Typical Microcirculatory Remodeling of CAD Inherited Real Risk.

Sergio Stagnaro and Simone Caramel*

Introduction

In the last decades several scientific works in human physiology and cardiovascular diseases have focused on non-linear oscillatory behavior of well defined biological systems, whose dynamics, as measured by statistic invariants typical of deterministic chaos and fractals, can have significant interpretation and importance for clinical diagnosis and therapeutic monitoring [1]. The main characteristics of deterministic chaos are the uncertainty and unpredictability, but it is possible to bedside detect and investigate it and to get qualitative information through invariant statistic measures. In literature there are several researches [2-7] aimed to test the non-linear behavior of heart muscle: fractal measures, heart rate variability (HRV) analysis methods and other non-linear statistics. In all these studies nonlinear complexity appears to degrade in characteristic ways with aging and disease, reducing the adaptive capacity of the individual. These researches provide the same results, independently of the different statistical approach: fractal dimension and the rate of unpredictability of a biological system with nonlinear dynamics helps in differentiating patients with Coronary Artery Disease (CAD) from healthy subjects. As higher is the rate of unpredictability of a system as much the bio-system is physiologically healthy, presenting higher orders of high complexity typical of dissipative systems far from equilibrium studied by Prigogine [8]. On the contrary, as much the trend of the investigated system is predictable, as much it tends to pathology or chronic phases. In parallel, the fractal dimension decreases, demonstrating an altered and reduced level of structural organization, impacting negatively on the physiology of the system, with loss of flexibility, adaptability and learning, while rigidities, obstructions and inharmonious behaviors are emerging [9].

These pioneering works, even if corroborating the correlation between deterministic chaos and the presence or absence of 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 [10-12] and microvascular [13, 14] dysfunction are novel but separated and fragmented researches and insights into the pathogenesis and epidemiology [15] of CAD. Furthermore, CAD is a growing epidemic, often asymptomatic.

For all these reasons new diagnostic approaches need to be explored, such as those introduced by Quantum Biophysical Semeiotics (QBS), which through bed-side evaluation, not only can diagnose the presence or absence of CAD, even silent and asymptomatic, but it can also assess the existence of pre-metabolic syndrome that can last for years or decades, pre-clinical stages of the disease still potential or evolving to pathology, so allowing for an effective, pre-primary and primary prevention. QBS theory [16] offers an approach ‘as a whole’ of the patho-physiology of inherited mitochondrial degenerative diseases, as well as that of cardiovascular diseases in its various forms, characterized by the Inherited Real Risk (IRR) of Coronary Artery Disease [17].

Microcirculatory remodeling and Inherited Real Risk of CAD

QBS is a new discipline in medical field and an extension of the classical medical semeiotics with the support of quantum and complexity theories, i.e., deterministic chaos and mit-genome fractal dimension [18-20]. It is a scientific trans-disciplinary approach that is based on the 'Congenital Acidosic Enzyme-Metabolic Histangiopathy’ (CAEMH) [21], a unique mitochondrial cytopathy that is present at birth and subject to medical therapy. The presence of intense CAEMH in a well-defined area (i.e., myocardium) is due to gene mutations in both n-DNA and mit-DNA. This is the basis for one or more QBS constitutions [22] which could bring about their respective IRR [17, 23-26]. It is unavoidable to divide CAD risk factors in two groups: A) Environmental risk factors, and

B) QBS Constitutions-Dependent, IRR, recognized quickly from birth with a stethoscope: CAD environmental risk factors (about 300!) can facilitate and worsen CAD onset, but exclusively in individuals involved by CAD IRR, bedside recognized in quantitative way in a few seconds [16, 27]. The QBS method allows the clinical and pre-clinical [28] diagnosis of the most severe diseases such as the IRR of CAD [16-19]; this is achieved in the easier way through the auscultatory percussion of the stomach [23, 26-29]. Made with the aid of gastric aspecific reflex, this diagnosis is consistent and dually reflects the informative nature and quality of parameters collected by QBS microcirculatory investigations [30]. The patho-physiology of QBS reflexes is based upon local microvascular conditions. In case of genetic alteration of both DNAs, intense CAEMH, and IRR of CAD there is a microcirculatory remodeling, especially intense under environmental risk factors, due to vasomotility and vasomotion impairment (e.g., functional imperfection) and structural obstructions, i.e., pathological Endoarteriolar Blocking Devices (EBDs) in coronary small arteries, and Arteriovenous Anastomosis (AVA) [31].

According to QBS, most of these inherited impairments are already present, in a similar form, in micro-vascular biological systems and clinically observable since birth, through ureteral reflexes diagnosis. Briefly, in healthy, from the microcirculatory point of view, during stress tests both vasomotility (chaotic-deterministic oscillations of arterioles) and vasomotility (chaotic deterministic fluctuations of nutritional capillaries and post-capillary venules) are maximally activated [26, 30-32], particularly in cardiovascular 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 dissociated form of microcirculatory activation appears, characterized by increased vasomotility and decreased vasomotion. The flow- and flux-motion in the coronary microcirculatory bed appears to be clearly decreased, due to the dangerous phenomenon of the so -called “microcirculatory blood-flow centralization”.

Bedside Diagnosis of CAD Inherited Real Risk

In following, we suggest an useful, reliable and clinical manoeuvre, easy to apply, that proved to be efficacious to recognize clinically silent CAD, its IRR [16, 23, 30-32] and heart ischaemic diseases before they occur. Moreover, it is well known that patients with CAD may have no symptoms at all for years or decades. In addition, the electrocardiographic features of ischaemia may be induced by exercise without accompanying angina [23, 30]. QBS is able to make diagnosis of CAD IRR in particular through the auscultatory percussion of the stomach [33, 34], easier to understand and apply in the daily practice, i.e., revealing if any subject, from the moment of birth, is at risk of coronary artery disease. Among the several QBS signs, one of these is the simultaneous heart gastric aspecific reflex (GAR) in case of “intense” digital pressure on heart trigger points. This reflex is related with the non-local quantum behavior of biological systems [20].

In health, an “intense” digital pressure on heart’s trigger points (any point of the precordium), does not provoke simultaneously the heart GAR (the reflex appears just after 16 seconds due to physiological tissue acidosis), thus there is not IRR of CAD (negative Caotino’s sign): this is the physiological state [23, 35].

If the stomach dilates simultaneously, from about 1 cm to 1,5 cm or more (reflex’ intensity is related to the seriousness of underlying disorder), there is IRR of CAD, and respectively IRR in evolution, or finally overt CAD (if the stomach dilates more than 1 cm): positive Caotino’s sign.

In presence of IRR of CAD, the physicians must refine the diagnosis making an investigation more focused on the correct localization of the underlying clinical cardiovascular disorder, and in order to determine the severity of the metabolic (CAD in progress) or pre-metabolic (grade of evolution of IRR of CAD) syndrome [28]. This is achieved through QBS assessment of the related specific signs, i.e., myocardial Ischaemic Preconditioning [19, 31-33].

In fact, Caotino’s sign is an aspecific reflex, but it becomes specific if the microcirculatory remodeling [23, 26, 30] is locally present in the small areas of the related CVD disorder.

In health, digital pressure of mean intensity, applied upon heart skin projection area, brings about a GAR (in the stomach, fundus and body are dilated; on the contrary, antral- pyloric region contracts) after a latency time (lt) of 8 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) [16, 23, 26]. A second, successive evaluation, performed after an interval of 5 s exactly, provokes the identical reflex, but with doubled latency time - 16 s: physiological myocardial preconditioning, type I. On the contrary, in patients involved by CAD, even initial and/or silent, i.e., subclinical, latency time increases in no statistically significant way, showing to be less than 16 s, as in presence of IRR of CAD, or results clearly lower than the basal value in the second one, in overt severe CAD. The gastric diagnosis is consistent and dually reflects the informative nature and quality of parameters collected by QBS microcirculatory investigations that are in accord with clinical microangiology. The patho-physiology of QBS reflexes is based upon local microvascular conditions [23, 29-32].

Microcirculation shows three basic types of activation, ignoring the many transitional forms:

1) type I, Associated (the term 'associated' means that vasomotility and vasomotion show the same physiological behavior);
2) type II Intermediate, partially dissociated (pre-metabolic syndrome, dissociated because there is an impairment, vasomotility and vasomotion have a different behavior);
3) type III Completely Dissociated (pathological microcirculation, typical of overt disease).

In case of IRR of CAD, there is a functional alteration of microcirculatory dynamics evidenced by a microcirculatory activation, type 2, dissociated, as well as structural abnormalities such as the presence of pathological EBDs [23, 29, 31]. These functional and structural abnormalities increase along time, with the evolution of the IRR of CAD (pre-clinical stage) to the overt pathology (microcirculatory activation, type 3, dissociated).

Microcircle's oscillations have physiological nonlinear and complex dynamics, whose quantitative and qualitative behaviors can be determined through the invariant statistic measure of fractal dimension (fD) [18-20, 23]. There are well defined QBS techniques to calculate the fD, such as, e.g., considering the vasomotility and vasomotion oscillations' diagram, and particularly taking the ratio between the highest spikes – HS (maximum points of the oscillation) and the minimal points of coronary microvessels' fluctuation. In health, microvessels' physiological behavior is denoted by a fractal dimension of 3.81. In patients where a biological system is evolving towards any chronic disease there is a lower fractal dimension, i.e., $1 < fD < 3$, and, finally, in chronic situations fD is equal to 1, topological dimension, i.e., from IRR to overt CAD. Fractal Dimension, simply calculated as the time of the disappearance of gastric aspecific reflex, before the appearance of the next, is an universal measure, independent of the investigated parenchyma, informing the physician about the health condition of the visited patient, and it is directly related to local MFR, the presence or not of the local congenital Real Risk and the GAR latency time (and then with tissue pH), while is inversed related to GAR duration.

Inherited Real Risk of CAD: primary and pre-primary prevention

QBS tools are not only useful for diagnostic purposes, but also for therapeutic advices, because they are able to measure the microcirculatory activity before and after each preventive treatment, in order to understand the effectiveness of remedies.

In particular, we have successfully used a Quantum Therapy for the pre-primary prevention of Type 2 Diabetes Mellitus [25, 36], Coronary Artery Disease [17], cancer [37] and Alzheimer's Disease [38].

Conclusions

QBS method offer an original approach for microcirculatory dynamics evaluation giving a flurry of worthy information useful for the clinical and pre-clinical diagnosis of Coronary Artery Disease, even silent and asymptomatic. Furthermore QBS is able to make a diagnosis of CAD not only at

the first very initial stages, usually very difficult to do, but even many years and decades before disease onset, allowing thus an efficacious primary prevention, prescribing proper preventive treatments, which proved to be really efficacious in healing the real risk of cardiovascular disease.

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Correspondence:
* **Simone Caramel**
International Society of Quantum Biophysical Semeiotics (SISBQ)
Department of Advanced Research
CP 18 - 31020 Lancenigo - Italy
email simonecaramel@yahoo.it
Cell. +39 338 8129030