Papillary muscle free strain- promosing parameter to predict sudden cardiac death in hypertrophic cardiomyopathy?

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August 31, 2024

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Hypertrophic Cardiomyopathy (HCM) generally have a good prognosis. In the long follow-up study over 5 decades annual overall HCM-related mortality was 1.3%/y (0.7% first decade to 1.8% in second and third decades). The sudden cardiac death (SCD) mortality rate was also low (0.1%/y first decade to 0.44% in second and third decades)[1]. SCD is the most feared HCM complication and the only effective treatment for this is Implantable Cardioverter Defibrillator (ICD) that is responsible for >10-fold decrease in HCM related mortality[2]. In 2014,the European Society of Cardiology (ESC) come out with risk score comprising 7 variables but this risk score have low sensitivity[3,4]. This led to the search for additional risk factors such as percentage of late gadolinium enhancement (LGE) in the left ventricle, presence of apical aneurysm and left ventricle ejection fraction <50% .The American Society of Cardiology/American Heart Association (ACC/AHA) incorporate this for their guidelines in 2020[5].Eventhough this guidelines have high sensitivity, it have low ability to identify low risk patients which can lead to inappropriate ICD implantation[4]. The ongoing challenge is to identify the small yet significant group of patients who are at risk of sudden cardiac death, heart failure, and death resulting from heart failure.

Neither the 2014 nor the 2020 SCD risk calculators/predictors, nor even the latest 2022 ESC guidelines, have incorporated the relatively new echocardiography technique of speckle-tracking strain measurements. This technique is non-doppler oriented, angle independent and have been shown to be highly reproducible with

high sensitivity and specificity[6]. These techniques can measure Global longitudinal strain (GLS), left atrial reservoir (LArS), conduit (LAcS) and booster (LAbS) strain and right ventricle global (RVGLS) and free wall strain (RVFWS). The most studied of these is Global Longitudinal Strain (GLS) and a recent study showed GLS have the highest accuracy to predict fatal arrhythmia and accurate ICD indication compare to all the other echocardiographic parameters that was previously considered important like diastolic left atrial (LA) diameter, left ventricular wall thickness and ejection fraction[7].This is consistent with another study of large cohort of 427 HCM patients showing independent association between GLS and all cause mortality, heart transplantation, aborted SCD, and appropriate ICD therapy[8]. Furthermore, the latest meta-analysis of 13 studies with 2441 HCM patients showed significant correlation between impaired GLS and major adverse cardiovascular outcomes (MACE). The same correlation was also found with LA strain. A recent meta-analysis in 2023 shows significant association between all aspect of LA strain (reservoir, conduit and booster) with MACE as well as development of new atrial fibrillation (AF)[9]. This is not only true with echocardiography derived strain. In a Cardiac MRI (CMR) strain study published in 2024, the combination of left ventricle circumferential strain and left atrial reservoir strain model shows high diagnostic value of SCD with staggeringly high area under the curve (AUC) of 0.95[10]. All of these studies show how powerful is strain study in HCM SCD prognosis and it is natural to then look at papillary muscle (PM) strain as this structure is frequently abnormal in HCM[11].

It is widely known that papillary muscle abnormalities are part of HCM phenotypes, in addition to elongated mitral valve leaflets and hypertrophied muscle with excessive contractility (the sine qua non of HCM)[11]. Abnormal papillary muscle morphology is independently associated with increase left ventricular outflow tract (LVOT) obstruction with anteroapically displaced PM and double bifid PM patients having higher resting LVOT gradients than control independent of septal thickness, use of rate control medications and resting heart rate[12]. The variations of papillary muscle abnormalities are anterior and apical displacement of the PM usually involving ALPM, bifid PM characterized by the presence of more than one muscle head (If both PM involved it is called double bifid morphology), accessory PM that extend from the LV apex and inserted to basal myocardium without insertion into the mitral leaflets and anomalous insertion of the PM itself[12,13,14].In HCM, the PM are frequently hypertrophied, with a mass measuring roughly twice the healthy controls. HCM patients also tend to have larger number of PM (2.5 muscles vs 2.1 in control) with half of the patients demonstrating multiple (3 or 4) PM[15].

In this issue of *Echocardiography* Atilla Koyuncu et al look at 79 patients with HCM that were divided into low/intermediate-risk (n=57, ESC risk score <6 points) and high risk (n=22, ESC risk score [?]6 points) groups based on the ESC risk calculator. Their mean follow-up duration is 6.2 years. They specifically look for PM abnormalities and measured anterolateral papillary muscle (ALPM) and posteromedial papillary muscle (PMPM) free strain in addition to other conventional 2-dimensional echocardiographic parameters and GLS. They enrolled all HCM phenotypic groups with or without obstruction and they exclude patients with hypertension, valvular heart diseases, hepatic/renal failure or inflammatory diseases. Of note, they did not perform left atrium (LA) or right ventricle (RV) strain. Papillary muscle strain is a relatively new tool and the measurements of ALPM strain is done in apical 4 chamber view and measurement for PMPM strain is done in apical 3 chamber view. The majority of patients have sigmoid or reverse curvature phenotype (70.9%). Interestingly 5 patients (6.3%) had anteriorly displaced papillary muscles, 7(8.8%) had bifid ALPM, 5(6.3%) had bifid PMPM and 2 patients have both bifid ALPM and PMPM (double bifid morphology).

They found that the high SCD-risk group had greater wall thickness, interventricular septum thickness, posterior wall thickness and left ventricle mass index and lower GLS, ALPM (-16.88 ± 4.41% vs. -14.34 ± 3.68%, p = .028) and PMPM (-18.48 ± 6.31% vs. -15.28 ± 6.88%, p = .042) free strain. Furthermore, the SCD risk score was positively correlated with GLS, ALPM (r=0.658, p<0.001) and PMPM (r=0.600, p<0.001) strain. Also important is the fact that patient who have papillary muscle abnormalities had significantly worse ALPM and PMPM free strain. Finally, in multivariate analysis, LVMI, presence of syncope, worse GLS and ALPM-free strain were predictors of death. In terms of PM free strain value in normal healthy populations, one study done in 2016 shows between -32.5% to -48% for ALPM and -34.5% to -39.5% for PMPM but for the moment at least there are no guidelines for normal values[16].

What is the relevance of this paper for our understanding of HCM? It introduces an additional parameter that is easy to measure and reproducible alongside GLS and LA strain, aiding in the prediction of SCD. Although the technique is new and the sample size is limited, further studies with larger populations are necessary to establish its predictive value for SCD, similar to GLS. As strain measurements are generally robust and reproducible, papillary muscle strain has the potential to replace traditional parameters like left atrial dimension, wall thickness, and ejection fraction. Moreover, this paper highlights the importance of considering papillary muscle involvement in HCM, drawing attention to abnormalities such as bifid papillary muscles and anterior displacement during strain measurement. Ultimately, by integrating papillary muscle free strain with GLS, RV, and LA strain, we can enhance our ability to predict sudden cardiac death and ensure more appropriate ICD implantation. For clinicians focused on managing HCM, these are exciting times, and this paper provides valuable insights into the field.

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