).

These emerging data support the notion that cardiac remodeling in hypertrophy is heterogeneous and complex; and the conventional geometric patterns of LV remodeling is not adequate to risk-stratify patients with LVH.

Study limitations

The study populations included in the meta-analysis were heterogeneous. It is possible that the conventional remodeling patterns has incremental prognostic value in certain cardiac conditions. Unfortunately, the limited number of studies precluded stratified analyses to examine the prognostic value of LV geometric patterns in the different cardiovascular conditions. The definitions used for classifying geometric patterns were not consistent across the different studies. This is concerning and reinforces the necessity to apply consensus definitions in future studies².

Conclusions

Concentric and eccentric hypertrophy are associated with increased and similar all-cause mortality. Possible explanations for these observations include the heterogeneous populations, inconsistent definitions used in the classification and the inherent limitations of the conventional patterns of LV geometry to adequately risk stratify LVH. Well-validated novel approaches

Figure 5. Relationship between geometric patterns of cardiac remodeling, mechanical stress and prognosis. Geometric patterns of left ventricular remodeling are useful to identify the mechanisms of mechanical stress; but may not adequately identify the transition between myocardial adaptation and decompensation.

to improve risk stratification of LVH should be explored in future research.

Data availability

Underlying data

All data underlying the results are available as part of the article and no additional source data are required.

Extended data

Open Science Framework: Prognosis associated with geometric patterns of left ventricular remodeling: systematic review and network meta-analysis. <https://doi.org/10.17605/OSF.IO/3CJMW>¹¹.

This project contains the following extended data:

- Data file.xlsx (Sheet 1 contains study questions, search date, search terms and eligibility criteria; Sheet 2

contains a list of the studies identified; Sheet 3 contains the six composites used in this study).

Reporting guidelines

Open Science Framework: PRISMA checklist for “Prognosis associated with geometric patterns of left ventricular remodeling: systematic review and network meta-analysis”. <https://doi.org/10.17605/OSF.IO/3CJMW>¹¹.

Data are available under the terms of the [Creative Commons Zero “No rights reserved” data waiver](#) (CC0 1.0 Public domain dedication).

Grant information

The author(s) declared that no grants were involved in funding this work.

References

- Verdecchia P, Porcellati C, Reboldi G, *et al.*: **Left ventricular hypertrophy as an independent predictor of acute cerebrovascular events in essential hypertension.** *Circulation*. 2001; 104(17): 2039–44.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Lang RM, Badano LP, Mor-Avi V, *et al.*: **Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging.** *J Am Soc Echocardiogr*. 2015; 28(1): 1–39.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Levy D, Garrison RJ, Savage DD, *et al.*: **Prognostic implications of echocardiographically determined left ventricular mass in the Framingham Heart Study.** *N Engl J Med*. 1990; 322(22): 1561–6.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Zoccali C, Benedetto FA, Mallamaci F, *et al.*: **Prognostic impact of the indexation of left ventricular mass in patients undergoing dialysis.** *J Am Soc Nephrol*. 2001; 12(12): 2768–74.
[PubMed Abstract](#)
- Elliott PM, Gimeno Blanes JR, Mahon NG, *et al.*: **Relation between severity of left-ventricular hypertrophy and prognosis in patients with hypertrophic cardiomyopathy.** *Lancet*. 2001; 357(9254): 420–4.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Lieb W, Gona P, Larson MG, *et al.*: **The natural history of left ventricular geometry in the community: clinical correlates and prognostic significance of change in LV geometric pattern.** *JACC Cardiovasc Imaging*. 2014; 7(9): 870–878.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
- Krumholz HM, Larson M, Levy D: **Prognosis of left ventricular geometric patterns in the Framingham Heart Study.** *J Am Coll Cardiol*. 1995; 25(4): 879–84.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Ghali JK, Liao Y, Cooper RS: **Influence of left ventricular geometric patterns on prognosis in patients with or without coronary artery disease.** *J Am Coll Cardiol*. 1998; 31(7): 1635–40.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Katz DH, Beussink L, Sauer AJ, *et al.*: **Prevalence, clinical characteristics, and outcomes associated with eccentric versus concentric left ventricular hypertrophy in heart failure with preserved ejection fraction.** *Am J Cardiol*. 2013; 112(8): 1158–64.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
- Paoletti E, De Nicola L, Gabbai FB, *et al.*: **Associations of Left Ventricular Hypertrophy and Geometry with Adverse Outcomes in Patients with CKD and Hypertension.** *Clin J Am Soc Nephrol*. 2015; 11(2): 271–9.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
- Chin C: **Prognosis associated with geometric patterns of left ventricular remodeling: systematic review and network meta-analysis.** 2019.
<http://www.doi.org/10.17605/OSF.IO/3CJMW>
- Hayden JA, van der Windt DA, Cartwright JL, *et al.*: **Assessing bias in studies of prognostic factors.** *Ann Intern Med*. 2013; 158(4): 280–286.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Salanti G, Ades AE, Ioannidis JP: **Graphical methods and numerical summaries for presenting results from multiple-treatment meta-analysis: an overview and tutorial.** *J Clin Epidemiol*. 2011; 64(2): 163–71.
[PubMed Abstract](#) | [Publisher Full Text](#)
- White IR: **Network meta-analysis.** *Stata J*. 2015; 15(4): 951–985.
[Publisher Full Text](#)
- Verma A, Meris A, Skali H, *et al.*: **Prognostic implications of left ventricular mass and geometry following myocardial infarction: the VALIANT (VALsartan In Acute myocardial iNfarcTion) Echocardiographic Study.** *JACC Cardiovasc Imaging*. 2008; 1(5): 582–91.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Gardin JM, McClelland R, Kitzman D, *et al.*: **M-mode echocardiographic predictors of six- to seven-year incidence of coronary heart disease, stroke, congestive heart failure, and mortality in an elderly cohort (the Cardiovascular Health Study).** *Am J Cardiol*. 2001; 87(9): 1051–7.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Milani RV, Lavie CJ, Mehra MR, *et al.*: **Left ventricular geometry and survival in patients with normal left ventricular ejection fraction.** *Am J Cardiol*. 2006; 97(7): 959–63.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Lavie CJ, Milani RV, Ventura HO, *et al.*: **Left ventricular geometry and mortality in patients >70 years of age with normal ejection fraction.** *Am J Cardiol*. 2006; 98(10): 1396–9.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Berger J, Ren X, Na B, *et al.*: **Relation of concentric remodeling to adverse outcomes in patients with stable coronary artery disease (from the Heart and Soul Study).** *Am J Cardiol*. 2011; 107(11): 1579–84.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Verdecchia P, Schillaci G, Borgioni C, *et al.*: **Prognostic value of left ventricular mass and geometry in systemic hypertension with left ventricular hypertrophy.** *Am J Cardiol*. 1996; 78(2): 197–202.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Kohara K, Zhao B, Jiang Y, *et al.*: **Relation of left ventricular hypertrophy and geometry to asymptomatic cerebrovascular damage in essential hypertension.** *Am J Cardiol*. 1999; 83(3): 367–70.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Apostolakis S, Sullivan RM, Olshansky B, *et al.*: **Left ventricular geometry and outcomes in patients with atrial fibrillation: the AFFIRM Trial.** *Int J Cardiol*. 2014; 170(3): 303–8.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Shah N, Badheka AO, Grover PM, *et al.*: **Influence of left ventricular remodeling on atrial fibrillation recurrence and cardiovascular hospitalizations in patients undergoing rhythm-control therapy.** *Int J Cardiol*. 2014; 174(2): 288–92.
[PubMed Abstract](#) | [Publisher Full Text](#)

24. Debry N, Maréchaux S, Rusinaru D, *et al.*: **Prognostic significance of left ventricular concentric remodelling in patients with aortic stenosis.** *Arch Cardiovasc Dis.* 2017; **110**(1): 26–34.
[PubMed Abstract](#) | [Publisher Full Text](#)
25. Shigematsu Y, Hamada M, Ohtsuka T, *et al.*: **Left ventricular geometry as an independent predictor for extracardiac target organ damage in essential hypertension.** *Am J Hypertens.* 1998; **11**(10): 1171–7.
[PubMed Abstract](#) | [Publisher Full Text](#)
26. Gerds E, Cramariuc D, de Simone G, *et al.*: **Impact of left ventricular geometry on prognosis in hypertensive patients with left ventricular hypertrophy (the LIFE study).** *Eur J Echocardiogr.* 2008; **9**(6): 809–15.
[PubMed Abstract](#) | [Publisher Full Text](#)
27. Fabiani I, Pugliese NR, La Carrubba S, *et al.*: **Incremental prognostic value of a complex left ventricular remodeling classification in asymptomatic for heart failure hypertensive patients.** *J Am Soc Hypertens.* 2017; **11**(7): 412–419.
[PubMed Abstract](#) | [Publisher Full Text](#)
28. Park CS, Park JB, Kim Y, *et al.*: **Left Ventricular Geometry Determines Prognosis and Reverse J-Shaped Relation Between Blood Pressure and Mortality in Ischemic Stroke Patients.** *JACC Cardiovasc Imaging.* 2018; **11**(3): 373–382.
[PubMed Abstract](#) | [Publisher Full Text](#)
29. Lavie CJ, Milani RV, Patel D, *et al.*: **Disparate effects of obesity and left ventricular geometry on mortality in 8088 elderly patients with preserved systolic function.** *Postgrad Med.* 2009; **121**(3): 119–25.
[PubMed Abstract](#) | [Publisher Full Text](#)
30. Capoulade R, Clavel MA, Le Ven F, *et al.*: **Impact of left ventricular remodelling patterns on outcomes in patients with aortic stenosis.** *Eur Heart J Cardiovasc Imaging.* 2017; **18**(12): 1378–1387.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
31. Rymuza B, Zbroński K, Scislo P, *et al.*: **Left ventricular remodelling pattern and its relation to clinical outcomes in patients with severe aortic stenosis treated with transcatheter aortic valve implantation.** *Postępy Kardiol Interwencyjnej.* 2017; **13**(4): 288–294.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
32. Meerson FZ: **Compensatory hyperfunction of the heart and cardiac insufficiency.** *Circ Res.* 1962; **10**: 250–8.
[PubMed Abstract](#) | [Publisher Full Text](#)
33. Bader HS: **Biological significance of cardiac hypertrophy.** *Am J Cardiol.* 1964; **14**: 133–8.
[PubMed Abstract](#) | [Publisher Full Text](#)
34. Diwan A, Dorn GW 2nd: **Decompensation of cardiac hypertrophy: cellular mechanisms and novel therapeutic targets.** *Physiology (Bethesda).* 2007; **22**: 56–64.
[PubMed Abstract](#) | [Publisher Full Text](#)
35. Lorell BH, Carabello BA: **Left ventricular hypertrophy: pathogenesis, detection, and prognosis.** *Circulation.* 2000; **102**(4): 470–9.
[PubMed Abstract](#) | [Publisher Full Text](#)
36. Khouri MG, Peshock RM, Ayers CR, *et al.*: **A 4-tiered classification of left ventricular hypertrophy based on left ventricular geometry: the Dallas heart study.** *Circ Cardiovasc Imaging.* 2010; **3**(2): 164–71.
[PubMed Abstract](#) | [Publisher Full Text](#)
37. Bang CN, Gerds E, Aurigemma GP, *et al.*: **Four-group classification of left ventricular hypertrophy based on ventricular concentricity and dilatation identifies a low-risk subset of eccentric hypertrophy in hypertensive patients.** *Circ Cardiovasc Imaging.* 2014; **7**(3): 422–9.
[PubMed Abstract](#) | [Publisher Full Text](#)
38. de Simone G, Izzo R, Aurigemma GP, *et al.*: **Cardiovascular risk in relation to a new classification of hypertensive left ventricular geometric abnormalities.** *J Hypertens.* 2015; **33**(4): 745–54; discussion 754.
[PubMed Abstract](#) | [Publisher Full Text](#)
39. Garg S, de Lemos JA, Ayers C, *et al.*: **Association of a 4-Tiered Classification of LV Hypertrophy With Adverse CV Outcomes in the General Population.** *JACC Cardiovasc Imaging.* 2015; **8**(9): 1034–1041.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
40. Gaasch WH, Zile MR: **Left ventricular structural remodeling in health and disease: with special emphasis on volume, mass, and geometry.** *J Am Coll Cardiol.* 2011; **58**(17): 1733–40.
[PubMed Abstract](#) | [Publisher Full Text](#)
41. Goh VJ, Le TT, Bryant J, *et al.*: **Novel Index of Maladaptive Myocardial Remodeling in Hypertension.** *Circ Cardiovasc Imaging.* 2017; **10**(9): pii: e006840.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)

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Current Peer Review Status:

Version 1

Reviewer Report 23 October 2019

<https://doi.org/10.5256/f1000research.21845.r55256>

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Tee Joo Yeo

National University Heart Centre Singapore, National University Health System, Singapore, Singapore

Zheng et al performed a systematic review and meta-analysis of echocardiographic studies that included prognostic characteristics of 4 geometric patterns of cardiac remodeling.

Through the combined total of 22 studies comprising diverse populations, including hypertension, aortic stenosis, heart failure with preserved ejection fraction, ischemic strokes, chronic kidney disease etc, the authors conclude that the presence of concentric LVH and eccentric hypertrophy was associated with a higher risk of all-cause mortality.

The overall aim of this study is commendable. Nonetheless, there are a few areas of note:

- The study includes populations both with and without pre-existing cardiovascular disease; in such a situation, the baseline risk profiles differ significantly (eg. an apparently healthy individual with newly diagnosed hypertension has a substantially lower risk profile compared to an individual with pre-existing or longstanding aortic stenosis although both may develop LVH eventually).
- A suggested approach would be to stratify the risk of LVH based on aetiology (e.g. hypertension-related, aortic stenosis related, multifactorial etc.) which would make the meta-analysis more applicable to the above sub-groups of patients rather than providing a single risk ratio for an entire phenotypic category of cardiac remodeling.
- The authors may consider excluding the studies involving the general population to limit the study population to those with pre-existing disease, as the absolute number of Framingham subjects with LVH was actually small.
- Importantly, the classification of LVH and RWT differed in certain studies, so applicability is affected. Although the authors listed this as a limitation, studies with substantial differences in quantifying LVH might need to be excluded in order to keep the study population

homogenous.

- In Table 2, regional (or relative, as stated by the American Society of Echocardiography and other international echocardiography societies) wall thickness for all 4 categories of cardiac remodeling ranged between 0.95 to 1.29. Do check if this is correct, as that would classify all subjects in the concentric geometry.
- For the conclusion, the authors are right to say that the study populations were heterogeneous. As such, it might be more appropriate to generate different risks for the larger subsets of patients (eg. LVH from hypertension vs LVH from aortic stenosis vs LVH from combined causes) rather than to generalise risk for all patients regardless of aetiology.

Are the rationale for, and objectives of, the Systematic Review clearly stated?

Yes

Are sufficient details of the methods and analysis provided to allow replication by others?

Yes

Is the statistical analysis and its interpretation appropriate?

I cannot comment. A qualified statistician is required.

Are the conclusions drawn adequately supported by the results presented in the review?

Partly

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Sports cardiology; Athlete's heart; physiological vs pathological cardiac remodeling in athletes.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Reviewer Report 16 October 2019

<https://doi.org/10.5256/f1000research.21845.r54455>

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Bruno Trimarco

Department of Advanced Biomedical Sciences, University of Naples Federico II, Naples, Italy

The paper titled "Prognosis associated with geometric patterns of left ventricular remodeling:

systematic review and network meta-analysis" by Zheng *et al* aims to identify different prognostic profile of different left ventricular remodeling patterns. Although the aim is of interest, the method to select data from the international literature is quite messy.

In fact, populations are not homogenous (from population-based studies like the FHS, to patients with stable CAD, to patients with hypertension, aortic stenosis, HFpEF, etc). In addition, methods reported in studies to categorize left ventricular remodeling are still not homogeneous. Consequently, conclusions of the paper are erroneous.

Authors stated that the new classification of left ventricular remodeling proposed by Khouri is "complex" and "more guidance is needed before this complex classification can be integrated into routine clinical practice", so that they propose a more simple index (the remodeling index) which at moment is tested by the authors in a trial of hypertensive patients.

We thank the Author for the suggestion, i.e. to use their index; of course, to demonstrate in the future that their index is superior to that used in the past, they will have to perform a correct statistical analysis, confronting their index with clear-cut values suggested by guidelines and more recently by Khouri, (which, I guess, is very easy to use into clinical practice) for the identification of left ventricular remodeling patterns.

Are the rationale for, and objectives of, the Systematic Review clearly stated?

Yes

Are sufficient details of the methods and analysis provided to allow replication by others?

No

Is the statistical analysis and its interpretation appropriate?

No

Are the conclusions drawn adequately supported by the results presented in the review?

No

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Hypertension

I confirm that I have read this submission and believe that I have an appropriate level of expertise to state that I do not consider it to be of an acceptable scientific standard, for reasons outlined above.

Author Response 16 Oct 2019

Calvin Chin, National Heart Center Singapore, Singapore, Singapore

We thank the Reviewer for the comments. We wish to highlight the issues raised by the Reviewer are inherent to the individual studies and not the methodology of the meta analysis. We agree with the Reviewer that the study populations included in the study are heterogeneous. Unfortunately, the limited number of studies precluded further analyses to examine prognostic value of LV geometric patterns in different cardiovascular conditions.

The definitions used for classifying geometric patterns were not consistent in the studies as highlighted by the Reviewer, a limitation that reinforces the necessity of applying consensus definitions in future studies. Both of these points have already been listed as study limitations.

Competing Interests: None

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