Highlights and comments on EHRA/HRS/APHRS/LAHRS expert consensus on risk assessment in cardiac arrhythmias: use the right tool for the right outcome

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Abstract

Patients with heart disease, or at high risk of developing a cardiac condition, usually undergo risk assessment by primary care physicians, internal medicine doctors, or cardiologists. There are several methods that can be used for this risk assessment, and their applicability differs with respect to availability, complexity, and usefulness in different geographic populations. This document focuses on some of the many relevant clinical topics recently presented in the "Expert Consensus on Risk Assessment in Cardiac Arrhythmias: Use the Right Tool for the Right Outcome," which include statements based on the best available evidence. In this review, we want to highlight and make some pertinent comments on some of the most relevant points of this Consensus.

Keywords Cardiac arrhythmias · Cardiac electrophysiology · Electrocardiography · Invasive electrophysiological study · Atrial fibrillation · Ventricular tachycardia

1 Introduction

One of the most important roles for professional medical societies is to develop expert consensus guidelines and documents that can help define policies and strategies for the best medical care of our patients. Heart Rhythm societies and associations all over the world are focused on the field of arrhythmia diagnosis and management and gather clinical and interventional electrophysiologists that could work on many of these documents to address many critical clinical topics. From a continental point of view, there are four such societies: Latin American Heart Rhythm Society (LAHRS), Heart Rhythm Society (HRS), European Heart Rhythm Association (EHRA), and Asian Pacific Heart Rhythm Society (APHRS). All have a similar interest and expertise in many relevant topics on the field, emphasizing that best arrhythmia management is a collaborative process among multiple professional societies from around the world.

Recently these four Societies developed an Expert Consensus on Risk Assessment in Cardiac Arrhythmias: Use the Right Tool for the Right Outcome [1–3], to create tools for clinicians to perform rational and evidence-based risk stratification in cardiac arrhythmias. It is known that patients with cardiac diseases, or at high risk of developing a heart condition, undergo risk assessment by cardiologists and primary care physicians. There are several methods used for this risk assessment, and they differ with respect to availability, complexity, and usefulness in different patient populations. This document focuses on some of the many relevant clinical topics presented in the Consensus, whose statements are based on the best available evidence to date. In this review,

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we want to highlight some of the most relevant points of the Consensus and provide some thoughts on their importance.

2 Comments on "General tools for risk assessment, strengths, limitations, and pretest probability"

Proper evaluation of any patient includes as major and first step, a detailed medical history. This is really important to determine the arrhythmia patterns, its duration, triggers, and, very relevant, the mode of onset (beginning) and termination (end) of tachycardias. Also relevant are the accompanying symptoms when the event occurs, and, in cases with heart failure, the functional class (still mostly evaluated by the New York Heart Association (NYHA) classification) and left ventricular ejection fraction (LVEF) to guide diagnosis and to perform the best treatment for each patient [1–4].

After clinical history, the most straightforward and essential tool in arrhythmia evaluation is still the 12-lead electrocardiogram (ECG). With this tool, we can identify ventricular preexcitation, tachyarrhythmias, and conduction disturbances, but also the presence of structural heart disease, and many cardiac ion channel diseases ("channelopathies"). But the ECG is not only useful for diagnosis; there is growing data that confirms its utility for prognosis. For example, some P wave characteristics had been shown to be predictive of atrial fibrillation (AF) [5, 6]. P wave duration (atrial depolarization) is an independent risk factor for AF occurrence in 10 years [7]. QRS duration (depolarization component) has been associated with all-cause mortality among patients with heart failure [8]. QT interval measurement (as a surrogated of repolarization) is key for the diagnosis of both congenital and "acquired" long QT syndrome, but also for monitoring the effects of several drugs that prolongs the QT interval as has been clearly demonstrated during this coronavirus pandemic. Different ST segment and T wave (ST-T or repolarization components) characteristics could be predictors of malignant arrhythmias, as when macroscopic T-wave alternans appeared on any 12-lead ECG, Holter monitoring, or treadmill-stress test. A very specific ECG pattern called "Early repolarization syndrome" (not the traditional early repolarization pattern) has been established as a new entity with a high possibility of sudden cardiac death (SCD) and is easily observed in the 12-lead ECG [9]. Finally, ambulatory ECG monitoring (Holter monitoring) can register continuous heart rhythm and allow us to detect and quantify arrhythmias. To establish the burden of atrial and ventricular arrhythmias is relevant for treatment decisions, including drug treatment and catheter ablation. Advances on ambulatory monitoring include new personal portable devices, long-term monitoring through patch monitors, and implantable subcutaneous loop recorders (ILR).

New portable device (wearable/direct to consumer products) technology refers to several equipment that monitor physiological parameters (i.e., ECG) and can be used to facilitate arrhythmia detection, but it is imperative to integrate them into clinical context and physician judgment. The ILR provides long-term continuous monitoring up to 3 years, improving the diagnosis of unexplained syncope, allowing to provide specific treatment of tachyarrhythmias, and even to detect AF as a cause of "cryptogenic" stroke or ESUS, embolic stroke of undetermined source [1–3].

Many other data may also be acquired with new Holter monitoring systems. In this sense, 24-h heart rate variability can help to predict adverse outcomes in the subset of patients with ischemic cardiomyopathy [10].

3 Comments on "Risk assessment of ventricular arrhythmias using imaging modalities"

LVEF remains the most crucial parameter for SCD prediction, especially in subjects with structural heart disease in which it guides implantable cardioverter-defibrillator (ICD) implantation. Therefore, echocardiography, due to its large availability, is still the main tool for risk stratification of SCD. But primary prevention rate all over the world is still low, with only 1 to 5% of patients with an ICD implanted based upon low LVEF (LVEF > 35%) [6, 11]. On the other hand, up to 70% of all SCD occur in individuals with a LVEF greater than 35% [11, 12]. These data implies that many patients that could be prevented from SCD are either not implanted with an ICD (when they should) or do not receive an ICD because an incomplete risk stratification. Using other imaging techniques, like cardiac magnetic resonance imaging (MRI) with late gadolinium enhancement, it is possible to broaden the spectrum of patients who can benefit from an ICD or other interventional therapies. For example, information about fibrosis or scar tissue could guide ventricular tachycardia (VT) ablation around scar reentry circuits [13, 14]. Quantification of myocardial fibrosis could guide ICD implantation in some diseases like hypertrophic cardiomyopathy. Unfortunately, this technology is not widely available in Latin American countries. Therefore, echocardiography is still the most frequently used imaging tool in Latin America, due to lower cost and availability.

4 Comments on "Invasive electrophysiological study"

Invasive electrophysiology (EP) studies are still a useful tool to identify the cause of unexplained syncope, mainly in subjects with previous myocardial infarction or other

scar-related conditions (i.e., congenital heart disease) [15]. It can identify conduction disturbances in which a pacemaker is mandatory, VT in patients with an unclear indication for ablation or slight decrease of LVEF, and may have prognostic value for SCD in specific subgroups, like in asymptomatic patients with Brugada syndrome. It is also essential to know when we should not perform an EP study: (a) in patients with a LVEF < 35% (with or without ischemic heart disease) or other scenarios distinct than asymptomatic Brugada syndrome [1–3].

5 Comments on "Biomarkers, tissue, and genetics"

Biomarkers are useful to stratify many illnesses and are used with increasing frequency all over the world [1–3]. Nowadays, the value of molecular genetic studies is clear, for diagnosis and for risk stratification in channelopathies and many myocardial diseases. Unfortunately, both tools, biomarkers and molecular genetic studies, are difficult to be applied in most developing countries. Therefore, for molecular genetic diagnosis, collaborations with laboratories from Europe or the USA are crucial for Latin American patients [1–3].

6 Comments on "How to assess risk for AF in people at higher risk for AF"

AF has a prevalence in the Western world of 1–2%, and it will increase as our population tends to be older [16, 17]. Risk assessment for AF is crucial since this arrhythmia is associated with the risk of stroke, cognitive impairment, heart failure, and even death [18, 19]. Risk assessment should focus on two main areas: risk of developing AF and risk of developing AF-related complications. The following must be considered for the former [1–3]. Age continues to be one of the most important risk factors for developing AF. Gender has a special interest since women have higher incidence of AF, usually have more comorbidities, are less symptomatic, and are at higher risk of complications [20]. Heart failure has a bidirectional relationship with AF as subjects with heart failure are at increasing risk of developing AF but also AF could precipitate heart failure in specific subsets of patients. In both situations, the combination of heart failure and AF increases the risk of suffering AF-related complications [21–23]. Frequent interrogation of implantable devices (ICD or CRT-D devices) commonly used in heart failure patients, alongside with an increased use of "home monitoring" platforms, is crucial for an early diagnosis and management of AF. Careful consideration of individual risk factors like obesity, diabetes, sleep apnea, and structural heart disease is emphasized, as well as the use

of clinical risk scores [1–3]. Clinical tools go from amazingly simple strategies, as to train patients on pulse palpation, to more complex analysis of risk factors with the use of CHA_2DS_2-VASc score to stratify patients to oral anticoagulation therapy. Nowadays, it is possible to download many applications that include calculators for CHA_2DS_2-VASc and HAS-BLED scores.

7 Comments on "Risk of developing complications because of AF"

In the Consensus, cognitive assessment is highly recommended in AF patients since it has been clearly shown that AF is a risk factor for cognitive decline or impairment of cognitive function [24]. This may be related to directly to manifest or silent stroke but also to other mechanisms that are independent from thromboembolism. There is evidence that early anticoagulation therapy using risk factor stratification may reduce the rate of this cognitive decline [24]. Therefore, cardiologists should interact with their counterparts, neurologists, in order to prevent this deficit.

8 Comments on "How to assess risk for adverse outcome (disease progression or death) in patients with AF"

Stroke is the most known adverse outcome in AF [23–25] and anticoagulation therapy is the cornerstone therapy for stroke prevention in AF. Stroke risk scores must be used to guide therapy and the most widely used is the CHA_2DS_2-VASc [26]. Male patients with a score > 1 or woman with > 2 points should be considered for long-term oral anticoagulation. For high-risk patients in which long-term anticoagulation is contraindicated, left atrial appendage occlusion (LAAO) has emerged as an alternative therapy. Although there is no definitive evidence on its use, randomized trials found a non-inferior strategy in LAAO when compared to warfarin [27]. More solid evidence is needed on this topic before its widespread use.

Catheter ablation is an acceptable therapy in symptomatic patients with AF and may have benefits in hard clinical endpoints (death and hospitalization for worsening heart failure) in selected populations, like patients with impaired LVEF as shown in the CASTLE-AF trial [28–30]. In the CABANA trial, where not only patients with impaired LVEF were included but hard clinical endpoints did also not differ between drug and ablation therapy [31].

Discrepancy regarding a rhythm or rate control strategy has been a discussion since the publication of the AFFIRM trial in the early 2000 [32] that did not show any difference in outcomes. However, the recently published EAST-AFNET 4

Trial showed that the ablation strategy has a statistically significant difference in the composite primary endpoint (death and stroke) that favored a rhythm-control strategy (3.9% vs 5.0% $P = 0.005$) [33]. It is important to address that EAST/AFNET 4 trial could not be included in this Consensus, as it was recently released (August 2020). Another recent trial on cryoballoon ablation versus drugs also confirms the EAST-AFNET 4 results [34].

9 Comments on "How to assess risk for VT in specific populations"

Coronary heart disease is the most frequent etiology of SCD, with approximately 70% of cases [35]. For primary prevention of SCD, current approach to risk stratification relies mainly on the evaluation of LVEF: values below 30–35% allow the identification of ICD candidates, who are at the highest relative risk of SCD. In other words, many patients with EF 35% and a high risk of VT/VF are not protected, and patients with a LVEF > 35% account for the highest absolute number of SCDs [36]. For this reason, many researchers emphasize that EF is an inadequate marker for detecting patients who are at high risk for SCD despite having a normal or subnormal EF.

In secondary prevention, SCD risk is significantly higher, and thus risk stratification is certainly more standardized. Both the ischemic substrate and the ischemic triggers for malignant ventricular arrhythmias must be evaluated whenever considered appropriate with coronary angiogram, functional ischemic evaluation by nuclear scan, stress-echocardiography, or MRI [15, 36, 37].

Non-ischemic HF includes a heterogeneous group of patients with reduced ventricular function due to cardiomyopathies from different etiologies, and at high risk for VT. Reduced cardiac function remains a powerful predictor of VT and appropriate ICD therapy in these patients as a primary prevention. Cardiac MRI shows promising results in some subsets [38, 39].

Inflammatory cardiomyopathies encompass a broad spectrum of disorders characterized by myocardial inflammation as the primary cause of cardiac dysfunction. In patients who present with ventricular arrhythmias and diagnosed with non-ICM, the incidence of inflammatory cardiomyopathy may be as high as 50% [40].

Cardiac MRI scan is the gold standard for diagnosing myocarditis and inflammatory cardiomyopathies [41]. The presence of late gadolinium enhancement is significantly associated with increased risk of adverse cardiac events. Although randomized data on the possible use of a higher EF for risk stratification in these patient populations is lacking, given the risk of VT noted in retrospective studies, the use

of MRI and cardiac positron emission tomography to evaluate the etiology of non-ischemic heart disease is warranted.

Ventricular arrhythmias in patients with congenital heart disease may be observed the pediatric age group but also in adults with repaired congenital defects group [42]. In the pediatric patient with congenital heart disease, ventricular overload, surgical scars and patches or baffles, ventricular dysfunction, and previous conduction defects are recognized risk factors for VT [43, 44]. In adult patients with congenital heart disease, an increasing group in Latin American countries, VTs are mainly observed after correction of tetralogy of Fallot and left ventricular outflow tract defects [45]. Older age at surgery, poor hemodynamic status, and prolonged QRS represent the most common risk factors for ventricular arrhythmias. In adult patients with congenital heart disease,

In Arrhythmogenic Right Ventricular Cardiomyopathy, the most important features of a high arrhythmic risk include sustained ventricular arrhythmias, non-fatal cardiac arrest, severe right and/or left ventricular dysfunction, and the presence of a positive genotype [46]. Ambulatory ECG monitoring is crucial to detect premature ventricular complex burden or the presence of non-sustained VT. Inducibility of VT/VF on EPS can prompt an ICD therapy in these patients [46]. Abnormal cardiac MRI is an independent predictor of clinical events with a cumulative effect of the abnormalities including morphology, wall motion, and fat/fibrosis [47].

In patients with Chagas' disease, a disease with a high prevalence in Central and South American countries, the highest risk of death is observed associated with the presence of HF with a NYHA class III/IV and non-sustained VT on Holter or patients in NYHA class I/II with left ventricular dysfunction and NSVT on Holter. All those patients should be considered candidates for invasive therapeutic management [48]. In patients with syncope and a bundle branch block, an invasive EPS is useful in assessing risk of sustained ventricular arrhythmias [49]. When available, cardiac MRI should be considered to evaluate for arrhythmogenic substrate as part of a risk stratification strategy in those patients with cardiomyopathy.

10 Conclusions

The Expert Consensus developed by the four major EP international societies have an important role for helping guide clinicians in conditions associated with arrhythmias. Although a wide range of tools is available for risk assessment, choosing the best method and tool, considering the individual patients' characteristics and the suspected arrhythmia, is not always an easy decision. Even though many of the content of this document is not easily available in our region, there are clearly many tools that are relevant to clinical cardiologists and arrhythmia specialists working

on the field in Latin America and that can lead to better care for our patients.

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