**Thematic Units**

Basic and Clinical Research

Bioengineering and Medical Informatics

Cardiopulmonary Revascularization

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Cardiovascular Surgery

Chagas Disease

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Education

Epidemiology and Cardiovascular Prevention

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Hemodynamics - Cardiovascular Interventions

High Blood Pressure

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Pediatric Cardiology

Vascular Disease

Women and Heart Disease

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**Brief Communications**

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**ABSTRACT**

We introduce an approach 'as a whole' of the pathophysiology of inherited mitochondrial degenerative cardiovascular diseases in its various forms, characterized by the Inherited Real Risk (IRR) of Coronary Artery Disease (CAD), taking into account both the mitochondrial and microvascular dysfunctions, novel but separated and fragmented researches and insights into the pathogenesis and epidemiology of CAD. We present the bed-side diagnosis of CAD IRR through Quantum Biophysical Semiotics (QBS) clinical method to assess, since birth, the presence or not of QBS Constitutants and its congenital Real Risks, independent of all the environmental risk factors. The clinical and electrocardiographic diagnosis of the Inherited Real Risk of CAD permits a biological preventive evaluation, because biological systems function modification parallels genes' mutations. This method can be used both for diagnostic purposes and for therapeutic advice, because it is to measure the coronary microcirculatory and its nonlinear dynamics, before and after each preventive treatment. In order to understand the effectiveness of remedies, so orienting and monitoring any choice according with biological activities modifications and improvements, allowing a proper primary and pre-primary prevention.

**INTRODUCTION**

In the last decades several scientific works in human physiology and cardiovascular diseases have focused on oscillatory behavior of well defined biological systems, whose nonlinear dynamics, as measured by statistical invariants typical of deterministic chaos and fractals, i.e., fractal measures and heart rate variability (HRV) analysis methods, have significant interpretation for clinical diagnosis and therapeutic monitoring, by testing the non-linear behavior of heart muscle. In all these studies nonlinear complexity appears to degrade in characteristic ways with aging and disease, reducing the adaptive capacity of the individual. These pioneering works, even if corroborating the correlation between deterministic chaos and the presence or absence of Coronary Arterial Disease (CAD), still leave many open questions and unresolved issues. First, these are purely statistical approaches, not easy to do at the bed-side, useful for clinical diagnosis; second, they do not address the underlying problem, namely investigating the causes of CAD, for example, by analyzing the lifelong behavior of coronary parenchymal cells, microvascular tissue or blood flow in microvessels, even if mitochondrial [1,6] and microvascular [7,8] dysfunction are roved, but separated and fragmented researches and insights into the pathogenesis and epidemiology [9] of CAD. Furthermore, CAD is a growing epidemic, often asymptomatic, for all these reasons new diagnostic approaches should be explored, such as those introduced by Quantum Biophysical Semiotics (QBS), which through bed-side evaluation of parenchymal and microvascular behaviors, not only can diagnose the absence or presence of CAD, even silent and asymptomatic, but it can also assess the existence of pre-metabolic syndromes that can last for years or decades, and in clinical stages of the disease still potential or evolving to pathology, so allowing for an effective, pre-primary and primary prevention [11]. QBS is a new discipline in medical field and an extension of the classical medical semiotics with the support of quantum and coherency theories [12,13]. It is a scientific trans-disciplinar approach based on the 'Conjunctive Acidic Enzyme-Metabolic Histology' (CAEMH) [14], a unique mitochondrial cytopathy that is genetic and metabolic, and in the presence of intense CAEMH is in a well defined area (i.e. the myocardium) and in genes mutations in both nDNA and mtDNA. CAEMH is the basis for one or more QBS constitutants [15] which could bring about their respective Inherited Real Risks (IRR) [11,16]. The QBS method allows the clinical and pre-clinical diagnosis of the most severe diseases, such as the IRR of CAD [15,17]; this is achieved in the easier way through the auscultatory percussion of the stomach [18,19]. Made with the aid of gastric specific reflex (GAR), this diagnosis is consistent and dually reflects the informative nature and quality of parameters collected by QBS microcirculatory investigations. QBS clinical method allows CAD biological preventive evaluation, because biological system functional modification parallels gene mutation according with Anglobiopsy Theory [11].

**OBJECTIVES**

The objectives of this manuscript are to explain how to assess the coronary microvascular conditions in any subject at the bed-side; to diagnose, clinically, the IRR of CAD; to monitor any therapeutic CAD primary prevention; to favor an effective primary and pre-primary prevention of CAD.

**MATERIALS AND METHODS**

We introduce an useful, reliable and clinical manœuvre, easy to apply, that proved to be efficacious to recognize clinically silent CAD, its IRR [11,13,18,21] and heart ischaemia diseases before they occur. Moreover, it is well known that patients may have no symptoms at all for years or decades. In addition, the ECG features of ischaemia may be induced by exercise without accompanying angina [11,13,18]. QBS is able to make diagnosis of CAD IRR in particular through the auscultatory percussion of the stomach, easier to understand and to apply in the daily practice, revealing if any subject, single or collective, is at risk of CAD. Among the several QBS signs, one of these is the simultaneous cardiac GAR in case of intense digital pressure on heart trigger points. This paramout reflex is related with the non-local quantum behavior of biological systems [21]. In health, an "intense" digital pressure on heart's trigger points (any point of the precordium), does not provoke simmultaneously the cardic-GAR (the reflex appears after 16 seconds due to physiological tissue acidosis), thus there is not CAD IRR (negative Caosino's sign). The presence of CAD IRR, the physicians must refine the diagnosis making a deeper investigation on the correct localization of the underlying clinical cardiovascular disorder. This is achieved through QBS assessment of the relevant specific signs, i.e., myocardial ischaemic Preconditioning [22]. In fact, Caosino's sign is an specific reflex, but it becomes specific if the microcirculatory remodeling [16,20,23] is located precisely in the small areas of the related CVD disorder. In healthy subjects, digital pressure of mean intensity, applied upon heart skin's projection area, brings about a GAR - in the stomach, fundus and body are dilated; on the contrary, antir- pyloric region contracts - after a latency time (LT) of 4 s, that lasts less than 4 s. The later parameter value is of paramount significance, since it parallels the efficacy of coronary Microcirculatory Functional Reserve (MFR) [11,18,21,23]. A second, successive evaluation, performed after an interval of 5 s, provokes the identical reflex, after a doubled LT...
RESULTS

QBS tools are useful both for diagnostic purposes and for therapeutic advices. QBS diagnosis, corroborated by more than 100 clinical and experimental evidences over the last five decades, further provides additional information complementary to those usually collected according to Official Protocols. QBS therapeutic monitoring allows to measure the microcirculatory activity before and after each preventive treatment, in order to understand the effectiveness of remedies. In case of CAD IRR, preventive treatments (24,25) are suggested to activate the activity of mitochondria respiratory chain by acting on metabolism, but also improving it, as far as to normalize mitochondrial and tissue oxygenation, expression of the normal activity of mitochondrial oxidative phosphorylation. By this way the hypoxia, but also the genetic alteration of mtDNA still remains: CADMM, QBS Constitutions and CAD IRR are yet positive, but the IRR turns ‘residual’. By the way, recent experimental evidences show the chance of an efficient pre-primary prevention with effective resources to reverse the genetic alteration of mtDNA, we successfully tested a quantum therapy based on millimeter waves with Extremely High Frequencies (EHF), for the pre-primary prevention of CAD (26) and other degenerative diseases, such as Type 2 Diabetes Mellitus (26) and cancer (27).

DISCUSSION

QBS theory (11,15,18) offers an approach ‘as a whole’ of the pathophysiology of inherited mitochondrial degenerative diseases, as well as that of cardiovascular diseases in its various forms, characterized by CAD IRR (11,16,17), condotto sine qua non of Coronary Artery Disease (16,22). QBS clinical and experimental evidences (11-26) allows to divide IRR into two groups: A) environmental risk factors in two groups: A) Environmental risk factors, and B) IRR, early and quickly recognized from birth with a stethoscope (11,17,18). CAD environmental risk factors (about 3000) can facilitate and worsen CAD onset, but exclusively in individuals involved by CAD IRR, beside recognized in quantitative way in a few seconds (22). The pathophysiology of QBS reflexes is based upon local microvascular conditions (17,20,22). In case of genetic alteration of both DNA, increasing IRR, and IRR of CAD there is a coronary microcirculatory remodeling, especially intense under environmental risk factors, due to vasomotor and structural imbalance, both on normal and pathologic endothelial blocking Devices (EBDs) in coronary small arteries, and Arteriovenous Anastomosis (AVA) (17,20,22,27). As far as CAD is concerned, notably coronary IRR, as well as sub-clinical, and consequently very dangerous, coronary heart disease is very prevalent among individuals, both with or without IRR for CAD, which is independently associated with actually known CAD risk. The risk of CAD acute events substantially increases, among individuals with hyper tension, dyslipidemia, and diabetes mellitus (27), due to the pressure of newborn-pathological type I, subtype b) associated, EBDs in coronary small arteries, according to Hammanssen. According to :QBS, most of these inherited impairments are already present, in a similar form, in microvascular biological systems and clinically observable since birth, through uterine reflexes diagnosis. Briefly, in healthy, from the microcirculatory point of view, during stress test both coronary circulation (aufonic-deterministic oscillations of arterioles) and vasomotor (chaotic deterministic fluctuations of nutritional capillaries and post-capillary venules) are maximally activated (11-13,17,22), particularly in coronary regions. On the contrary, in individuals with a family history positive for CAD and, of course, in patients in the first stages of CAD, under identical conditions, a deep degree of microcirculatory activation appears, characterized by increased vasomotor and decreased vasoconstriction. The flow and the fluidity in the coronary microvascular bed appears to be clearly altered, due to this phenomenon of the so-called "microcirculatory blood-flow centralization". Microcirculation shows three basic types of activation, ignoring the many transitional forms (17,20,23): 1) type I, Associated (the term 'associated' means that the same physiological behavior); 2) type II, Intermediate, partially associated (pre-metabolic syndrome, dissociated because there is an internal imbalance, and vasoconstriction and vasodilation have a different behavior); 3) type III, Completely Dissociated (pathological microcirculation, typical of overt disease). In case of CAD, there is a functional alteration of microcirculatory dynamics evidenced by a microcirculatory activation (MA), type 2, dissociated, as well as structural abnormalities such as the presence of pathological EBDs (20,23). These functional and structural abnormalities increase along time, with the evolution of the IRR of CAD (pre-clinical stage) to the overt pathology (MA, type 3, dissociated). The chronic pathological physiological nonlinear and complex dynamics, whose quantitative and qualitative behaviors can be determined through the involuntary statistic measure of fractal dimension (10) (11,13,20,23), that is directly related to local MFR, the presence or not of the local IRR and the GARI frequency time (expressing tissue pHi), while it is Inverted related to GAR duration.

CONCLUSIONS

QBS method offers an original, clinical, approach for microcirculatory dynamics evaluation giving a flurry of worthy information useful for the bedside diagnosing CAD, even silent and asymptomatic. Importantly, QBS is able to diagnose CAD not only at the first very initial stages, usually before to diastolic function, but even many years and decades before disease onset, termed Inherited Real Risk of CAD, allowing thus an efficacious primary prevention through early bed-side diagnosis and therapeutic monitoring.

REFERENCES
