Analysis of clinical characteristics, risk factors and complications associated with Brugada Syndrome: An integrative review

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ABSTRACT

Brugada Syndrome is a channelopathy resulting from genetic alterations that influence the regulation of sodium channels in the heart muscle, leading, consequently, to arrhythmias, detected by means of an electrocardiogram with ST-segment elevation, given the variably asymptomatic condition of young people with hereditary development of the disease. The diagnosis, when evidenced through clinical manifestations, occurs through syncope or cardiac arrest. Data were analyzed through an integrative literature review and sampling data didactically represented in weighted base articles. Based on digital researches platforms such as PUBMED, SCIELO, SCOPUS and BVS, it is possible, through inclusion and eligibility criteria, to understand the findings and comparatively understand symptoms, clinical conditions, family members and treatment before the target audience.

Keywords: Brugada syndrome, Channelopathy, Hereditary development.

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INTRODUCTION

Brugada Syndrome is a hereditary arrhythmogenic disease identified by the presence of specific electrocardiographic features with or without clinical symptoms. In addition, it is important to highlight the anatomical and physiological aspects of the heart in order to add a concept and understanding of this syndrome, which affects mostly young patients, who are at increased risk of sudden death due to ventricular fibrillation (VF). (MILITZ, et al, 2021)

As for the anatomical and physiological aspects, it is legitimate to postulate that the heart has four cavities, two right and two left. The two cavities that are present on the right side receive poorly oxygenated blood from the systemic circulation through the superior and inferior vena cavae, and pump it through the pulmonary artery to the lungs, where it will be oxygenated. The blood then returns to the left atrium through the pulmonary veins, goes to the left ventricle, and, through the aortic artery, returns to the systemic circulation. (BRANCO, et al, 2018).

With regard to Brugada Syndrome, it is worth mentioning that it belongs to a group of channelopathies caused by alterations that occur in genes that encode or regulate the sodium channels of the heart muscle. This pattern of genetic transmission has an autosomal dominant trait with mutations of the SCN5A and SCN10A genes linked to the Brugada phenotype. (MILITZ, et al, 2021).

In addition, the recognition of Brugada Syndrome can be done by means of a 12-lead ECG, demonstrating elevation of the J point in the right precordial leads. However, diagnosing the existence of the syndrome among the general population becomes complicated, since some patients have an unstable Brugada electrocardiographic pattern. (MILITZ, et al, 2021).

As for the risk factors of Brugada syndrome, genetic inheritance can be included, which due to heredity increases the risk of developing the pathology as it is more frequent in men than in women. Brugada syndrome occurs more often in Asians than in people of other races. In addition, an alarming factor that does not cause the syndrome but can irritate the heart and cause fainting or sudden cardiac arrest is fever, especially if it is in children. (Wylie, et al, 2020).

Under these aspects, it is relevant to highlight the complications of this syndrome. Studies show that Brugada syndrome has distinct consequences such as syncope, sudden cardiac arrest, which if not treated immediately, can lead to sudden loss of heart function, breathing and consciousness and which usually occurs during sleep, AF, conduction disorders or pathological mutations, these factors are present in patients with Brugada ECG and also exist in patients with genetic cause of the syndrome. In view of the above, the objective was to analyze the clinical characteristics, risk factors and complications associated with Brugada Syndrome. (Brugada, 2023).

METHODOLOGY

This is an integrative literature review that listed the stages of problem/hypothesis construction, in addition to the general and specific objectives of the review, establishment of inclusion and exclusion criteria for articles (sample), defining the information that was extracted from the selected articles that emerged from research carried out on the clinical characteristic, risk factors and complications associated with Brugada Syndrome.

To define the guiding question, the PVO strategy was used, in which P (population) patients with Brugada Syndrome, V (variable) clinical characteristic, risk factors and complications, and O (Ouctomes/outcome) know the clinical patterns among patients. Thus, the guiding question was established in order to function as a research question or hypothesis. Thus, the question for the direction of this study was: "What are the risk factors associated with eating disorders among college students?" (BIRUEL; PINTO 2011). (TABLE 1).

Table 1: Components of the question according to PVO strategy.

Acronym	Definition	Description
P	Population	Patients with Brugada syndrome
V	Variable	Clinical characteristic, risk factors and complications
Or	Ouctomes/outcome	Know the clinical patterns among patients

Source: authors (2023)

After this stage, data were manually searched in electronic databases of the Virtual Health Library (VHL), namely: Scientif Electronic Library Online (SCIELO), National Library of Medicine (PUBMED) and SciVerse Scopus (SCOPUS). The following descriptors were used, "brugada syndrome", "signs and symptoms", "risk factors", "complications", "diagnostic" to locate the publications. In which they were combined by the Boolean operator AND to relate the search terms. Regarding the study, the following steps were followed: 1) detection of the descriptors by means of the Descriptors in Sciences and Health (DECs), selecting those that were closest to the theme; 2) articles were searched using these descriptors in the databases above, which were in the period from 2013 to 2023; 3) filtration was performed by applying the eligibility criteria for the selection of the articles that were used in this review.

A priori, the titles and abstracts of the articles were read to analyze the publications. The inclusion criteria were those that fit the time frame of the last 10 years, that were in the Portuguese and English languages and that were related to the proposed theme. Those that did not have the full text and did not fit within the required time frame were excluded. The search for the study sample

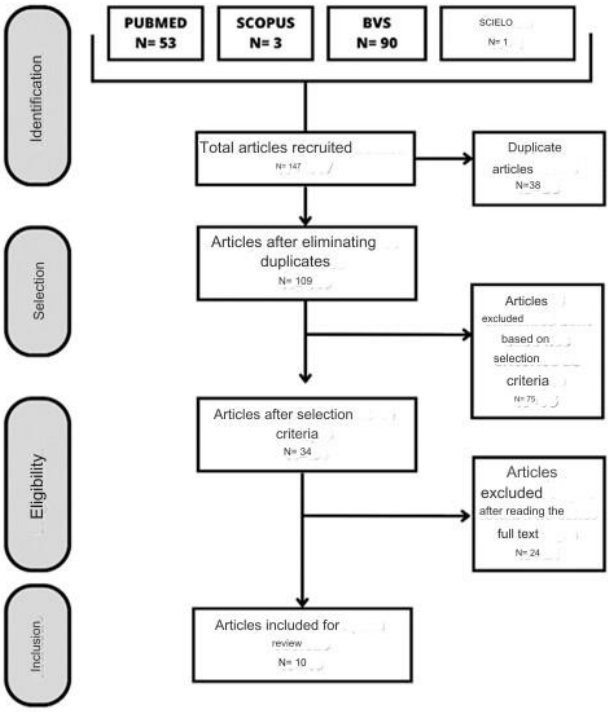
was carried out in March 2023. A flowchart was developed to recognize the methodological path adopted (Figure 1).

The data obtained from the previously selected articles were transcribed into a validity instrument, and this mechanism was adapted to accommodate the study objectives. Instrument that contains variables of interest to the research in question, and its items are composed of: title, authors, year, sample, research location, study objective, method/level of evidence and main results. The proposal described by Melnyk and Fineout-Overholt (2022) was adopted to evaluate the research design and classify the scientific evidence of the article.

RESULTS

A total of 147 articles were identified in electronic databases using the science and health descriptors "Brugada Syndrome", "risk factors" and "signs and symptoms", "complications" and "diagnosis". Of these, 53 were in the PUBMED database, 1 article in SCIELO, 3 articles in SCOPUS and 90 were found in the VHL. After applying the eligibility criteria, 10 articles fit perfectly according to the inclusion and eligibility criteria, relating to the proposed theme, as evidenced in the flowchart based on the PRISMA model (Figure 1).

Figure 1: Methodological path of sample collection



Source: Authors (2023)

Chart 2 – Presentation of the sample according to the variables: title, author, year| sample, location| study objective| method and level of evidence| main results.

Title/ Authors/ year	**Sample/ Location**	**Purpose of the study**	**Method| Level of evidence**	**Main results**
Brugada syndrome. Pedro Brugada. 2023	8 patients	The goal was the discovery of Brugada Syndrome and its risks to the patient	Cross-sectional study	In this article, the syndrome was discovered through 8 patients who showed a very unusual ECG with ST-elevation in the right precordial leads and what appeared to be a right bundle branch block.
Risk stratification of ventricular fibrillation in Brugada syndrome using non-invasive scoring methods; KAWAZOE, Hiroshi et al. 2016.	143 Japanese patients with SBr with VF (n=35) and without VF (n=108).	The aim of this study was to construct a new prediction model for VF risk in patients with RRB using non-invasive parameters.	Cross-sectional study	The frequency of syncope history, spontaneous type 1 ECG, and maximum T-wave alternation were associated with the occurrence of VF in univariate analyses. The new prediction method makes it possible to assess the risk of VF in patients with rBS.
Prevalence of spontaneous ECG pattern type 1, syncope, and other risk markers in survivors of sudden cardiac arrest in Brugada syndrome. LEONG, Kevin MW et al.2019.	133 patients with SBr	Evaluate patients with rSB, based on medical examinations or interviews and through risk factors	Cross-sectional study	A total of 133 patients with rBS were identified, only 8 had episodes of ventricular fibrillation and 2 required cardiopulmonary resuscitation. It was concluded that most patients with the syndrome had no history of previous syncope or risk factors.
Clinical characteristics, management and prognosis of elderly patients with Brugada syndrome. CONTE, Giulio et al. 2014	**437 patients with BS in an elderly population.**	The aim of this study was to investigate the clinical characteristics, management, and prognosis of BS in an elderly population.	Cross-sectional study	In the study, it was found that the elderly have a lower frequency of family history of sudden death compared to young people. However, a familial screening was done among 58 family members most of whom have BS. Therefore, the clinical features and benign prognosis of BS patients older than 70 years are likely to identify a category of patients at lower risk compared to younger individuals.
Syncope in Brugada syndrome: prevalence, clinical significance, and anamnesis clues to distinguish arrhythmic from non-arrhythmic causes.	342 patients with SBr	The aim of this study was to distinguish arrhythmic events from non-arrhythmic syncope in the SBr and to establish the clinical relevance of non-arrhythmic syncope.	Cross-sectional study	One study identified that 23 patients (7%) had ECG-documented ACA and 118 (34%) syncope; of these 118, 67 (57%) were diagnosed with suspected non-arrhythmic syncope. Therefore, non-arrhythmic syncope frequently occurs in BrS and should be considered a risk factor.

NORTH BATTLE, Louise Ra Olde et al.2015				
Number of electrocardiogram leads in the diagnosis of spontaneous Brugada syndrome. ARNAUD, Marinho et al, 2020	1613 patients	To investigate the value of a single-lead diagnosis in patients with Brugada syndrome and a spontaneous type 1 electrocardiogram.	Cross-sectional study	The study among 1613 patients was based on the recently recommended single shunt criterion for the diagnosis of Brugada syndrome, as this disorder can lead to a high risk of sudden cardiac death. However, after research, it is concluded that the number of leads is not necessary for diagnosis.
Fever-induced Brugada syndrome is more common than previously suspected: a cross-sectional study of an endemic area. Ratanwong, Patara et Al, 2016.	401 patients	The aim of this study was to identify the prevalence of fever-induced SRB	Cross-sectional study	A total of 416 patients were included in the study, including all 158 febrile patients and randomly selected 258 non-febrile patients presented to the emergency departments of Buriram Hospital concluded the highest prevalence of fever-induced SBr ever reported.
Low serum levels of eicosapentaenoic acid and docosahexaenoic acid are risk factors for cardiogenic syncope in patients with brugada syndrome. Yagi, Shusuke et al. 2017	62 men	The objective of this study was to verify whether fatty acids are risk factors for cardiogenic syndrome	Cross-sectional study	Serum levels of EPA and DHA were evaluated among these men, and it was concluded that low levels of EPA and DHA are associated with the incidence of syncope in patients with SBr.
Identification of a patient with high-risk Brugada syndrome by combined analysis of late potential and T wave amplitude variability on electrocardiograms. Yoshioka, Koichiro et al. 2013.	127 patients	To evaluate how the electrocardiogram changes in Brugada Syndrome (late potentials and variability of T wave amplitude)	Cross-sectional study	In this study, the research was carried out in the outpatient clinic to investigate how the electrocardiogram behaved in these patients and it was concluded that the analysis of late potentials and the variability of the amplitude of the T wave is useful in the identification of patients with high-risk syndrome.

Arrhythmic events in a patient with Brugada syndrome induced by fever. ROTERBERG, Gretje et al. 2020.	53 patients	The aim of this study is to further explore baseline characteristics and the association of fever with syndrome-related arrhythmic events.	Cross-sectional study	The study did a genetic screening performed on 14 patients (26%) and revealed an SCN5A mutation in 21% of the patients and these were seen that fever symptoms included life-threatening arrhythmia, ventricular fibrillation, tachycardia, syncope and cardiac arrest, concluding that fever is a major risk factor for arrhythmia events in patients with SBr.

DISCUSSION

Brugada syndrome (BS) is a rare autosomal inherited syndrome that leads to an increased risk of sudden death (SC). It mainly affects adult patients with an average age of 45 years, and the prevalence of diagnosis is eight times higher in men (NORDKAMP, *et al.*, 2015)

The clinical presentation of the disease is variable, however, some patients may remain totally asymptomatic. However, arrhythmic syncope is considered one of the most frequent symptoms of BS and this should be considered from the risk stratification since it allows the analysis of electrocardiographic changes, cardiac arrest and cardiogenic syncope, thus avoiding sudden death. In addition, it is also worth mentioning that male patients over 45 years of age are more prone to these events. (OLDE N L R., et al 2015; KRAHN AD., et al, 2022)

Some studies show that one third of patients with BS are diagnosed after symptoms of syncope or cardiac arrest, most of which occur at rest with vagal symptoms or during the night. An increase in the prevalence of atrial fibrillation in BS was evidenced, which highlights the need for screening for BS by the physician, especially for young men. On the other hand, two-thirds of patients with BS are asymptomatic at diagnosis, and one-third of these are identified during family screening. For diagnosis based on a specific ECG pattern, symptoms are not required (NORDKAMP, *et al.*, 2015).

In addition, there are 3 patterns that can be considered characteristic for this syndrome. Pattern 1 is the most common and the one that presents ST segment elevation to more than 2 mm together with T wave inversion in the right precordial leads and J point elevation also above 2 mm. While patterns 2 and 3 have an ST-segment elevation ECG in saddle type (KRAHN AD., et al, 2022). It has been observed that patients with spontaneous type I ECG have twice the risk of arrhythmic events than patients who develop such an ECG pattern when submitted to the use of sodium channel blocking medication. (BRUGADA, et al., 2023).

Previous findings in the literature indicate that implantable cardioverter defibrillators, or ICDs, can actively prevent cardiac events with a worse prognosis in BS, especially in male patients and patients with ventricular arrhythmias that can be induced. However, new studies show that the

use of ICDs is not suitable for all types of patients with this syndrome, since their use is associated with high complications, and is better indicated, for example, for individuals who have survived a cardiac arrest due to ventricular fibrillation or hemodynamically unstable ventricular tachycardia (KAWAZOE., et al, 2016).

It is also noteworthy that in a study that evaluated the clinical characteristics, management, and prognosis of BS in elderly patients, it was found that they more frequently presented, compared to younger patients, some type of conduction disorder of the baseline ECG, in addition to also presenting transient advanced atrioventricular (AV) block before the diagnosis of BS. In addition, it was found that the incidence of AV conduction disorders or advanced AV block was significantly higher in patients over 70 years of age compared to people aged 60 to 70 years (CONTE, *et al.*, 2014).

However, it was identified that elderly patients reported less family history of MS compared to younger patients and had fewer sustained ventricular arrhythmias induced by programmed ventricular pacing. Therefore, the prognosis of BS patients over 70 years of age highlighted a lower risk of complications compared to younger individuals (LEONG, *et al.*, 2019)tag.

As for the treatment, some studies have shown that quinidine and its subcompounds are useful to treat Brugada Syndrome, because quinidine has antiarrhythmic therapeutic properties, in addition to inhibitory power in the action action of potassium during the action potential, especially in phase 2. However, its use can cause diarrhea, significant neurological events, and thrombocytopenia (KRAHN AD., et al, 2022)

CONCLUSION

In view of what has been postulated, it can be observed that Brugada Syndrome (BS) is a hereditary pathology with an arrhythmogenic aspect, with specific electrocardiographic characteristics, with the ECG1 pattern being the most common among them. As for its clinical condition, BS can present both symptomatically and asymptomatically, with arrhythmic syncope and cardiac arrest as its most frequent symptoms. In addition, through the articles included in the present study, it was also possible to analyze the risk factors and the main complications associated with BS, with malignant syncope, history of sudden family death and SCN5A mutation as indicative of risk for the development of this syndrome, whose complications are the ephemeral loss of cardiac function. atrial fibrillation and conduction disorders or pathological mutations.

This integrative review is of remarkable importance for the university environment, since, through the analysis of scientific articles, it is possible to highlight the main risk factors and complications of Brugada Syndrome, in addition to focusing on its most common clinical presentations.

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