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OPEN PEER REVIEW

Predictors and Prognosis of End-Stage Hypertrophic Cardiomyopathy

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SUBMITTED	REVISED	ACCEPTED
3 Jul 2022	25 Dec 2022	28 Dec 2022

About this report

This open peer review (OPR) report shows the public comments made on this article during peer review, by the reviewers, the associate editor and the editor-in-chief, for every revision round, together with the authors' replies. Comments appear only with the consent of the people who wrote them. Reviewers who chose to sign their report are named; the others are shown as "Referee". Comments are edited for language only, and confidential remarks to the editors are not included.

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1 Original submission

6 comments · 3 Aug 2022 – 28 Aug 2022

Referee 1 Reviewer

REJECT 3 Aug 2022

Thanks for submitting this manuscript.
I reviewed the article; unfortunately, the results of this research have no novelty.

Referee 2 Reviewer

ACCEPT 3 Aug 2022

This manuscript is acceptable and can be published.

Referee 3 Reviewer

MAJOR REVISION 3 Aug 2022

Abstract:

In Method:
Add the type of study, sample size, sampling method, ethical considerations, parameters and variables, tools, methods of measuring variables, statistical methods, and software.

Why were patients who did not complete the follow-up not included in the study? These patients are censored, and one of the capabilities of the Cox model is that it handles such data. Eliminating these people can cause bias. Please consult an experienced biostatistician.
What is this "(LVEF ¿ 50%?"
The manuscript should be revised grammatically.
Main body.
Method:
Add the type of study, sample size, sampling method, parameters and variables, tools, methods of measuring variables, and statistical methods.
Why were patients who did not complete the follow-up not included in the study? These patients are censored, and one of the capabilities of the Cox model is that it handles such data. Eliminating these people can cause bias. Please consult an experienced biostatistician. (Reanalysis is necessary.)

Version 16 is a free version in our country.
Multivariate Cox proportional is not appropriate. You had a multiple Cox model.
The Cox model yielded the hazard ratio (HR), not the odds ratio (table 2). Please consult an experienced biostatistician.
Add the confidence interval for HR in table 2.
The figure does not make sense to me; please clarify it.
The p-value must be reported to 3 decimal places, as in (p=0.038).
Please reformat the table and split it into two tables. The table is very messy. Please remove the word "positive" from this table and mention it in the table legend.

Referee 4 Reviewer

ACCEPT 28 Aug 2022

The paper is well-designed and accepted.
Please pay attention to the grammatical mistakes.

Associate Editor

MINOR REVISION 28 Aug 2022

Please make the corrections.

Editor-in-Chief

MINOR REVISION 28 Aug 2022

Dear authors,
Please make the statistical revisions and revise the references based on the comments.

2

Revision 1

AUTHORS' RESPONSE TO REVIEWERS

Authors' reply to reviewers

The next pages contain the authors' point-by-point reply to the comments of this revision round, as submitted with the revised manuscript. It is published as the authors wrote it.

Dear Editors of International Cardiovascular Research journal:

After consult with an experienced biostatistics, we have corrected the statistic method in our manuscript.

Statistical analysis was performed using SPSS 16.0 software. Continuous variables with normally distribution explained as mean ±SD and variables without normally distribution explained as median (interquartile range) . Categorical variables are explained as number and percentage.

Continuous variables have compared between 2 groups using the t test, or a nonparametric test (Wilcoxon test) for variables without normal distribution. Categorical variables have compared between 2 groups using the Fisher exact test. Generalized estimating equation (GEE) regression performed to assess the association between patient characteristics and BO. Clinical features that demonstrated a $P<0.1$ by univariate GEE analysis were included in a multivariate model to identify independent predictors.

In method we corrected type of study ,sample size and we explained more about the method of study.

Study patients

In this retrospective study reevaluated 401 consecutive patient who referred to echocardiography ward of Rajeev Heart Center for evaluation of HCM during the period from January 2010, to February 2018. All transthoracic echocardiographic studies were performed on Philips EPIQ devices, All ultrasonography systems were equipped with 1–5 MHz TTE transducers , as well as continuous wave , pulsed wave Doppler and Color Doppler imaging. Subjects were examined in the left lateral supine position . All echocardiographic examinations were recorded and for further evaluation we reanalysis patient's data. In all echo study, patients evaluated with 2D and Doppler . Analysis of LVEF was done with visual assessment and Simpson biplane method. Mitral regurgitation (MR) and TR regurgitation severity was analyzed by visual assessment, Doppler and PISA method. . HCM was diagnosed with trans thoracic echocardiography (TTE) as hypertrophied, nondilated LV (maximum LV wall thickness [MLVWT] ≥15 mm in adult patients, in the absence of another cardiac or systemic disease capable of

producing a similar magnitude of hypertrophy by echocardiography or cardiac magnetic resonance imaging. These patients had been followed by TTE for a mean period of 5 years, and a final index TTE was done by echocardiography experts to determine the changes in HCM characteristics BO-HCM was defined by the detection of a LV ejection fraction (LVEF) <50% on echocardiography during follow-up. Patients were excluded for the following reasons: A history of surgical or ablative septal reduction therapy; a history of coronary artery disease or documented coronary arterial narrowing (≥50% stenosis of at least one major artery by angiography), and patients without follow-up TTE. Echocardiography was performed using Philips EPIQ ultrasound equipment. The magnitude of LV hypertrophy was assessed from two-dimensional images in accordance with the recommendation of the American Society of Echocardiography. Continuous variables with normally distribution explained as mean ±SD and variables without normally distribution explained with median (interquartile range) . Categorical variables are explained as number and percentage.

Continuous variables have compared between 2 groups using the t test, or a nonparametric test (Wilcoxon test) for variables without normal distribution. Categorical variables have compared between 2 groups using the Fisher exact test. Generalized estimating equation (GEE) regression performed to assess the association between patient characteristics and BO. Clinical features that demonstrated a P<0.1 by univariate GEE analysis were included in a multivariate model to identify independent predictors.

Ethical approval for this study was obtained from Iran University of medical science. The ethical code is IR.RHC,REC.1400.030

3-P value has been reported with 3 decimals.

4-we reformatted and split table 1 to 2 table and remove “positive” word

5-Figure 1 was removed.

2 Revision 1

2 comments · 1 Oct 2022 – 1 Oct 2022

Associate Editor

MAJOR REVISION 1 Oct 2022

major revision

Editor-in-Chief

MAJOR REVISION 1 Oct 2022

Needs major revision

3

Revision 2

AUTHORS' RESPONSE TO REVIEWERS

Authors' reply to reviewers

The next pages contain the authors' point-by-point reply to the comments of this revision round, as submitted with the revised manuscript. It is published as the authors wrote it.

With greetings and respect to the respected reviewer of the Cardiovascular Journal of Shiraz University of Medical Sciences

The statistical analysis was performed again by Dr. Alipour, associate professor of epidemiology at Mazandaran University of Medical Sciences, and the design of the tables was also changed. The confidence intervals were also given in Table 5. The table headings were also corrected

Table 5. Echocardiographic and demographic predictors of burned out HCM

Demographic parameters	Odds ratio (95% Confidence interval)	P-value
AGE	1.02 (1.002- 1.0471)	0.030
Family history of HMC*	1.14 (0.4690- 28100)	0.762
Mild RV** dysfunction	2.37 (1.1399- 4.9337)	0.021
Moderate RV dysfunction	4.61 (1.0307- 206991)	0.046
Systolic pulmonary artery pressure	1.02 (0.9952- 1.0597)	0.097

*HCM: Hypertrophic cardiomyopathy; **RV: Right ventricle

3 Revision 2

2 comments · 19 Dec 2022 – 19 Dec 2022

Associate Editor

MINOR REVISION 19 Dec 2022

needs revision

Editor-in-Chief

MINOR REVISION 19 Dec 2022

minor revision

4

Revision 3

AUTHORS' RESPONSE TO REVIEWERS

Authors' reply to reviewers

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With greetings and respect to the respected reviewer of the Cardiovascular Journal of Shiraz University of Medical Sciences

Respectfully, the stated issues, which were due to writing errors, are corrected, and the final analysis tables are submitted as an attachment

.

BO	Odds Ratio	Robust Std. Err.	z	P>|z|	[95% Conf.	Interval]
RVsize	7.356306	3.020754	4.86	0.000	3.289477	16.45101
_cons	.0010351	.0013472	-5.28	0.000	.0000807	.0132687

.

BO	Odds Ratio	Robust Std. Err.	z	P>|z|	[95% Conf.	Interval]
SRV	.7492019	.066257	-3.27	0.001	.6299721	.8909973
_cons	7.032821	6.130508	2.24	0.025	1.273906	38.82592

.

BO	Odds Ratio	Robust Std. Err.	z	P>|z|	[95% Conf.	Interval]
LVsizes	2.099248	.3945641	3.95	0.000	1.452366	3.03425
_cons	.0435292	.0265237	-5.14	0.000	.0131861	.143696

(Std. Err. adjusted for clustering on idno)

BO	Odds Ratio	Robust Std. Err.	z	P>|z|	[95% Conf.	Interval]
age	1.024495	.0114403	2.17	0.030	1.002316	1.047165
famil_his	1.148095	.5243256	0.30	0.762	[illegible]	[illegible]
RVF_mild	2.37151	.8863944	2.31	0.021	1.139916	4.933746
RVF_mod	4.619161	3.534854	2.00	0.046	[illegible]	[illegible]
PAP	1.026996	.0164728	1.66	0.097	.9952126	1.059795
_cons	.0321142	.0290694	-3.80	0.000	.0054475	.1893194

4 Revision 3

2 comments · 21 Dec 2022 – 21 Dec 2022

Associate Editor

MINOR REVISION 21 Dec 2022

Needs revision

Editor-in-Chief

MINOR REVISION 21 Dec 2022

Please make the revisions.

5

Revision 4

AUTHORS' RESPONSE TO REVIEWERS

Authors' reply to reviewers

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Greetings to the respected reviewer of the Cardiovascular Journal of Shiraz University of Medical Sciences

The requested changes were applied to the table

5 Revision 4

3 comments · 28 Dec 2022 – 28 Dec 2022

Referee 3 Reviewer

MINOR REVISION 28 Dec 2022

Hello. They have not made any changes and have submitted the same version as before. Perhaps they made a mistake.

They were supposed to remove the chart and correct the table.

Hello. Tell them that the information in the chart does not match the table. They should include the same table as before, with confidence intervals. They should remove only the variable with a large upper confidence limit from the model because it is not stable.

Associate Editor

MINOR REVISION 28 Dec 2022

Please do the revisions.

Editor-in-Chief

MINOR REVISION 28 Dec 2022

Please make the revisions.

6

Revision 5

AUTHORS' RESPONSE TO REVIEWERS

Authors' reply to reviewers

The next pages contain the authors' point-by-point reply to the comments of this revision round, as submitted with the revised manuscript. It is published as the authors wrote it.

Greetings to the respected reviewer of the Cardiovascular Journal of Shiraz University of Medical Sciences

The requested changes were applied to the table

6 Revision 5

1 comment · 3 Jan 2023

Editor-in-Chief

ACCEPT 3 Jan 2023

Accept