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Brief Communications

"Inherited Real Risk of Coronary Artery Disease: pathophysiology, diagnosis and primary prevention"

Sergio Stagnaro; Simone Caramel.

Società Internazionale di Semeiotica Biofisica Quantistica (SISBQ).
Clinical Diagnosis & Prevention. Advanced Research. Treviso. Veneto. Italia

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 in due 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 Semeiotics (QBS) clinical method able to assess, since birth, the presence or not of QBS Constitutions and its congenital Real Risks, independent from all the environmental risk factors. The clinical and pre-clinical diagnosis of the Inherited Real Risk of CAD permits a biological preventive evaluation, because biological systems functional modification parallels genes' mutations. This method can be used both for diagnostic purposes and for therapeutic advices, because it is able to measure the coronary microcirculatory activity 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 statistic invariants typical of deterministic chaos and fractals, i.e., fractal measures and heart rate variability (HRV) analysis methods, can have significant interpretation and importance for clinical diagnosis and therapeutic monitoring [1,4] 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 Artery 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 [5,6] and microvascular [7,8] dysfunction are novel, 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 to be explored, such as those introduced by Quantum Biophysical Semeiotics (QBS), which through bed-side evaluation of parenchymal and microvascular behaviours, 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 [10] 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 [11]. 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 [12,13]. It is a scientific trans-disciplinary approach that is based on the 'Congenital Acidosic Enzyme-Metabolic Histangiopathy' (CAEMH) [14], a unique mitochondrial cytopathy that is generally present at birth. 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. CAEMH is the basis for one or more QBS constitutions [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 [16,17]; this is achieved in the easier way through the auscultatory percussion of the stomach [18,19]. Made with the aid of gastric aspecific 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 a CAD biological preventive evaluation, because biological system functional modification parallels gene mutation according with Angiobiopathy Theory [11].

OBJETIVES

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 manoeuvre, easy to apply, that proved to be efficacious to recognize clinically silent CAD, its IRR [11,13,18,21] 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 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 apply in the daily practice, revealing if any subject, since birth, is at risk of CAD. Among the several QBS signs, one of these is the simultaneous cardio-GAR in case of "intense" digital pressure on heart trigger points. This paramount 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 simultaneously the cardio-GAR (the reflex appears after 16 seconds due to physiological tissue acidosis), thus there is not CAD IRR (negative Caotino's sign): this is the physiological state [16,18,21]. On the contrary, if the stomach dilates simultaneously, 1 - 1,5 cm or more (reflex' intensity parallels the seriousness of underlying disorder), there is CAD IRR, and respectively CAD IRR in evolution, or finally overt CAD (if the stomach dilates more than 1 cm): positive Caotino's sign. In 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 related specific signs, i.e., myocardial Ischaemic Preconditioning [22]. In fact, Caotino's sign is an aspecific reflex, but it becomes specific if the microcirculatory remodeling [16,20,23] is locally present 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, 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) [11,18,21,23]. A second, successive evaluation, performed after an interval of 5 s, provokes the identical reflex, after a doubled Lt

(16 s): physiological myocardial preconditioning, type I. On the contrary, in patients involved by CAD, even initial and/or silent, subclinical, Lt increases in no statistically significant way, showing to be less than 16 s, as in presence of CAD IRR, or it 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, i.e., clinical microangiology [23] and patho-physiology of QBS cardio-ureteral reflexes (see Discussion).

RESULTS

QBS tools are useful both for diagnostic purposes and for therapeutic advices. QBS diagnosis, corroborated by more than 100,000 clinical and experimental evidences over the last five decades, favors CAD primary prevention providing additional information complementary to those usually collected according with Official Protocols. QBS therapeutical 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 stimulates 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 tissue oxygenation and mitochondrial activity improve, but the genetic alteration of mit-DNA still remains: CAEMH, 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 recursive effects able to reverse the genetic alteration of mit-DNA and CAEMH. In particular, 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 [24] and cancer [25].

DISCUSSION

QBS theory [11,15,18] 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 CAD IRR [11,16,17], conditio sine qua non of Coronary Artery Disease [16,22]. QBS clinical and experimental evidences [11-26] allows to divide CAD risk factors in two groups: A) Environmental risk factors, and B) QBS Constitutions-Dependent, IRR, early and quickly recognized from birth with a stethoscope [11,17,18]. 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 [22]. The patho-physiology of QBS reflexes is based upon local microvascular conditions [17,20,22]. In case of genetic alteration of both DNAs, intense CAEMH, and IRR of CAD there is a coronary microcirculatory remodeling, especially intense under environmental risk factors, due to vasomotility and vasomotion impairment, both functional and structural, i.e., pathological Endoarteriolar Blocking Devices (EBDs) in coronary small arteries, and Arteriovenous Anastomosis (AVA) [17,20,22,27]. As far as CAD is concerned, notoriously coronary IRR, as well as sub-clinical, and consequently very dangerous, coronary heart disease is very prevalent among older individuals, always positive for IRR of CAD, which is independently associated with actually known CAD risk. The risk of CAD acute events substantially increases, among individuals with hypertension, dyslipidemia, and diabetes mellitus [27], due to the presence of newborn-pathological, type I, subtype b) aspecific EBDs in coronary small arteries, according to Hammersen. 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 [11-13,17,22], 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". Microcirculation shows three basic types of activation, ignoring the many transitional forms [17,20,23]: 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 (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). 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) [11,13,20,23], that is directly related to local MFR, the presence or not of the local IRR and the GAR latency time (expressing tissue pH), while it is inversed 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 very difficult to do till now, 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

1. Goldberger AL, Rigney DR, West BJ. (1990). Chaos and fractals in human physiology. Sci Am 1990;262:40-49.
2. Ristimäe T., Juhani Airaksinen K.E., Peng C.K., Goldberger A.L., Huikuri H. V. (1998). Heart Rate Dynamics in Patients With Stable Angina Pectoris and Utility of Fractal and Complexity Measures - The American Journal of Cardiology Volume 81, Issue 1, Pages 27-31.
3. Goldberger AL, Amaral LAN, Hausdorff JM, Ivanov PCh, Peng CK, Stanley HE. (2002). Fractal dynamics in physiology: alterations with disease and aging. Proc Natl Acad Sci USA. 99[suppl 1]:2466-2472.
4. Antanavičiusa K., Bastysa A., Blužasb J., Gargasasb L., Kaminskienėb S., Urbonavičienėb G., et al. (2008). Nonlinear dynamics analysis of electrocardiograms for detection of coronary artery disease, Computer Methods and Prog in Biomedicine. 92(2): 198-204.
5. Kofler B, Mueller EE, Eder W, Stanger O, Maier R, Weger M, et al. (2009) Mitochondrial DNA haplogroup T is associated with coronary artery disease and diabetic retinopathy: a case control study BMC Medical Genetics 2009, 10:35.
6. Luk TH, Dai YL, Siu CW, Yiu KH, Li SW, Fong B, et al. (2012) Association of lower habitual physical activity level with mitochondrial and endothelial dysfunction in patients with stable coronary artery disease. Circ J. 2012;76(11):2572-8. Epub 2012 Jul 13.
7. Jones E, Eteiba W, Merz NB. (2012) Cardiac syndrome X and microvascular dysfunction. Trends Cardiovasc Med. Aug;22(6):161-8.
8. Fischer-Rasokat U, Spyridopoulos I, Walter J, Honold J, Zeihe (2012). Microvascular dysfunction and pulse wave reflection characterize different vascular pathologies in patients at cardiovascular risk. Vasa. 2012 May;41(3):192-9.
9. Mueller EE, Eder W, Ebner S, Schwaiger E, Santic D, Kreindl T, et al. (2011). The mitochondrial T16189C polymorphism is associated with coronary artery disease in Middle European populations. PLoS One. 2011 Jan 26;6(1).
10. Stagnaro S. (2009). Pre-Metabolic Syndrome and Metabolic Syndrome: Biophysical-Semeiotic Viewpoint. Atherosclerosis Society. http://www.athero.org/commentaries/comm904.asp
11. Stagnaro S. (2009) Reale Rischio Semeiotico Biofisico. I Dispositivi Endoarteriolari di Blocco neoformati, patologici, tipo I, sottotipo a) oncologico, e b) aspecifico. Ediz. Travel Factory, Roma.
12. Stagnaro S., Moscatelli G. (1996). Biophysical Semeiotics, Deterministic Chaos and Biological System, Gazz Med It Arch Sci Med 155, 125
13. Stagnaro-Neri, M., and Stagnaro, S. (1997). Deterministic chaos, preconditioning and myocardial oxygenation evaluated clinically with the aid of biophysical semeiotics in the diagnosis of ischaemic heart disease even silent. Acta Med Medit. 13, 109.
14. Stagnaro S, Caramel S. (2010). The role of mitochondria and mit-DNA in oncogenesis. Quantum Biosystems. 2(1) 250-281.

15. Stagnaro S., Stagnaro-Neri M. (2004) Le Costituzioni Semeiotico Biofisiche. Strumento clinico fondamentale per la prevenzione primaria e la definizione della Single Patient Based Medicine. Travel Factory, Roma.
16. Stagnaro S, Caramel S. (2013). The Inherited Real Risk of Coronary Artery Disease, Nature PG., European Jour Clin Nut.
17. Stagnaro S. (2005). Biophysical-Semeiotic Bed-Side Detecting CAD, even silent, and Coronary Calcification. 4to Congreso International de Cardiologia por Internet, 2005, http://www.fac.org.ar/ccvc/llave/tl016/tl016.pdf
18. Stagnaro S, Stagnaro-Neri M. (2004) Introduzione alla Semeiotica Biofisica. Il Terreno oncologico. Travel Factory SRL., Roma.
19. Stagnaro S. (1985) Percussione Ascoltata degli Attacchi Ischemici Transitori. Ruolo dei Potenziali Cerebrali Evocati. Min. Med. 76, 1211, 1985 [MEDLINE]
20. Stagnaro S. (2009). CAD Inherited Real Risk, Based on Newborn- Pathological, Type I, Subtype B, Aspecific, Coronary Endoarteriolar Blocking Devices. Diagnostic Role of Myocardial Oxygenation and Biophysical-Semeiotic Preconditioning. IAS, International Atherosclerosis Society, www.athero.org, 29 April, 2009, http://www.athero.org/commentaries/comm907.asp
21. Stagnaro S. (2012) Caotino's Sign and Gentile's Sign in bedside Diagnosing CAD Inherited Real Risk and Acute Myocardial Infarction, even initial or silent. Patho-Physiology and Therapy. Lectio Magistralis. III SISBQ Congress, 9-10 June, 2012, Porretta Terme (Bologna). www.sisbq.org. http://www.sisbq.org/uploads/5/6/8/7/5687930/presentazione_stagnaro_it.pdf
22. Stagnaro S. (2006). Role of Coronary Endoarterial Blocking Devices in Myocardial Preconditioning - c007i. Lecture, V Virtual International Congress of Cardiology. http://www.fac.org.ar/qcvc/llave/c007i/stagnaros.php
23. Stagnaro-Neri M., Stagnaro S. (2013). Clinical Microangiology. From the book: "Semeiotica Biofisica. Microangiologia Clinica." Travel Factory, Roma. In press. Available at: http://www.semeioticabiofisica.it/microangiologia/common_eng.htm
24. Stagnaro S, Caramel S. (2013) The Role of Modified Mediterranean Diet and QuantumTherapy in Type 2 Diabetes Mellitus Primary Prevention. LifeScienceGlobal, February 2013, Journal of Pharmacy and Nutrition Sciences, 2013, 3.
25. Stagnaro S, Caramel S. (2013). The Role of Modified Mediterranean Diet and Quantum Therapy in Oncological Primary Prevention. Bentham PG., Current Nutrition & Food Science ISSN: 1573-4013; VOLUME: 9, ISSUE: 1.
26. Caramel S, Stagnaro S, Pyatakovich F, Yakunchenko TI, Makkonen KF, Moryleva ON. (2013) Background Millimeter Radiation Influence in Cardiology on patients with metabolic and pre-metabolic syndrome. J of Infrared and Millimeter Waves. China (in press).
27. Stagnaro S, Caramel S. (2013). Inherited Real Risk of Type 2 Diabetes Mellitus: bedside diagnosis, pathophysiology and primary prevention. Frontiers in Endocrin, 4:17.http://www.frontiersin.org/Diabetes/10.3389/fendo.2013.00017/full [Pub-Med]

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