Value of ECG in Hypertrophic Cardiomyopathy (HCM) - 2021

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In an era of fast technological development and evolving diagnostic possibilities, the ECG is living an authentic "rebirth" in cardiomyopathies.

Currently, the ECG remains an irreplaceable first step when evaluating patients with HCM and an abnormal ECG may be the only manifestation of disease at an early stage. In some instances, specific electrical anomalies may differentiate HCM from cardiac amyloidosis and glycogen storage diseases. +

The exponential growth in knowledge of the complexity of HCM has led to new challenges in terms of early identification of the disease, differential diagnosis, risk stratification, and development of targeted therapies.

In this scenario, the apparently "old fashioned" ECG and the array of ECG-based techniques, ranging from Holter monitoring and loop recorders to exercise testing, are as contemporary as ever (**Gherardo Finocchiaro 1, et al. The electrocardiogram in the diagnosis and management of patients with hypertrophic cardiomyopathy. Heart Rhythm. 2020 Jan;17(1):142-151. doi: 10.1016/j.hrthm. 2019.07.019.**).

The ECG in the diagnosis and management of patients with HCM is altered in > 90% of cases. In presence of HCM diagnosis a normal ECG is indicative of good prognosis (**Calore C, Cianfrocca C, Iacovella I, et al. Hypertrophic cardiomyopathy with normal ECG: clinical meaning and prognostic implications. Circulation 2018; 124: A15703**.)

The most common abnormalities are LVH, ST-segment alterations, T-wave inversion, deep narrow Q waves in lateral leads or lateroinferior leads and the peculiar diminution of R waves in the lateral precordial leads seen in this patient.

ECG features in HCM

1) **Sinus Node Dysfunction/ SSS:**

Characterization: Periods of inappropriate and often severe sinus bradycardia; Sinus pauses, sinus arrests and sinus exits blocks that can happen with and without appropriate escape rhythm, alternating tachycardia and bradycardia, referred to as a tachy-brady syndrome, which could also be associated with supraventricular tachycardia.

Meaning: Abnormal automaticity, conduction, or both of the SAN and surrounding tissues. Patients with HCM may have SSS together or SSS may develop in later years. Antiarrhythmic drug therapy should be given carefully and 24-hour ambulatory electrocardiogram monitoring should be done in certain periods. (**Zafer Yalim, Ibrahim Etem Dural, Volkan Emren, Ersel Onrat, Coexistence of Sick Sinus Syndrome and Hypertrophic Cardiomyopathy in Patient with Syncope. International Journal of Contemporary Medical Research Volume 3 | Issue 12 | December 2016 | ICV (2015): 77.83 | ISSN (Online): 2393-915X; (Print): 2454-7379**)

2) **Abnormal His-Purkinje conduction** These are observed in 15-30% of HCM patients (**Patrick Fitzgerald, Fred Kusumoto) The effects of septal myectomy and alcohol septal ablation for hypertrophic cardiomyopathy on the cardiac conduction system. J Interv Card Electrophysiol. 2018 Aug;52(3):403-408. doi: 10.1007/s10840-018-0433-0. Epub 2018 Aug 10**.).

Meaning: Abnormal His-Purkinje system conduction may result in CHB. (**Fananapazir L, et al. Electrophysiologic abnormalities in patients with hypertrophic cardiomyopathy. A consecutive analysis in 155 patients. Circulation. 1989 Nov;80(5):1259-68. doi: 10.1161/01.cir.80.5.1259**.)

3) **P-wave.**

Characterization possibilities: Normal, **LAE, RAE** or **BAE**. **LAE:** broad, bifid P wave in lead II "P mitrale" and enlarges the terminal negative portion of the P wave in V1. In lead II Bifid P wave with > 40 ms between the two peaks P wave duration > 110 ms. In V1: biphasic P wave with terminal negative portion > 40 ms duration and > 1mm deep.
LAE reflects diastolic dysfunction, high filling pressures, LVOTO, functional mitral regurgitation and progression toward the end-stage phase.
RAE: Peaked P wave ("P pulmonale") with amplitude: > 2.5 mm in the inferior leads (II, III and aVF) > 1.5 mm in V1 and V2. RAE is present in 14% t of patients with HCM, and reflects increased pulmonary pressures because of severe diastolic and/or systolic LV dysfunction. Patients have a higher prevalence of sarcomeric gene mutations, troponin T mutations and complex genotypes. RAE is a marker of disease progression and adverse outcome in sarcomeric HCM. (**Giuseppe Limongelli, et al. Clinical and genetic characterization of patients with hypertrophic cardiomyopathy and right atrial enlargement. J Cardiovasc Med (Hagerstown). 2017 Apr;18(4): 249-254. doi: 10.2459/JCM.0000000000000361**.)

RAE as an independent predictor of MACE.
BAE: lead II (Amplitude ≥ 2.5mm + Duration ≥ 120 ms), lead V1 or a combination of leads. lead V1 or a combination of leads. Biphasic P waves with initial positive deflection ≥ 1.5mm tall + terminal negative deflection ≥ 1mm deep + terminal negative deflection ≥ 40 ms duration. The diagnosis of BAE requires criteria for LAE and RAE to be met BAE is diagnosed when criteria for both RAE and LAE are present on the same ECG.
Poor prognosis when present in HCM. Patients with HCM and impaired LV relaxation develop progressive LAE and P wave modifications. This ECG feature is observed in approximately 20% of cases as a consequence of

- **Diastolic dysfunction:** DD is dangerous and is believed to be associated with congestive heart failure symptoms in patients who have what's called preserved left ventricular ejection fraction,

➢ **High filling pressures:** Filling pressures are considered elevated when the mean pulmonary capillary wedge pressure (PCWP) is >12 mm Hg or when the LVEDP is >16 mm Hg. HCM) is a primary myocardial disease, characterized by LVH, normal or supernormal **systolic function** and impaired **diastolic function**, including chamber stiffness and impaired relaxation (**Maron BJ, Bonow RO, Cannon RO, III, Leon MB, Epstein SE. Hypertrophic cardiomyopathy: Interrelation of clinical manifestation, pathophysiology, and therapy. *N Engl J Med.* 1987;316:844–52.**) (**Wigle ED, Rakowski H, Kimball BP, Williams WG. Hypertrophic cardiomyopathy. Clinical spectrum and treatment. *Circulation.* 1995;92:1680–92.**)

➢ **Left ventricular outflow tract obstruction (LVOTO)** is a recognized feature of HCM. It is caused by the thickened heart muscle and the abnormal movement of the mitral valve. This is the main mechanism of debilitating symptoms in HCM patients. About two-thirds of patients have obstructive form. In most patients, LVOTO occurs via systolic anterior motion (SAM) of the mitral valve in which the elongated leaflets contact the septum in mid-systole due to the high-velocity flow of blood directly on the leaflets. The narrower diameter of the LVOT due to increased septal wall thickness contributes to this obstruction. This leads to increased intraventricular pressures that over time can lead to LV dysfunction. Symptoms may include chest pain, dyspnea, exertional fatigue, dizziness, palpitation, and other symptoms of heart failure. Patients may experience near-syncope or syncope due to outflow obstruction or arrhythmia. A systolic ejection murmur may be heard at the lower left sternal border and apex that varies with the subaortic gradient.

➢ **Functional mitral regurgitation:** The systolic anterior motion of the mitral valve contributes to the development of mitral regurgitation and further narrows the LVOT, leading to more severe symptomatology. Cardiac magnetic resonance imaging accurately measures the left ventricular mass, the degree of diastolic function and it may also be used to distinguish phenotypic variants.

The presence of LAE is a marker of poor prognosis (**Gherardo Finocchiaro, Francois Haddad, Joshua W Knowles, Colleen Caleshu, Aleksandra Pavlovic, Julian Homburger, Yael Shmargad, Gianfranco Sinagra, Emma Magavern, Myo Wong, Marco Perez, Ingela Schnittger, Jonathan Myers, Victor Froelicher, Euan A Ashley Cardiopulmonary Responses and Prognosis in Hypertrophic Cardiomyopathy: A Potential Role for Comprehensive Noninvasive Hemodynamic Assessment. JACC Heart Fail. 2015 May;3(5): 408-418. doi: 10.1016/j.jchf.2014.11.011**.)
augmentation of left ventricle (LV) end diastolic pressure and diminution of LV compliance **(Savage, Seides et al. 1978). (Savage, D. D., S. F. Seides, C. E. Clark, W. L. Henry, B. J. Maron, F. C. Robinson and S. E. Epstein (1978). "Electrocardiographic findings in patients with obstructive and nonobstructive hypertrophic cardiomyopathy." Circulation 58(3 Pt 1): 402-408.)**

Impaired relaxation in HCM results in a reduced rate and volume of filling during the rapid filling period of diastole, with a resultant compensatory increase in atrial systolic filling, which results in a loud and often palpable fourth heart sound. In this hemodynamic situation is frequent registered left atrial enlargement (LAE) ("P mitrale") consequence of the left ventricular diastolic dysfunction that may lead to compensatory LAE. In LAE, the P wave of increased duration is ≥ 110 ms in adults, ≥ 120 ms in seniors, and 90 ms in children.
Chronic LAE can produce AF eventually in its evolution, which results in severe hemodynamic deterioration because of the importance of atrial systole in the presence of the impaired relaxation (Wigle, Sasson et al. 1985). (**Wigle, E. D., Z. Sasson, M. A. Henderson, T. D. Ruddy, J. Fulop, H. Rakowski and W. G. Williams (1985). "Hypertrophic cardiomyopathy. The importance of the site and the extent of hypertrophy. A review." Prog Cardiovasc Dis 28(1): 1-83**.)
Biatrial enlargement (BAE) is observed in the dilated phase with right ventricular heart failure (Biolato, Montalto et al. 2010). Asymmetric septal hypertrophy is a common cause of LVOTO. In these cases, mitral valve regurgitation is present in 30% of those patients as well as BAE (Opfermann, Doll et al. 2003). (**Opfermann, U. T., N. Doll, T. Walther**

and F. W. Mohr (2003). "Combined mitral valve repair, LVOT myectomy and left atrial cryoablation therapy." Interact Cardiovasc Thorac Surg 2(4): 501-502.)

RAE is observed in the so-called Bernheim's syndrome characterized by RVH cardiomyopathy leading to right ventricular outflow tract dynamic obstruction by right eccentric hypertrophy of the right side of ventricular septum (Sanen 1960). (Sanen, F. J. (1960). **"[Stenosis of the right ventricle caused by excentric hypertrophy of the left ventricle or ventricular septum (Bernheim's syndrome)]." Z Kreislaufforsch 49: 331-336**.)

4) **PR interval:** possibilities Normal PR interval, Prolonged/First-degree atrioventricular block (AVB) or short PR interval. First-degree AVB is observe in » 20% of the cohort demonstrated PR prolongation ≥200 ms, which associated in multivariable analyses with HCM−related death as well as a secondary end point of SCD or potentially lethal arrhythmic events. Higuchi et al demonstrates an association between first−degree AVB and cardiac outcomes among patients with HCM, even after moderate risk adjustment for common risk factors. (**Higuchi S, et al. Prognostic implication of first−degree atrioventricular block in patients with hypertrophic cardiomyopathy. J Am Heart Assoc. 2020; 9:e015064. DOI: 10.1161/JAHA.119.015064**.) (**Timothy C Wong. First-Degree Atrioventricular Block and Hypertrophic Cardiomyopathy: "I Have a Bad Feeling About This" J Am Heart Assoc. 2020 Mar 17;9(6):e015911. doi: 10.1161/JAHA.120.015911**.). » 20% of the cohort demonstrated PR prolongation ≥200 ms, which associated in multivariable analyses with HCM−related death as well as a secondary end point of SCD or potentially lethal arrhythmic events. Higuchi et al demonstrates an intriguing association between first−degree AVB and cardiac outcomes among patients with HCM, even after moderate risk adjustment for common risk factors. (**Higuchi S, et al. Prognostic implication of first−degree atrioventricular block in patients with hypertrophic cardiomyopathy. J Am Heart Assoc. 2020; 9:e015064. DOI: 10.1161/JAHA.119.015064**.)(**Timothy C Wong. First-Degree Atrioventricular Block and Hypertrophic**

Cardiomyopathy: "I Have a Bad Feeling About This" J Am Heart Assoc. 2020 Mar 17;9(6):e015911. doi: 10.1161/JAHA.120. 015911..). Short PR interval (<120ms) is considered an early detectable marker of myocardial storage diseases mainly FD. mild cardiac phenotype with symmetric distribution of LVH is suggestive of FD (**Martin S Maron et al, Identification of Fabry Disease in a Tertiary Referral Cohort of Patients with Hypertrophic Cardiomyopathy. Am J Med. 2018 Feb; 131(2):200.e1-200.e8. doi: 10.1016/j. amjmed.2017.09.010**.) (**Jiwon Seo et al, Fabry disease in patients with hypertrophic cardiomyopathy: a practical approach to diagnosis J Hum Genet. 2016 Sep;61(9):775-80. doi: 10.1038/jhg.2016.52**.)(**Pochis, W. T., et al. Electrophysiologic findings in Fabry's disease with a short PR interval. Am. J. Cardiol. 74, 203–204 (1994**). (**Mehta, J., et al. Electrocardiographic and vectorcardiographic abnormalities in Fabry's disease. Am. Heart J. 93, 699–705 (1977**).

A definite diagnosis of FD was defined as follows: a GLA mutation with ≤ 5% GLA activity (leucocytes, mean of reference value, males only) with ≥ 1 characteristic FD symptom or sign (neuropathic pain, cornea verticillata, angiokeratoma) or increased plasma (lyso)Gb3 (classical male range) or family members with definite FD. Subjects with LVH failing these criteria have a GVUS and an uncertain diagnosis. The gold standard is defined as characteristic storage in an endomyocardial biopsy on electron microscopy. Abnormally low voltages on ECG and severe LVH (MWT>15 mm) <20 years exclude FD. (**B E Smid et al, Uncertain diagnosis of Fabry disease: consensus recommendation on diagnosis in adults with left ventricular hypertrophy and genetic variants of unknown significance. Int J Cardiol. 2014 Dec 15;177(2):400-8. doi: 10.1016/ j.ijcard.2014.09.001**.).

WPW syndrome. may be associated with as HCM. The association of LVH, with ventricular preexcitation should raise suspicion of a glycogen storage disease produced by LAMP2 or PRKAG2 mutations, or FD.

5) QRS complex in HCM:

a) Deep and narrow("dagger-like") Q waves in lateral (I, aVL, V5-6) or lateral-inferior leads inferior (II, III, aVF) leads: Non-Q wave myocardial infarction;

b) Q wave >3mm in depth and/or >40ms in duration in at least two leads except aVR) showed the highest sensitivity (50% in the young, 29% in adults) while retaining a high specificity (90% in the young, 97% in adults), resulting in the highest accuracy (69% in the young, 52% in adults). Using this criterion criterion, abnormal Q waves were present 27.6% of preclinical carriers, and in 5.4% of non-carriers

c) It is caused by transmural fibrosis and or disproportionate hypertrophy of the basal interventricular septum and/or basal LV free wall. (**Tetsuo Konno et al, Diagnostic value of abnormal Q waves for identification of preclinical carriers of hypertrophic cardiomyopathy based on a molecular genetic diagnosis. Eur Heart J. 2004 Feb;25(3):246-51. doi: 10.1016/j.ehj.2003.10.031**.)

d) Small 'septal' q waves are typically registered in the lateral leads (I, aVL, V5 and V6)

e) The absence of small septal q waves in leads V5-6 should be considered abnormal. Absent q waves in V5-6 is most commonly due to LBBB.

f) Deeper Q waves (>2 mm) may be seen in leads III (+120°) and aVR(-150°) as a normal hearts

g) Q waves are considered abnormal if: > 40 ms (1 mm) wide, > 2 mm deep > 25% of depth of QRS complex. These need to be present in at least 2 contiguous leads to be considered abnormal (lead II and III for example, not leads II and aVF). The exception is the lateral leads V6, I, and aVL where the Q wave duration only needs to be 30 ms to be deemed abnormal.

h) **Low QRS voltage, compared to the degree of hypertrophy on TTE or CMRI,** This ECG signal is indicative of poor prognosis. Additionally, abnormally low QRS voltages on ECG and severe LVH (MWT>15 mm) <20 years exclude

FD. (**B E Smid et al, Uncertain diagnosis of Fabry disease: consensus recommendation on diagnosis in adults with left ventricular hypertrophy and genetic variants of unknown significance. Int J Cardiol. 2014 Dec 15;177(2):400-8. doi: 10.1016/j.ijcard. 2014.09.001**.)

i) Dominant S wave in V4,

j) Large Q and S waves in lead III: distinguished athlete heart from patients with HCM, independent of axis and well-known ECG markers associated with HCM. The correlation between interventricular septum thickness in patients with HCM and III_{Q+S} suggests a partial explanation for this association. Our hypothesis was driven by the understanding that patients with HCM commonly exhibit asymmetric septal hypertrophy on echocardiogram. The authors hypnotized that since the normal interventricular septum, typically, originate an small initial r wave representing septal depolarization towards lead III would be expected, but in a smaller proportion of instances, this r wave may be 'buried' inside a large Q wave if there is a larger septal thickness or underlying conduction system abnormality. (**Alvin S Chen 1, Rachel E Bent 1, Matthew Wheeler 1, Joshua W Knowles 1, Francois Haddad 1, Victor Froelicher 1, Euan Ashley 1, Marco V Perez Large Q and S waves in lead III on the electrocardiogram distinguish patients with hypertrophic cardiomyopathy from athletes, Heart. 2018 Nov;104(22):1871-1877. doi: 10.1136/ heartjnl-2017-312647**).

The observation that athletes rarely have Q waves wider than 40ms is already captured in the existing International Criteria. Recent studies showing that a Q to R ratio in lead aVF may be more useful than absolute Q wave measurements improves on the methods of Q wave analysis. Reverse cumulative frequency plots evaluated in all limb leads revealed that Q+S amplitude in lead III

showed the largest difference between the HCM and athlete populations, while lead aVF also showed a smaller difference and lead II showed no significant difference. This suggests that depolarization away from the lead III vector is the primary reason for this finding, as opposed to augmented superior depolarization. Existing Q wave criteria do not take into account that lead III may be more directly involved and that patients with HCM often have deep S waves instead of Q waves. Further optimization by measuring the (Q+S) to R ratio in lead III could be considered in future studies. The correlation between IIIQ+S and interventricular septal thickness in diastole (IVSd) on echocardiography that the authors reported further supports this hypothesis that the large negative deflections in lead III may represent septal depolarization towards the LV. Additionally, septal hypertrophic subtypes of HCM when compared with non-septal subtypes of HCM trended towards higher IIIQ+S amplitudes, although this did not reach statistical significance. This was likely due to the relatively small sample size of patients for whom the documented subtype of HCM was available.

Characteristics Favoring HCM and Athlete's Heart Favors HCM Asymmetrical hypertrophy, Diastolic dysfunction, Late gadolinium enhancement on CRMI Favor Athlete's Heart. Homogeneous hypertrophy with maxima thickness of 15mm, Ellipsoid LV shape, Regression iwth deconditioning

k) Prolonged QRS duration: RBBB: After alcohol septal ablation (37-70% of patients); LBBB: After Septal Myectomy (50-100% of patients) and

l) **Fragmented QRS** (f-QRS) complex is a myocardial conduction abnormality that indicates myocardial scar. It is defined as additional spikes, R' wave or notching of R or S wave within the QRS complex in two contiguous leads corresponding to a coronary territory in a routine 12-lead ECG (0.5–150 Hz) (**R. Jain, R. Singh, S. Yamini, M.K. DasFragmented ECG as a risk marker in cardiovascular diseases. Curr Cardiol Rev, 10 (3) (2014 Aug), pp. 277-286**).

Though initially fQRS was defined in the setting of normal QRS duration (<120 m s), later it has been expanded to include conditions with wide QRS complexes, ventricular ectopy and paced rhythm, when more than 2 notches are present. It is an important, yet often overlooked marker of mortality and arrhythmic events in many cardiac diseases. Several demonstrated the role of fQRS in predicting ventricular arrhythmias in the setting of HCM. In a prospective study of 167 HCM patients, ventricular arrhythmias and SCD were considered as the major arrhythmic events. The study established that fQRS is significantly associated with MACE and. fQRS was identified to be an independent predictor of VA and major arrhythmic events in HCM (**K.W. Kang, et al. Fragmented QRS as a candidate marker for high-risk assessment in hypertrophic cardiomyopathy. Heart Rhythm, 11 (8) (2014 Aug), pp. 1433-1440**).

6) **ST-segment depression:** ST-segment depression in the I and aVL leads could be of prognostic significance in HCM patients. (**Majid Haghjoo et al, ST-segment depression as a risk factor in hypertrophic cardiomyopathy. Europace. 2009 May;11(5): 643-9. doi: 10.1093/europace/eun393**.)

7) **Pseudo–ST-segment elevation myocardial infarction:** the ECG finding of convex ST-segment elevation and abnormal Q waves could be valuable for detection of disease progression in patients with HCM (**Maky Furuki et al.,Value of convex-type ST-**

segment elevation and abnormal Q waves for electrocardiographic-based identification of left ventricular remodeling in hypertrophic cardiomyopathy. Kobe J Med Sci. 2009 Jun 5;55(1):E16-29.).

8) **T-Wave Inversion (TWI)**

9) **QTc prolongation:** Predict appropriate ICD therapies in patients with HCM (**Gray B, Ingles J, Medi C, Semsarian C. Prolongation of the QTc interval predicts appropriate implantable cardioverter-defibrillator therapies in hypertrophic cardiomyopathy. JACC Heart Fail 2013;1:149–155**.)

10) **Supraventriculares arritmias:** AF: It is the most common arrhythmia observed in HCM. AF is present in 5 % of HCM patients at the time of diagnosis. AF 8 times higher risk of ischemic stroke. Causes: significant septal hypertrophy, significant mitral valve regurgitation, SAM, and LVOT obstruction. AF is the most common supraventricular arrhythmia observed in HCM and is frequently associated with acute and/or long-term clinical deterioration, embolic complications, and increased cardiovascular mortality due to heart failure and stroke (Olivotto, Cecchi et al. 2001). Factors that predispose to AF: significant septal hypertrophy, significant mitral valve regurgitation, systolic anterior motion (SAM), and LVOT obstruction. HCM is related to ischemic stroke and AF is under-recognized and consequently, many patients who should be on oral anticoagulation for stroke prevention go untreated. The consequences of AF on the long-term prognosis of HCM patients are not uniformly unfavorable; however, and in ≈ 30% of patients the arrhythmia is compatible with an uneventful course. AF is a common sustained arrhythmia in HCM patients and is primarily related to left atrial dilatation and remodeling. There are several clinical, ECG, and echocardiographic features that have been associated with development of AF in HCM patients; strongest predictors are left atrial size, age, and heart failure class. AF can lead to progressive functional decline, worsening heart failure and increased risk for systemic thromboembolism. The management of AF in HCM patient focuses on symptom alleviation (managed with rate and/or rhythm control methods) and prevention of complications such

as thromboembolism (prevented with anticoagulation). Finally, evidence suggests that early rhythm control strategy may result in more favorable short- and long-term outcomes. (**Lohit Garg 1, ET AL. Atrial fibrillation in hypertrophic cardiomyopathy: prevalence, clinical impact, and management. Heart Fail Rev. 2019 Mar;24(2): 189-197. doi: 10.1007/s10741-018-9752-6**.), Twenty-seven patients diagnosed with HCM and having a history of documented AF attack were compared with 53 age- and gender-matched patients who had no such history. LA diameter was significantly greater and gradient in the LVOT was lower in patients with AF than those without AF. Maximum P-wave duration (Pmax), P wave dispersion (PWD) and P-Terminal Force (PTF-V1) (normal PTF-V1 does not exceed 0.04 s in width and 1 mm in depth, i.e., 0.04 mm/s) values were significantly higher in patients with AF. A Pmax>134.5 ms separated the patients with AF from controls with a sensitivity of 92%, specificity of 89% and a positive predictive value of 80%. A PWD value > 52.5 ms separated patients from controls with a sensitivity of 96%, a specificity of 91% and a positive predictive accuracy of 84%. An LA diameter>4.2 cm separated patients from controls with a sensitivity of 96% and a specificity of 81%. The authors concluded that LA diameter and PWD values are the most significant predictors for AF occurrence in patients with HCM, and simply measuring Pmax and PWD values, could easily identify the patients with high risk, and prescribe the necessary treatment and follow-up protocols for such patients (Ozdemir, Soylu et al. 2004). Sinus rhythm is present in most cases. Possible acute AF is observed in ≈10% of cases as a consequence of LV impairment of relaxation, compliance diminution or diastolic stiffness of the LV and augmentation of end diastolic LV pressure and consequently augmentation of medium intra left atrial (LA) pressure, leading to LAE. In a large cohort of patients with HCM, a marked increase in LA dimension was a novel and independent marker of prognosis in HCM, particularly relevant to the identification of patients at risk of death related to heart failure (Nistri, Olivotto et al. 2006). **(Nistri, S., I. Olivotto, S. Betocchi, M. A. Losi, G. Valsecchi, B. Pinamonti, M. R. Conte, F. Casazza, M. Galderisi, B. J. Maron and F. Cecchi (2006). "Prognostic significance of left atrial size in patients with hypertrophic cardiomyopathy (from the**

Italian Registry for Hypertrophic Cardiomyopathy)." Am J Cardiol 98(7): 960-965.)

11) **Ventricular arrhythmias:** a) NSVT is defined as an episode of ventricular tachycardia that: Involves a heart rate of more than 100 beats per minute, Lasts for at least three heartbeats and persists ≤30" Most often, this either does not cause any symptoms at all or it causes palpitations. Occasionally, can produce lightheadedness, dizziness, or, more rarely, syncope. (**Al-Khatib SM, Stevenson WG, Ackerman MJ, et al. 2017 AHA/ACC/HRS guideline for management of patients with ventricular arrhythmias and the prevention of sudden cardiac death: A report of the American College of Cardiology/American Heart Association task force on clinical practice guidelines and the Heart Rhythm Society. Circulation. 2018;138(13). doi: 10.1016/ j.hrthm.2017.10.035**) https://www.verywellhealth.com/non-sustained-ventricular-tachycardia-nsvt-1746247 NSVT should be considered in the primary prevention of SCD. McKenna et al. found that NSVT was significantly associated with an increased risk of sudden death during a mean follow-up period of 2.6 years. (**W.J. McKenna, D. et al. Arrhythmia in hypertrophic cardiomyopathy I. Influence on prognosis. Br Heart J, 46 (1981), pp. 168-172**). In a large HCM cohort with no or only mild symptoms, myocardial fibrosis detected by CMR was associated with greater likelihood and increased frequency of ventricular tachyarrhythmias (including NSVT) on ambulatory Holter ECG. Therefore, contrast-enhanced CMR identifies HCM patients with increased susceptibility to ventricular tachyarrhythmias (**A Selcuk Adabag et al, Occurrence and frequency of arrhythmias in hypertrophic cardiomyopathy in relation to delayed enhancement on cardiovascular magnetic resonance; J Am Coll Cardiol. 2008 Apr 8;51(14):1369-74. doi: 10.1016/j.jacc.2007.11.071**.).
12) Exercise-induced Arrhythmias and blunted blood pressure response predict the risk of SCD, especially in ≤40 years HCM patients

III) PR or PQ interval duration

In HCM it is possible to observe normal, short and prolonged PR intervals, AV blocks of different degrees and even total AV blocks. Signs of Wolff-Parkinson-White WPW (short PR, delta wave) — ECG features of Wolff-Parkinson-White (WPW) were seen in 33% of patients with HCM in one study, and at least one genetic mutation has been identified that is associated with both conditions. Data concerning the familial occurrence of ventricular preexcitation, i.e. WPW syndrome, indicating autosomal dominant inheritance with a gene mutation on chromosome 7q3 has been described in familial HCM coexisting with WPW syndrome. (**MacRae CA, Ghaisas N, Kass S, 1995. Familial hypertrophic cardiomyopathy with Wolff-Parkinson White syndrome maps to a locus on chromosome 7q3. J Clin Invest 96: 1216–1220**.)

Bobkowski et al (**Bobkowski, W., Sobieszczańska, M., Turska-Kmieć, A., Nowak, A., Jagielski, J., Gonerska, M., … Siwińska, A. (2007). *Mutation of theMYH7 gene in a child with hypertrophic cardiomyopathy and Wolff-Parkinson-White syndrome. Journal of Applied Genetics, 48(2), 185–188.* doi:10.1007/bf03194677**) presented a case of a 7-year-old boy with HCM and coexisting WPW syndrome. On chromosome 14, molecular diagnostics revealed a C 9123 mutation (arginine changed into cysteine in position 453) in exon 14 in a copy of the gene for β-myosin heavy chain (MYH7). It was the first known case of mutation of the MYH7 gene in a child with both HCM and WPW. Since no linkage between MYH7 mutation and HCM with WPW syndrome has been reported to date, we cannot conclude whether the observed mutation is a common cause for both diseases, or this patient presents an incidental co-occurrence of HCM (caused by MYH7 mutation) and WPW syndrome.

Association of HCM and WPW has been reported in several manuscripts, but whether the prognosis or severity of arrhythmia is different compared to the individual disorders remains unsettled. Talle et al reported a case of HCM with WPW syndrome in a 28-year-old male Nigerian soldier presenting with recurrent syncope and lichen planus. (**Mohammed Abdullahi Talle, Faruk Buba, Aimé Bonny, Musa Mohammed Baba Hypertrophic Cardiomyopathy and Wolff-Parkinson-White Syndrome in a Young African Soldier with**

Recurrent Syncope. Case Rep Cardiol. 2019 Dec 4;2019:1061065. doi: 10.1155/2019/1061065)

Concurrence of HCM and WPW in a consecutive series of patients presenting with preexcitation, 7.62% were found to have HCM (***Perosio AM, Suarez LD, Bunster AM, Locreille A, Apkarian OA, Vallazza MA, Foye R* . Pre-excitation syndrome and hypertrophic cardiomyopathy. *J Electrocardiol. 1983 Jan; 16(1):29-40***).

Of the many phenocopies of HCM, cardiac hypertrophy and preexcitation are typically **caused** by a mutation of the g 2 subunit of the adenosine monophosphate-activated protein kinase (PRKAG2) Gollob et al identified a novel mutation (Arg531Gly) in the gamma-2 regulatory subunit (PRKAG2) of AMP-activated protein kinase (AMPK) to be responsible for a syndrome associated with ventricular preexcitation and early onset of atrial fibrillation and conduction disease.

M H Gollob 1, J J Seger, T N Gollob, T Tapscott, O Gonzales, L Bachinski, R Roberts Novel PRKAG2 mutation responsible for the genetic syndrome of ventricular preexcitation and conduction system disease with childhood onset and absence of cardiac hypertrophy Circulation 2001 Dec 18;104(25):3030-3. doi: 10.1161/ hc5001.102111.

These observations confirm an important functional role of AMPK in the regulation of ion channels specific to cardiac tissue. The identification of the cardiac ion channel(s) serving as substrate for AMPK not only would provide insight into the molecular basis of AF and heart block but also may suggest targets for the development of more specific therapy for these common rhythm disturbances.

Although both HCM and WPW are independently associated with various forms of arrhythmias and SCD, whether their concurrence will result in more frequent and severe arrhythmias or fatalities remains conjectural, and to our knowledge, this has not been reported in SSA. We present a case of HCM with WPW in a young African soldier presenting with recurrent syncope.