BACKGROUND

Predictive models for positive genotype in patients with hypertrophic cardiomyopathy (HCM) have been proposed in the past, including the Toronto model and Mayo model, along with respective scores based on the strength of the independent predictors. However, there is limited data on whether these models hold true for other HCM patients. Furthermore, many new pathogenic gene variants have been identified which were not pathogenic at the time these models were proposed. We aimed to validate these models using our own HCM patient population.

METHODS

Using a retrospective study design, all adult patients with HCM seen at our cardiomyopathy center from 2010 to 2021 were analyzed in our study. The primary objective was to validate these known predictors using our HCM patient population. The secondary objective was to evaluate the distribution of pathogenic mutation according to the left ventricular maximal wall thickness.

We used a multivariate regression model to evaluate these known independent predictors. Due to subjectivity in determining the phenotype, the phenotype was not included in the model. Receiver operating characteristic (ROC) curves were generated from the multivariate model to evaluate the strength of the model.

RESULTS

We analyzed data on 438 HCM patients. The mean age was 55 years. Females were 43%.

Pathogenic mutations were noted in 22.6%. MYBPC3 was the gene most commonly implicated (64%).

Our data showed that younger age (adjusted odds ratio [AOR] 0.97 per year, P=0.009), LVMWT (AOR 1.1 per 1 mm increase in thickness, P<0.001), family history of HCM (AOR 5, P<0.001), family history of sudden cardiac death (SCD; AOR 2.8, P=0.007) and absence of hypertension (AOR 0.5, P=0.008) were independent predictors of pathogenic mutation. Gender was not associated with a positive genotype. We also tested LGE in a separate multivariate model, but it could not be validated as an independent predictor either.

The ROC curve showed AUC of 0.82 (Figure 1A). The Hosmer-Lemeshow test showed that the data fit the model well.

Most patients with pathogenic mutation (84%) had a left ventricular maximal wall thickness (LVMWT) of ≥1.8 cm (Figure 1B).

DISCUSSION

We successfully validated most of the independent predictors suggested by Toronto and Mayo predictive models for a pathogenic mutation. However, we could not validate female sex as an independent predictor with our data. Hence, female sex as a predictor in Toronto HCM model was likely due to chance.

Family history of SCD associated with 180% increased risk as opposed to 45% increase in Mayo model.

Family history of HCM was the strongest predictor associated with 400% increased odds of mutation compared to 130-180% increased odds in previous models.

Finally, likelihood of finding a pathogenic mutation is high in patients with LV maximal wall thickness of ≥1.8cm.

CONCLUSION

We successfully validated most of the predictors of a pathogenic mutation except gender. Furthermore, due to increased recognition of pathological variants in patients with HCM, especially those with a family history of HCM and SCD, these are stronger predictors associated with higher odds of a positive genotype than has been seen in the past. Finally, likelihood of finding a pathogenic mutation is high in patients with LV maximal wall thickness of ≥1.8cm.

DISCLOSURE INFORMATION

None.