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Torsadogenic index for prevention of acute death

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ABSTRACT

This risk management project aims to apply a global preventive and predictive measure in potential victims of acute death and heart failure. Among the main causes are identified sub-diagnosed genetic mutations; prescription, interaction, self-medication or abuse of suspected drugs due to internet prospect's consult; and a parasitic pandemia, the Chagas disease (over 100 000 000 population is potentially infected worldwide). Promoting a global extensive determination of the torsadogenic index which was successfully published in Frontiers of Pharmacology Journal, will allow to monitor general population, set security patterns to categorize silent high risk groups of serious prognosis of tachyarrhythmias. For this purpose, applications of known QT determinations are proposed, recommending Dr. Rautaharju's formula, actually improved with gender adult versions. Torsadogenic index will allow to establish an individual traceability, obtain comparative samples that are alert to possible QT enlargements. Thus, torsadogenic index results a valuable, simple and costless resource to consider in the fight against acute death and cardiac arrest. Torsadogenic index represents a global indicator capable of predicting and preventing acute death and heart failure for most relevant reasons.

1. Introduction

Torsadogenic index allows the evaluation of QT enlargement, transforming itself into a preventive-predictive instrument for acute death and heart arrest for various reasons.

According to record of paper downloads in Frontiers of Pharmacology Journal during 2012–2013, torsadogenic index is a proposal to improve survival rates in cardiac arrests due to prescribed drugs and required as theme for session speaking during the International Drug Discovery Congress in Dubai and in the World Discovery Congress in Boston[1]. Torsadogenic index deserves to be proposed as a contingency strategy into a risk management project (ISO FDIS 31000: 2009 compliance), in order to mitigate the probability of its occurrence and death risk impact, as well as to avoid the materialization of these issues due to them[2].

It might seem an ambitious attempt to cover in one work different genetic mutations, torsadogenic drugs and a global endemic parasitosis. However, it happens that all of them converge into identical dangers, consequences and efforts to establish safeguards that involve simple and very low cost determinations.

1.1. Project risk goals (ISO FDIS 31000: 2009)

Therefore, it is imperative to establish the objectives of the aforementioned project, based upon the following priorities, in accordance with ISO FDIS 31000: 2009 standard[3]: (a) Risk identification to minimize issue's probability of occurrence; (b) Risk project analysis; (c) Risk monitoring until issues' disappearance; (d) Risk project control.

Understanding that meeting these goals is the optimal way of avoiding risks through the implementation of this International Standard; it is mandatory to propose a risk management process adapted to any kind of situation leading to conditions involving potential danger which may result in a Torsade de Pointes (TdP) and subsequent cardiac arrest.

This is the main basis for coupling a standard risk management to achieve the objective of safeguards proposed in this project.

1.2. Risk management process (ISO FDIS 31000: 2009)

Both ISO 9001: 2008 and ISO 31000: 2009 provide principles and generic guidelines on project and risk management

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to effectively identify, assess, analyze, treat and monitor risks[3,4].

The proposed quality model is presented in the Figure 1.

We will follow this 'logical stream of intervention', in order to achieve success in our management through ISO standards.

2. Methodological approach: torsadogenic index's risk management process cyclic sequence

Now we will start to break down, step by step, each statement that involves the proposed process.

2.1. Torsadogenic index risk project evaluation (ISO FDIS 31000: 2009)

We will address together the sequence of this project for top convergent conditions around this problem: genetic mutations, drugs and Chagas disease. The foregoing sets forth TdP as a preliminary step to ventricular fibrillation, a major cause of heart arrest.

2.2. Torsadogenic index risk project statements (ISO FDIS 31000: 2009)

(1) Risk identification; (2) risk probability and impact analysis; (3) risk control (for its negative, collateral or residual effects); (4) risk status and results (from handling and/or monitoring actions).

An expectable consequence of maintaining a strict and continuing surveillance through the presented sequence in the above project could result in a marked reduction of the sub-diagnosed cases of genetic mutations, in an unnecessary withdrawal from the market of suspected drugs and a controlled intervention over treated and potentially infected patients with Chagas disease.

This would make it possible to extend preventive measures to these risky pathological conditions, not only to those included in high risk groups (relatives of diagnosed cases of genetic mutations, relatives of victims of sudden death or cardiac arrest, contacts or relatives of patients treated for Chagas disease) but also to all the people in general, broadening the spectrum for identifying the presented conditions, proposing the same indicator to be also used as screening and follow-up tracer in newly discovered cases.

2.3. Risk project identification (ISO FDIS 31000: 2009)

While considering together these potential threats converging towards this project's implementation, we will evaluate and analyze each condition separately, in order to try to elucidate their mechanisms of action that allow us to identify them.

Regarding long QT syndrome (LQTS), it is a sarcolemmic intracellular ion channel dysfunction in the cardiac cell membrane by specific genes that regulate cardiomyocyte's potassium entry and are responsible for *sine materia* sudden deaths[5,6].

According to the worldwide recognized cardiology expert, Peter Schwartz, "The basic defect in LQTS is an unknown intracardiac abnormality that decreases electrical stability and makes the myocardium more vulnerable to the effect of sympathetic discharges[7]." The quoted situation may trigger a ventricular tachyarrhythmia that, in these patients, could directly lead to death. This risk is influenced by various causes: gender, genotype, exposure to triggers and history of previous events.

2.3.1. Statistical analysis of involved hazards

The above mentioned condition could also appear after congenital mutations (congenital LQTS) or for other secondary reasons (acquired LQTS)[7].

2.3.2. Congenital long QT inherited genetic syndromes

This group can be sub-divided into different types Table 1 [9,10].

Figure 1. Risk management process.

Referring to long QT inherited genetic syndromes, although there are many genotype variations, there are three most important conditions as genetic determinants: LQTS 1, LQTS 2 and LQTS 3 (Table 2).

According to Wu *et al.*, the most frequent type of congenital long QT syndrome is LQTS1 (more than 50% of the cases), which is caused by mutations in the KCNQ1 gene that encodes alpha-subunit of the slow component of delayed rectifier K^+ (Iks) major repolarizing current[10]. However, they discovered that at least 13 genes were responsible for different subtypes of the syndrome[10].

Dr. Schwartz warns us that neither the localization of a mutation nor its cellular electrophysiological effect could be enough to consistently unmask the presence and severity of mutation carriers LQT1 and predict the impact on their clinical manifestations[7]. As he claimed, "a borderline-normal QT may still be associated with severe risk of arrhythmia, as postulated long ago[7]." Schwartz, PJ: The long QT syndrome[11].

In acquired LQTS, there are also genetic conditioners gravitating over these genetic syndromes, like *CVP2D6* gene, and locus manifestation for cytochrome P450, which affects catalytic enzyme to metabolize drugs and toxics in 5%–10% of the Caucasian population.

According to Dr. Jufeng Wang, ex-chief science officer of Explorative Toxicological Assessment for Consumer Products in Harvard and current director of the Chinese National Drug Evaluation Center, "nearly 47% of LQTS has a congenital origin[12]." For this reason, we will necessarily be forced to identify and analyze the rest of the causes to try to stem the probability of impact which may lead to the same result, and ultimately, the cardiac arrest.

Thanks to his contribution, current Pharmacological Regulatory Committees identified sentinel effects of drugs already placed on the market.

Dr. Wang informed in 2010 that 1.5 million people required hospitalization and 100 000 died due to those TdP causing drugs, and situation that is the consequence of (1) inadequate drug prescription; (2) inadequate pharmacological interactions; and (3) self-medication or abuse of torsadogenic drugs.

All of them resulted from the unfortunate consequences of a lack of responsible cardiac surveillance of sentinel effects[13].

The above referred number climbed dramatically in 2012, when Colorado, Utah and New York Studies Summary Reviews estimated 198 000 cases of drug adverse effects (almost the double than in 2010) were registered and associated with death[14].

That evidences an unstoppable progression of the increasing mortality rate to truly catastrophic numbers by the end of this present decade (from 16 to 18 000 000 deaths in 2014 to 30 000 000 cardiovascular victims in 2020)[15].

In Table 3, pharmacological causes are shown in the listed causes of acute death. The drugs and their pharmacological causes of 'acute death' can be seen, together with the consequences arising there from. For other drugs with potential to cause QT prolongation, it is available at: www.qtdrugs.org or the First Worldwide Internet Symposium on drug-induced QT prolongation at http://www.lqts-symposium.org/2007/home.php.

As for the acquired LQTS, several causes are listed. Specifically regarding the quoted cases leading to TdP, and both drugs and Chagas disease are cited in Table 4.

Table 1
Congenital long QT inherited genetic syndromes (1/5 000 cases).

Subgroups of congenital long QT syndromes
- Jervell and Lange-Nielsen Syndrome (Oslo – associated with central deafness) Chromosome 11 – JLN1 Chromosome 21 – JLN2
- Romano – Ward Syndrome (Carlos Romano – O. Conor Ward) Autosomic dominant form Recessive form: Silvia Priori's Syndrome (1998)
- Benito Brugada's Syndrome[8] (1992) • Brugada subtype 1: sudden infant death syndrome – SIDS – *SNC5A* Gene *Affection of slow late output rectifier potassium channel • Brugada subtype 2: AVR sign (Eduardo Schapachnik) Channelopathy in right ventricular output *Rapid potassium output channel disorder (phase 3) (ST greater than or equal to 2 mm + positive or subphasic wave) • Brugada subtype 3: sudden unexplained death syndrome – SUDS
*Delayed sodium entry channel dysfunction (phase 2)
(Sudden death in south-east Asian young men?): Bangungot (Philippines) Pokkuri (Japan) Lai Tai (Thailand)
'Evil' polymorphic ventricular tachycardia – catecholaminergic ventricular tachycardia (ST > 1 mm)

Table 2
Genetic determinants: 3 most important variations[10].

Genetic determinants	Variations	Percentage (%)
LQTS 1 (9 years-old)	Chromosome 11 KCNQ1	63
LQTS 2 (12 years-old)	Chromosome 7 KCNH2 (Herg)	35
LQTS 3 (16 years-old)	Chromosome 3 SCN5A (Brugada subtype 1)	1

Table 3
Acute death's causes (American Colleague of Physicians).

Cause	Manifestation
Cardiac causes	Atrial fibrillation Cardiac tamponade Aortic dissection or rupture Arrhythmia infectological cases Cardiac fibroelastosis
Vascular causes	Traumatic loss of blood Spontaneous internal hemorrhage Gut rupture
	Anthrax *Clostridium perfringens* Colibacillosis
Pharmacological causes	Intravenous injection (inappropriate solutions) Intravenous injection (too rapidly): -Cardiac arrest -Pulmonary edema -Anaphylactic shock -Idiosyncratic reactions -Artificial poisons -Natural poisons: inadequate prescription, interaction, abuse or self-indicated Tdp drugs
Others	Electrocution Lightning injury

Table 4
Acquired LQTS causes[6].

Cause	Specification
Metabolic abnormalities	Hypothyroidism, hyperparathyroidism, pheochromocytoma
Antiarrhythmic drugs	Class 1A: quinidine, procainamide, disopyramide Class 1C: flecainide Class 3: amiodarone, ibutilide
Central nervous system injury	Subarachnoid hemorrhage, thalamic hematoma, stroke, encephalitis, head trauma
Other	Electrolyte disturbances Poisoning (arsenic, phosphorus organs) Malnutrition (anorexia nervosa, liquid protein diets) Peripheral nervous system (autonomic neuropathy, HIV)
Brady arrhythmias	Sinus arrhythmia Sinus bradycardia Chagas-Mazza disease Atrioventricular block

Regarding Table 4, the aforementioned antiarrhythmics, those of Class 1A (quinidine, procainamide, disopyramide), Class 1C (flecainide) or Class 3 (amiodarone, ibutilide), have been attributed, in many cases, disastrous consequences that lead to TdP.

Chagas-Mazza disease is endemic in Argentina. This is consistent with epidemiological information that more than 10% of the affected population, about 4 000 000 patients are currently under treatment, extending to over 10 000 000 potentially infected[16].

In case of South America, the figure reaches 34 million infected; and current estimates calculate the number at 100 000 000 infected worldwide.

About this parasitic pandemics, although it is postulated within the acquired LQTS, it also gets involved in genetic determinants. Even though the pathophysiological mechanism of cardiac Chagas-Mazza disease features QT interval dysautonomy and dispersion which result in chronotropic incompetence at high heart rates (even without symptoms), there are evidences of Gen 4 changes that are determinants of sinus bradycardia and consequent LQTS.

Protein B-2, also called ankyrin, is an acquired mutation over Gen 4 which involves preventive implant defibrillator in 23% of the patients or inappropriate therapies to cardioversion therapies in 36% of treated chagasic disease each year[17].

As you can see, even among the presented pathological conditions, there is a complex interplay of factors that determine them intrinsically.

2.4. Torsadogenic index risk project's probability and impact analysis (ISO FDIS 31000: 2009)

Risk analysis allows deductions from the project risk goals in order to reduce their potential danger[2].

After identifying the risk, you will also need to determine (1) risk probability of occurrence; (2) risk impact (magnitude of loss); (3) risk exposure (magnitude of the real global threat).

Having presented the information contained in the previous risk evaluation and identification steps, we are able to state the above mentioned risk which is in the absence of preventive or contingency measures, will continue to rise inexorably.

We will seek to describe each of the risk analysis items recently cited above.

2.4.1. Risk probability of occurrence (ISO FDIS 31000: 2009)

It specifies the real possibility for a quoted risk to turn into an issue[2].

Concerning the information about the lethal side effects of torsadogenic drugs, based upon the previously presented data obtained from USA studies, the mortality rates have increased nearly 100% in only 2 years (100 000 cases in 2010 and 198 000 reported cases in 2012)[2,14].

At present, there is no consideration for genetic studies to turn compulsory tests, so we have no objective information regarding the particular; there are only indirect registered data concerning mortality rates of acute death and cardiac arrest, which are on the rise[7].

To make matters worse, our country has excluded Chagas determination prior to labor admission due to the fact that it is considered "access to employment discrimination" by institutions governing the Ministry of Labor and Human Rights.

In other words, only victims are recorded in data, and there is no even an approximate knowledge about the potential carriers of genetic mutations for patients or relatives of victims with acute death and cardiac arrest; and luckily, those who are taking suspected drugs are properly controlled during treatment[7].

2.4.2. Risk impact

This is an indicator for measuring the extent of loss caused by a risk[2,18].

In a "triple constraint" concept, it is determined by three variables: cost, time and quality (Figure 2).

We will clarify each of these proposed triple constraint variables, available in all project management[18]:

Time: the torsadogenic index could be applied immediately to anyone and everywhere.

Cost: the torsadogenic index presupposes an easy implementation that implies zero cost.

Quality: Here we can consider this variable as "life-quality", by avoiding secondary or residual risk sequels (central nervous system lesions; neurological impairments, *etc*.) due to cardiac arrest.

2.4.3. Risk exposure

This indicator relates to the probability of occurrence to risk impact[2].

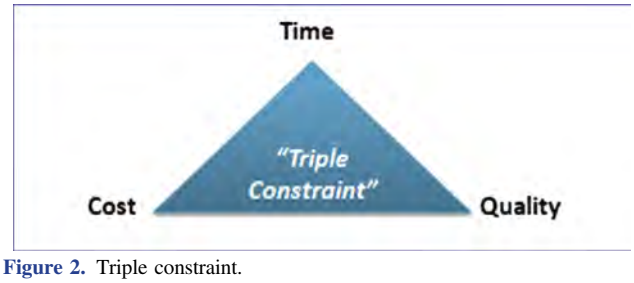


Figure 2. Triple constraint.

In these cases, we can infer from what was reported in the risk identification step and the following statements in the torsadogenic conditions analyzed in this work:

Although there are biochemical tests available for an early diagnosis of genetic mutations, it is not agreed as a compulsive practice by way of land in general population yet. This allows us to understand the existence of a large number of sub-diagnosed cases where it is not possible to deploy the aforementioned project[7].

Despite of the spontaneous or induced drug withdrawal from the market, risk exposure is yet high (*vide supra* USA studies) and it will increase in the next years if current existing drugs are still without a 10-year follow-up of true warnings of sentinel or dangerous side effects. There is a growing trend towards self-medication within the general population, which has now been adversely impaired due to widespread computers with free access to pharmacological prospect content[2,14].

Although Chagas disease is liable to be controlled through epidemiological sanitary general disclosure, it is not possible to prevent it through an extensive immunological protection device, as a vaccine would. For this reason, the WHO considered the Chagas-Mazza disease within the world's top thirteen neglected tropical diseases.

The quoted evaluation of risk exposure enables us to consolidate a risk diagnosis in the process of establishing an appropriate risk planning strategy.

2.5. Torsadogenic index risk management planning (operational strategy) (ISO FDIS 31000: 2009)

As it was introduced in the Boston World Drug Discovery Congress, the torsadogenic index risk strategy involves the following ISO FDIS 31000: 2009 steps[3]: (1) establishing a risk scale; (2)diagnosing risk status; (3) providing solutions containing major risks; (4) cost-threat balance for proper risk management; (5) risk management selection according to exposure (*vide supra*); (6) risk action plan definition.

The QTc and QTp are predictive clues to diagnose TdP.

The torsadogenic index sets alarm guidelines based on QT formulas in Figure 3 (Ex. Rautaharju) to determine the risk prior to prescription of suspected drugs.

According to the author of this formula, Dr. Pentti M. Rautaharju, the latest improvements and modifications have been made by their own creator, in order to enhance the accuracy of the obtained data. By this way, a new formula, QT index, is presented.

Here, I transcribe the words he has sent me:

> "I have substantially expanded my search for simple, best possible clinically practical formulas for the evaluation of QT prolongation. I have succeeded in deriving formulas for QT adjustment large well documented normal clinical trials and community-based population groups. These new formulas work better than the old QT index in older age groups and over a wide range of heart rates, and still maintain the simplicity of the old QT index".

This new value, QT index, is a more precise version of Dr. Rauraharju's old formula. Its calculation sequence is presented in Figure 4.

In his own words, Dr. Rautaharju concluded his explanation clarifying the practical simplicity of the proposed methodology: "To summarize briefly and to give you an idea about these new formulas, the calculations required with a simple hand-held calculator are as follows" (Figure 5).

2.6. Torsadogenic index risk monitoring and control (ISO FDIS 31000: 2009)

Risk monitoring and control involves (1) continuous analysis and monitoring performance of identified risks; (2) monitoring new collateral or residual risks; (3) maintaining new potential or residual risks; (4) permanent contingency plan revision; (5) risk mitigation by modifications of previous plans; (6) effective assessment of the risk through responsible quality performance.

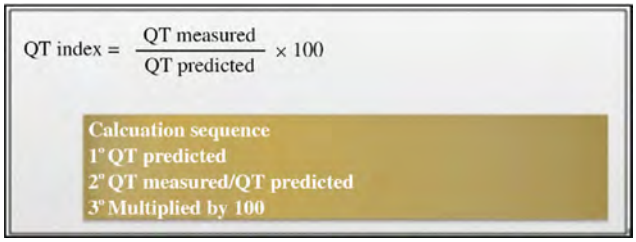


Figure 4. Dr. Pentti M. Rautaharju's new QT index formula.

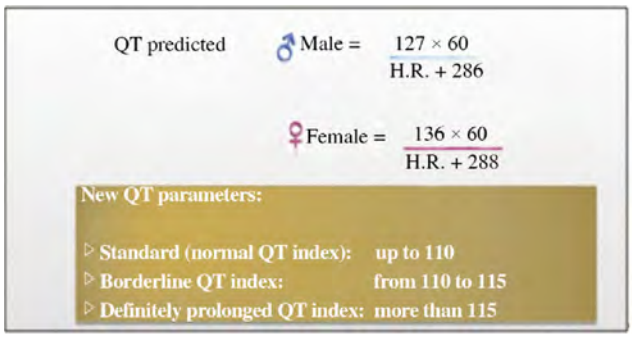
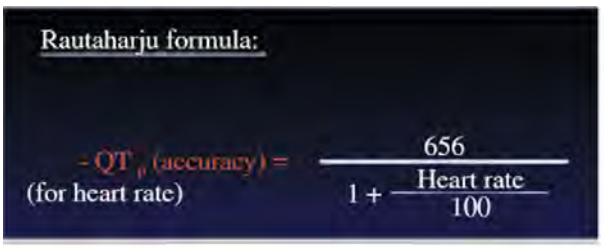


Figure 5. Dr. Pentti M. Rautaharju's new improved QT index formulas for adult men and women.



"I prefer always using variables that are model-based, with a biological reason for the risk. Otherwise, it's just a statistical hunting expedition"
Dr. Pentti M. Rautaharju

Figure 3. Dr. Pentti M. Rautaharju's QTp formula.

This continuous and cyclic process of that strict compliance and monitoring will lead to positive outcomes in managing risk of acute death and cardiac arrest.

2.7. Torsadogenic index safeguard against risk (ISO FDIS 31000: 2009)

Mandatory registration of torsadogenic index prior to TdP risk drug prescription allows an adequate monitoring and back-up of this risk management process.

Pérez Riera *et al.*, have suggested systematic electrocardiography to trace the relatives of victims with congenital LQTS. They agree to consider "the best diagnostic and prognostic parameter in relatives of patients with congenital LQTS"[8].

Thus, posed objectives for this risk management project will be achieved to upgrade the survival rates in acute death and heart arrest.

Milestones related to torsadogenic index are as following: (1) identification of high risk population (congenital or acquired LQTS); (2) electrocardiogram tests or analysis of possible early warning signs of TdP; (3) electrocardiogram and torsadogenic index screening during treatment (enhancement of timely decisions for positive effects); (4) careful assessment of TdP drugs through torsadogenic index, previewing occurrence probability of side effect[2].

Favorable consequences derived from the global application of the quoted indicator may lead to the following results: (1) effective evaluation of proposed contingency measures; (2) corrective actions based upon previous measures; (3) alternative strategies available to face new risks; (4) extended contingency plans over other stages of cardiac arrests; (5) risk management plan to improve data registration accuracy; (6) unexpected effect observations to allow taking new preventive measures, as well as avoiding new risks.

3. Discussion

The present proportion of drug collateral effects is rising from 50% to 70%. American College of Physicians judged "half of them to be preventable", but it is not clear whether the authors based their estimate on a real number of victims, or on a subjective assessment of the entire body of cases[14].

This was supported by the hierarchic opinion of Dr. Jufeng Wang, current President of Food and Drug Administration, China and Director of the National Chinese Drug Evaluation Center, "… more than 51% of pharmacological medical products have severe collateral effects after their inclusion in the commercial market."

As for those tests referred to congenital conditions, such as homogentisic acid and metabolic errors that require an early diagnosis, the torsadogenic index must be included into newborn compulsory tests, thus identifying nearly 50% of the total LQTS cases.

Cardiologist expert Peter Schwartz wrote his latest paper for the American College of Cardiology Foundation, and in his section of "Pitfalls and limitations of genetic testing", he expressed his doubt in this way[19]:

> "The methods to identify mutations are not 100% sensitive and therefore a negative genetic test cannot exclude the disorder by itself. There remain a substantial number of cases with classic symptoms and signs for one of the heritable arrhythmia syndromes which is negative for the many known genes … Certain types of mutations can be missed by standard testing exercises[19]."

The above written absolutely coincides with what was stated by Wu in this work:

> "Lethal arrhythmias can occur in these apparently healthy silent mutation carriers without any premonitory sign[10]".

Wu *et al.* identified that, referring to LQTS1, those cases with mutations over *KCNQ1*, *G269S* gene were heterozygous, and remained asymptomatic with their resting QTc intervals ranging from normal to borderline. However, they showed an excessive QT prolongation during exercise, triggering cardiac events during adrenergic stimulation. According to this study, these patients had lengthy QTc intervals after exercise[10].

Regarding Chagas-Mazza disease, it must be remembered that there is no vaccine or preventive medication available for this parasite, and further conventional treatment does not eliminate the disease, except for recent experimental results attributed to posaconazole, an antifungal of high cost in our country[20].

The torsadogenic index risk management project goals imply the development of promptly practical and costless security measures which will allow the prevention of possible severe cardiac conditions and lead to consider the Torsadogenic index as a preventive-predictive method, which is able to turn acute death prognosis into a preventable and predictable condition.

Expectable consequences of the torsadogenic risk management project will result in (1) improving pharmacological avoidable mortality; (2) upgrading cardiac arrest survival rates; (3) improving active cardio-safety preventive care; (4) promptly achieving practical-costless security.

Knowing in advance unrecognized acute death causes, and activating undiagnosed diseases interception before the appearance of lethal complications is very important.

Thus, a preventable death risk mitigation planning will help to discover unexpected causes prior to their extremely severe transformation.

4. Conclusions

With respect to the goals of this risk management project, the development of promptly practical and costless security measures to avoid severe cardiac conditions will help to consider the torsadogenic index as a preventive-predictive method that is capable of changing acute death prognosis.

Prescription and drug interaction stand as the fourth leading cause of death in USA with nearly 300 000 victims per year[21].

Regarding the risk impact, the torsadogenic index could dramatically impair the occurrence likelihood of TdP, reducing the risk before waiting its dangerous conversion into an issue.

Particularly referring to the pharmacological causes, inadequate prescription, interactions, self-medication or abuse of torsadogenic drugs recognize an annual current hospital admission of drug adverse effects of 2.9%–3.7% of overall hospital admission. So, American College of Physicians stated it as "… over half of those adverse events resulting from medical errors", meaning that quoted percentages can be efficiently prevented.

By this way, supporting the torsadogenic index risk management planning will turn this danger into a preventable measure over medical or pharmacological failures, avoiding fatal consequences due to inadequate drug prescription or combination, and thus improving the present health care possibility of changing these circumstances that frequently lead to death.

The deduction that may emerge from reading the aforementioned experts in LQTS and genetic mutations makes us conclude that, although the possibility of genetic registry represents a breakthrough for proper control of this problem, it could be realized that there are some cases in which, despite having referral genetic traits, they will never suffer from acute death or cardiac arrest, or, conversely, may die without the manifestations of LQTS genetics[20]. Therefore, genetic testing does not seem to constitute itself the solution to the problem of LQTS mutation.

In the words of the cardiologist Peter Schwartz: "the interpretation of a negative genetic test result in a symptomatic person is a real challenge. Therefore, interpreting genetic test results is often confounded by the discovery of variants of unknown significance."

In his extended study, Wu suggested that patients with *G269S* mutations and an excessive prolongation of QT intervals could benefit from beta-blocker therapy.

Therefore, continuous efforts must be made to identify them properly[10].

In his masterful work, Dr. Morillo CA emphasized medicolegal implications and the balance between the confidentiality of observation data and the duty to report and follow-up patients having tests with positive findings[20]:

> "Likewise, the physician who, after having obtained positive genotyping, and does not propose to initiate cascade screening within the family of the proband, has similarly fully decided to leave the affected family members uninformed about their status and unprotected".

Given the severity of all the nosological situations presented in this work, I guess the same consideration should be already extended for suspicious drugs, Chagas disease and to all other diagnostic attempts to safeguard the patients, by identifying their pathological conditions to enable timely medical intervention. The torsadogenic index, with its simplicity and low-cost implementation, should not be the exception to this rule.

Despite of this, Human Right's Defense and International Regulations poses our professional duty to provide full information to patients. Our commitment of a responsible risk assessment "… is the prevention of serious consequences of these diseases, and the respect of equal human rights, ensuring that all newborns have an access to an early diagnosis, preventing, thus death or disability for life", according to Dr. Magdalena Ugarte, Director of Center of Molecular Disease Diagnosis, Department of Biochemistry and Molecular Biology, Universidad Autónoma de Madrid[22].

In this way, supporting the torsadogenic index risk management planning will be considered another predictable and preventable measure over medical and pharmacological failures, by avoiding fatal consequences due to inadequate drug prescriptions or combinations, and improving actual medical possibilities of changing the circumstances that lead to death for all these reasons.

Quoted as a mandatory record of contingency strategy, the purpose of torsadogenic index risk management will maximize the success of the project, thus preventing or mitigating risks before they become real problems.

Conflict of interest statement

The author reports no conflict of interest.

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