SPECIAL ARTICLE

Fast Tilt Test, a New Paradigm in the Management of Reflex Syncope

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ABSTRACT

Introduction
Between 20% and 30% of the population present syncope throughout their lives being reflex syncope the most common cause. The differential diagnosis is based on the characteristics of the episode questionnaire and on the reproducibility of symptoms with the head-up tilt test. However, the tilt test has important limitations, which have led us to explore a new parameter in successive stages of research, which we called "time delay of the carotid pulse wave".

Objectives
To present the results of the research on the discovery, development and clinical applicability of the parameter: "time delay of the carotid pulse wave", capable of identifying patients with reflex syncope.

Methods
The development of the idea and the results of the analysis of the correlation between the parameter and the tilt test evaluated in a pilot study of 43 patients with syncope are described. The correlation is confirmed in 100 patients with syncope and in controls; the pathophysiological mechanism of the parameter is evaluated; the design of an automated device is described and its validation is confirmed in a multicenter study of 100 patients with history of syncope using drug-stimulated head-up tilt test. The search of a new gold standard for reflex syncope is described.

Results
The statistical analysis performing univariate and multivariate models and the construction of ROC curves on 243 patients undergoing head-up tilt test showed that, despite the different ages or methods used, the parameter correctly classified more than 80% of patients with history of syncope and positive head-up tilt test and 100% of volunteers without history of syncope who presented positive head-up tilt test. The measurement of the parameter without using a tilt table identified 100% of volunteers with history of syncope (7/30).

Conclusions
We developed a simple and non-invasive measurement parameter, capable of predicting a positive head-up tilt test within 5 minutes in patients with syncope and of identifying people with history of syncope without using the tilt table. The parameter could help to make rapid diagnostic decisions in patients with syncope, to understand the pathophysiological aspects and to evaluate the therapeutic interventions.

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Key words > Syncope vasovagal; Diagnosis; Cardiac Electrophysiological Techniques, Tilt table test

Abbreviations >

BP	blood pressure	**TT**	tilt test
HR	heart rate		

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INTRODUCTION

Syncope is a common manifestation that may occur in up to 20% of individuals throughout their lives (1). Although there are malignant arrhythmias related to rhythm disorders, the most common type is neurally-mediated syncope with good prognosis despite possible quality of life impairment (2). The differential diagnosis is based on the characteristic of the episodes questionnaire, which has been documented by the clinical score developed by Sheldon et al. with a good power of discrimination (3, 4). The use of the head-up tilt test (TT) began in the eighties, exposing patients to prolonged orthostatism that triggers a neurally-mediated response and may reproduce syncope and collaborate in identifying the mechanism (5, 6). However, TT has important limitations, as the high incidence of false negative results and its low reproducibility (7, 8) which have led some practice guidelines to withdraw it from their recommendations (9). In spite of the development of new diagnostic methods, medical history remains the gold standard (10, 11, 12). Eight-years ago, we began exploring a parameter observed in patients with neurally-mediated syncope, which we called "time delay of the carotid pulse wave". The aim of this publication is to present the results of the successive research stages of this parameter strongly related with neurally-mediated syncope, its discovery and development, and the clinical management outcome with the use of new technologies.

BIRTH OF THE IDEA:

Some publications made in 2003 on arterial compliance measurement in hypertensive patients (13) encouraged us to evaluate the efficacy of measuring the pulse wave velocity triggered from the onset of the QRS complex to study the pathophysiology of neurally-mediated syncope. With the help of bioengineers, we developed a device capable of measuring pulse wave velocity with a non-invasive, reproducible and reliable method during conventional head-up TT. The first three patients with reflex syncope showed, after changing position from supine to standing upright, significant prolongation of the parameter which preceded the late syncope appearance, thus giving impulse to the research.

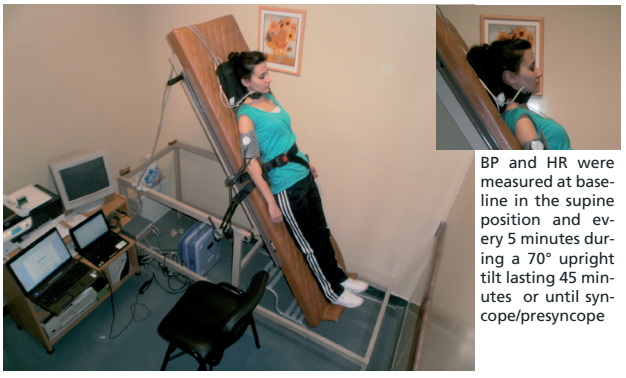
RESEARCH STAGES

First stage: Casual event or stable correlation?

In 2007, we evaluated the parameter performance during head-up TT through a prospective pilot study conducted on 43 consecutive patients referred to our department with history of syncope. After obtaining clinical data, the patients underwent conventional head-up TT. Heart rate (HT) and blood pressure(BP) were measured at baseline and every 5 minutes during a 70° upright tilt during 45 minutes or the presence of syncope, presyncope or symptoms associated with hypotension (Figure 1). The interval variation between the onset of the QRS complex and the onset of radial and carotid pulse waves determined by pressure transducers was measured using high precision digital calipers (± 2 ms) and recorded simultaneously on a computerized polygraph at 100 mm/s after changing position from supine to standing upright (Figure 2). The study results have been published. (14, 15). A time delay of the carotid pulse wave ≥ 17 ms measured at 5 minutes was an independent predictor of TT result, correctly classifying 88% of patients before the development of symptoms with a sensitivity of 83%, a specificity of 84%, a positive predictive value of 79% and a negative predictive value of 88%).

Second stage: "Confirming the correlation"

Due to the small number of patients and the lack of a control group in the pilot study, in May 2008 we began the prospective inclusion of 100 consecutive patients



BP and HR were measured at baseline in the supine position and every 5 minutes during a 70° upright tilt lasting 45 minutes or until syncope/presyncope

Fig. 1. Tilt-table testing at an angle of 70°. The right superior image shows the transducer placed over the carotid artery.

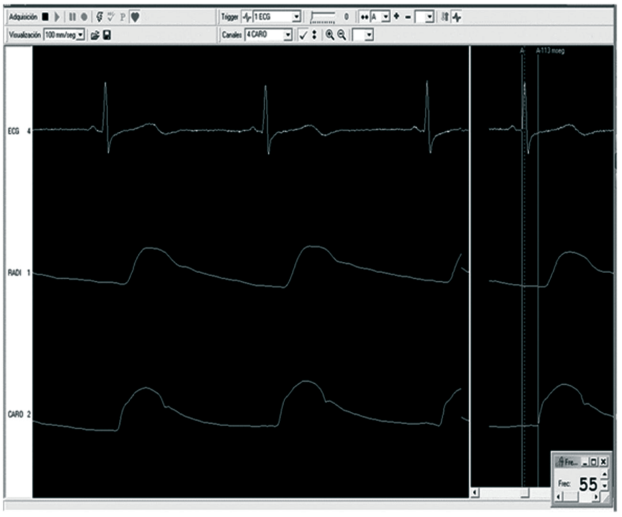


Fig. 2. Measurement of the parameter "time delay of the carotid pulse wave". Frozen digital polygraph screen with a recording velocity of 100 mm/s showing ECG record in channel 1, radial pulse wave in channel 2 and carotid pulse wave in channel 3. The right margin shows a digital trigger system for manual parameter by calipers from the onset of the QRS complex to the onset of the carotid pulse wave.

with history of syncope and of 30 volunteers without history of syncope. The study was similar to the former, using a conventional head-up TT and manual measurement of the "time delay of the carotid pulse wave". For statistical analysis, the population was divided into three groups according to TT results (positive, negative and control group). Baseline characteristics, differences in HR, BP and time delay of the carotid pulse wave at baseline and at 5 minutes were compared in univariate and multivariate analysis. There were no significant differences in the patients' characteristics with and without syncope. The results were similar to those of the pilot study. The parameter identified 80% of patients with history of syncope and positive TT and two volunteers in the control group who presented with syncope during head-up TT (16). Syncope may be provoked in 7% of patients without a history of syncope during TT, a number equivalent to our findings in the control group (17). A sub-analysis performed on 82 consecutive patients between 10 and 75 years with reflex syncope evaluated the parameter's capacity to predict TT result in patients of different ages. The population was divided into quartiles according to age (10-22, 23-43, 44-64 and 65-75) and ROC curves were made to perform statistical comparisons within the groups. The results showed that the parameter had a consistent capability to predict TT results in the different age groups (18).

Third research stage:

Correlation exists. What are we measuring?

The availability of a fast, simple and safe tool which can be correlated with syncope development during head-up TT may result of great interest, but certainly, the challenge of the research is to understand the origin of this manifestation called "time delay of the carotid pulse wave" and the reason of its accuracy to identify patients with high chance of developing neurally-mediated syncope independently of other parameters. Changes in the time interval from the onset of the QRS complex to the onset of the carotid pulse wave after changing position from supine to standing upright involve dynamic manifestations due to multiple vascular changes which include pre-ejection and ejection period. An observational study was performed to identify its time interval in the cardiac cycle. The delay of the carotid pulse wave and the pre-ejection period were simultaneously recorded using Doppler echocardiography. Five patients between 15 and 64 years with a history of spontaneous and provoked by head-up TT vasovagal syncope, with a delay in the carotid pulse wave > 20 ms during a 70° upright tilt, were selected. The time interval from the QRS complex to the onset of the carotid pulse wave and the time interval from the QRS complex to aortic valve opening (pre-ejection period) were simultaneously measured at baseline in the supine position with Doppler echocardiography with digital calipers at a speed of 50 mm/s (Figure 3). After 5 minutes of 70° upright tilt, and with a verified delay in the pulse wave ≥20 ms, both intervals were measured again and their changes were analyzed. The median time delay of the carotid pulse wave in the supine position and at 5 minutes of 70° head tilt was of 98.6 ms (90/105) and 131 ms (116/145) respectively, whereas the median interval from the onset of the QRS complex and aortic valve opening in the supine position with upright tilt was of 74.4 (55/98) and 78.8 (65/105), respectively, showing a change in the pre-ejection period of only 13% (4.4 ms) of the mean time delay of the carotid pulse wave (32.4 ms). The results were consistent in the 5 cases, demonstrating that prolonged delay of the carotid pulse wave after head-up tilting is predominantly related with the ejective period, i.e., with dynamic changes occurring from the aortic valve opening until pulse arrival to the carotid

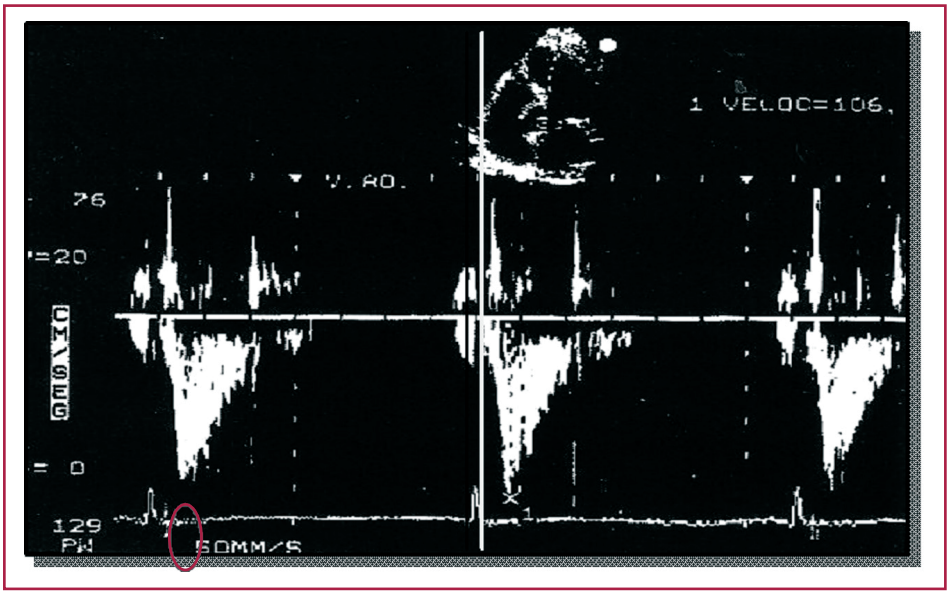


Fig. 3. Doppler echocardiography image recorded at 50 mm/s. Measurement of the pre -ejection time, from the onset of the QRS complex to aortic valve opening with the patient in the supine position and in 70° head-up tilt.

artery. In our opinion, such changes are related with peripheral vessels compliance variations after changing position from supine to standing upright with 2 to 3 minutes delay in the retrograde impact on the pulse wave velocity advancing towards the transducer placed over the carotid artery. The time delay of the carotid pulse wave after changing position from supine to standing upright could imply an exaggerated peripheral vasoconstrictor response (19).

Forth research stage:

Standardized and automated measurement

Considering that in the preceding studies parameter measurement depended on the operator and that the results came from a single center, we designed a device capable of automated measurement and began a collaborative study with the Hospital Británico de Buenos Aires (Figure 4). A total of 100 consecutive patients with a history of reflex syncope and a mean age of 50.2 years were included to validate automated measurement of the "time delay of the carotid pulse wave" versus manual measurement during nitrate-stimulated head-up TT. Sixty-eight percent of patients presented a positive TT, with a "time delay of the carotid pulse wave" > 17 ms manually and automatically measured at 5 minutes of upright tilt. This was the only parameter to be related with the result of the TT ($p < 0.001$). The area under the ROC curve (C statistic) of the time delay of the carotid pulse wave was 0.78 (95% CI 0.68 to 0.88) with a sensitivity of 83.8%, specificity of 72%, positive predictive value of 83.8% and negative predictive value of 71.9%. The study established that for every ms increase in parameter prolongation, the chance of positive responses during TT increased by 15% (Figure 5). The results confirmed that the parameter identified 78% of patients with history of syncope and positive TT (20). A sub-study conducted on the same population evaluated the correlation between automated and manual measurement of the "time delay of the carotid pulse wave". Both measurement modalities were performed on the 100 studies, statistically comparing the capability of the manual and automated measurement of the parameter at baseline and after 5 minutes during 70° upright tilt to predict TT result. The results validated automated measurement, showing a close correlation with manual measurement with even a slightly greater sensitivity and specificity, validating the method independently of the operator (21) (Figure 6).

Fifth research stage:

Looking for a new gold standard

So far, we have compared the parameter with head-up TT which has been questioned as gold standard for the diagnosis of neurally-mediated syncope. Compared to the results of TT, our method presents a moderate excess of positive tests which might be interpreted as false positive results, or, alternatively, as an expression of greater sensitivity (true positive results) if they were associated with anamnesis, a gold standard superior to TT. Thus, we believed that it was time to abandon head-up TT as comparative test and to try to correlate our parameter with syncope anamnesis. Taking into account that 20% to 30% of individuals present with syncope throughout their lives and that reflex syncope is particularly more common in patients without heart disease, a group of 30 volunteers was selected all of whom were high resistance athletes

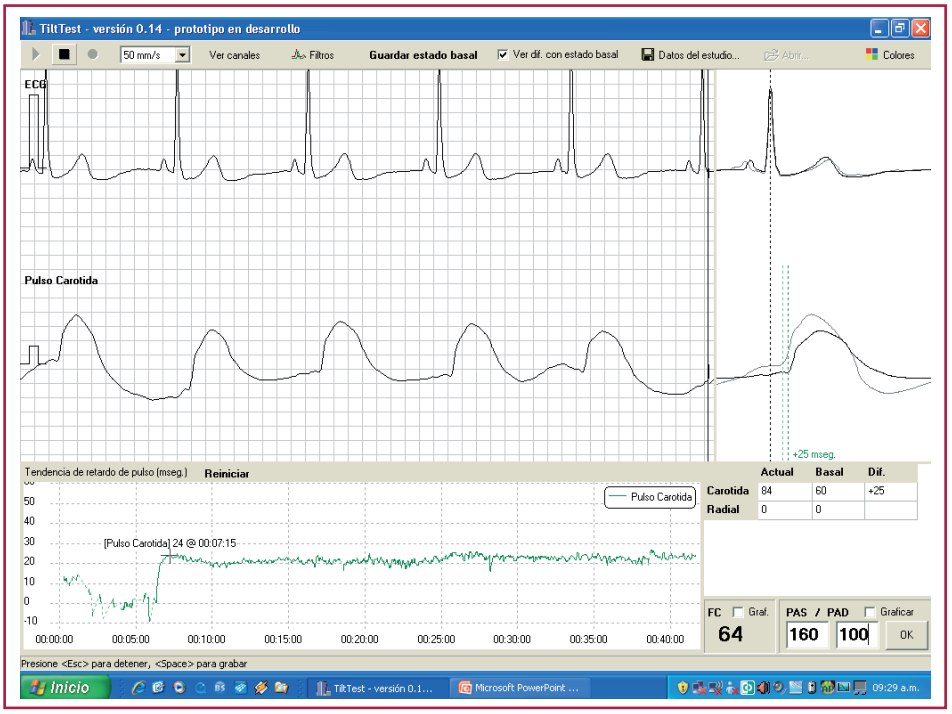


Fig. 4. Frozen image of the automated measurement system during a study showing an ECG recording and the carotid pulse wave at a velocity of 50 mm/s. The right superior box shows automated measurement of the delay of the carotid pulse wave with calipers triggered by the QRS complex and its instantaneous value after changing position from supine to standing upright, in this case of 25 ms. The inferior box shows a histogram of the values from study initiation, in the supine position and its variation after a 70° head-up tilt.

(20 men, mean age 48 years [34-60]). Five of them had mild hypertension which was well-controlled with low dose of angiotensin converting enzyme inhibitors, 3 had dyslipidemia and 2 had mild hypothyroidism. These athletes, who belong to a training group run 30 to 40 km, 3 to 4 times a week under the supervision of a Nike® trainer. We began an evaluation phase of the "time delay of the carotid pulse wave" parameter without using the tilt table. The athlete was asked to lie down in supine position on an exercise mat placed on the grass and the parameter was mechanically measured, then the athlete was asked to stand up and stay still for 3 minutes after which the parameter was measured again. We called this method "fast tilt test" (Figure 7). While one operator was in charge of asking the athletes to sign the informed consent form, retrieving clinical data and history of syncope and estimating the Calgary and Sheldon scores, another operator, blind to the questionnaire information, measured the "time delay of the carotid pulse wave" parameter. The information was statistically analyzed, assessing the prognostic accuracy of the parameter versus the history of syncope using ROC curve and the value with the best predictive accuracy was selected to calculate positive and negative predictive values. History of syncope was present in 7 volunteers. A carotid pulse delay ≥20 m had a sensitivity of 100%, a specificity of 87%, a positive predictive value of 70% and a negative predictive value of 100% for identifying persons with syncope. The area under the ROC curve was 0.90 (95% CI 0.79 - 1.00) (Figure 8). Mean time delay of the carotid pulse wave in the 7 volunteers with or without history of syncope was 24.8 ms and 9.5 ms respectively, ($p < 0.001$). Fast TT identified volunteers with a history of syncope in 3 minutes (22). Three volunteers without history of syncope presented a time delay of the carotid pulse wave > 20 ms but had no differences in their clinical characteristics compared to the other volunteers. These 3 athletes might belong to a group who has not suffered syncope yet but who possess the pathophysiological conditions to develop neurally-mediated syncope or it might correspond to false positive results due to limitations of a method still being developed

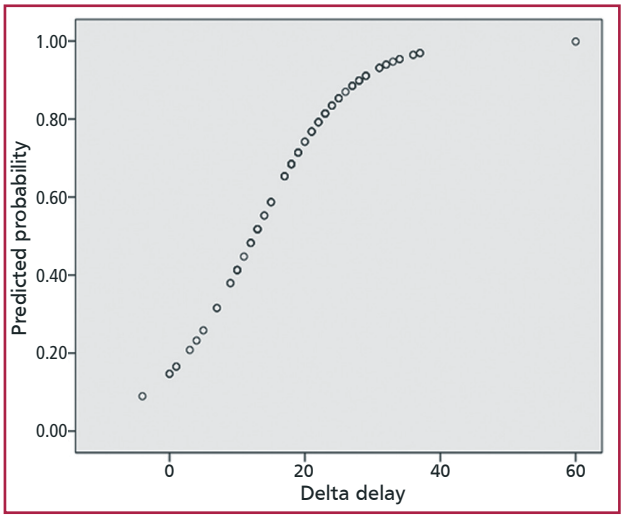


Fig. 5. Relation between the probabilities predicted by the logistic model and the delta delay. There is a close relation between the parameter with positive tilt-test responses.

DISCUSSION

We discovered and developed a simple and non-invasive measurement parameter capable of identifying in 5 minutes patients with a history of syncope in whom head-up TT would be positive, volunteers without history of syncope but with positive TT and volunteers with history of syncope without using the tilt table. During the last 8 years we have displayed five successive research stages with the purpose of answering different aspects of the "time delay of the carotid pulse wave" in order to provide the greatest information of this manifestation, its properties, pathophysiology and clinical usefulness. This article is the sum-

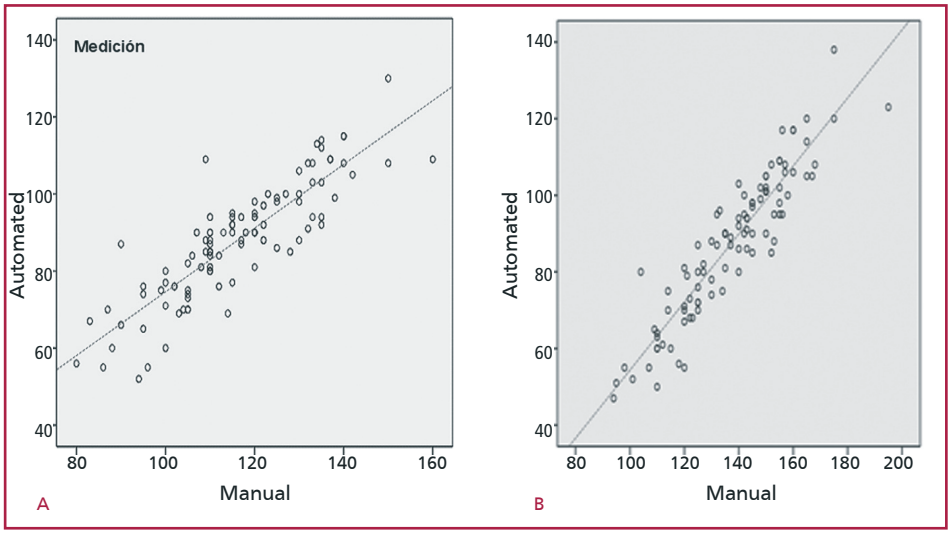


Fig. 6. Validation of the automated method versus the manual method to measure the "time delay of the carotid pulse wave" Correlation between baseline **(A)** and final **(B)** delays measured by both methods, considering that the absolute values are different: the manual measurement estimates the delay from the onset of the QRS complex to the onset of the carotid pulse wave, while the automated measurement estimates the delay from the zenith of the QRS complex to the onset of the carotid pulse wave; with the result of a lower absolute value.

Fig. 7. Measurement of the "time delay of the carotid pulse wave" in volunteer high resistance athletes using "Fast Tilt Test" without using the tilt table. Top: baseline measurement in the supine position. Bottom: measurement in the standing position.

mary of our objectives, where the reader can follow the working team from the birth and development of the idea and along the orderly steps which fulfilled each stage of the research. The parameter represents the time interval variation from the electrical activation of the heart until the pulse propagates through the carotid artery after standing up and the multiple biological responses occurring as an adaptation to the new posture. As this interval increases, the probability of developing neurally-mediated syncope is higher, suggesting the presence of a special pathophysiological condition in these patients associated with an excessive peripheral vasoconstriction that occurs after changing position from supine to standing upright. This manifestation has a delay of 2 to 3 minutes before it can be reflected in the velocity of the carotid pulse wave recorded by the transducer. In other words, the retrograde tidal wave rises in the upright standing position and, when opposing to the ejective blood flow would provoke a delay in the elastic carotid arteries, which can be measured by the novel digital computed techniques. In this regard, peripheral vascular resistance forms part of a wider concept called arterial impedance, which can be simply defined as the sum of the variables opposed to blood flowing through the arteries. Arterial impedance has three components: arterial compliance (typical or the great vessels), peripheral vascular resistance (in medium and small arteries) and pulse wave reflection originating in the aortic bifurcation and centripetally transmitted towards the aortic root, reaching the pulse wave in the final diastolic portion. (23). With our studies, we have demonstrated that the delay of pulse wave occurs mostly during the ejection period and does not differ in age groups with different arterial compliances; therefore, the manifestation seems to depend mostly on changes in peripheral resistance. In this sense, after our group of engineers developed a device to measure pulse wave

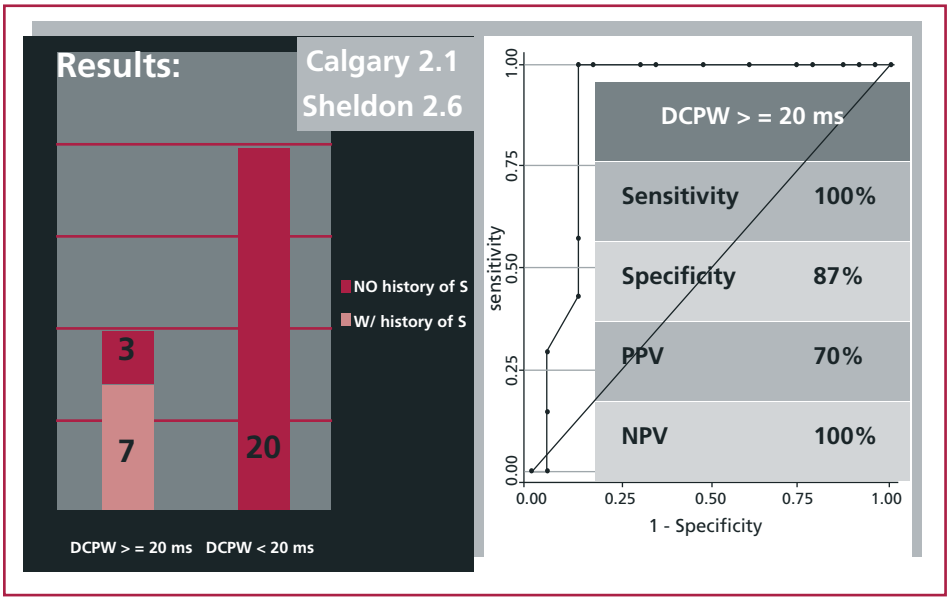


Fig. 8. To the left, population distribution with and without history of syncope with a time delay of the carotid pulse wave≥ 20 ms. Values obtained from the Calgary and the Sheldon scores in the population with history of syncope. To the right, Area under the ROC curve with its sensitivity, specificity and predictive values for a time delay of the carotid pulse wave ≥20 ms. S: Syncope. DCPW: Time delay of the carotid pulse wave. PPV: Positive predictive value. NPV: Negative predictive value.

velocity we are considering whether measuring this parameter during head-up TT can provide additional information on dynamic changes of peripheral vascular resistance. Finally, the research has concluded so far, but the steps taken seem solid enough to raise the interest of the medical community and promote its development and applicability in patients with syncope.

Limitations

The parameter can identify individuals with history of syncope and patients with positive head-up TT, but does not predict the exact moment of syncope occurrence. An ongoing study is analyzing changes in the parameter in the previous seconds to syncope during TT since additional delays have been observed at that instant. By improving the parameter measurement technique, we have learned that the correct measurement of the interval QRS complex-carotid pulse wave at baseline is crucial before changing position from supine to standing upright. When the patient is in the supine position, the venous pulse wave may be prominent and alter the carotid pulse wave initiation. The necessary time should be taken to modify the transducer position until achieving a clean carotid pulse wave which can be compared when the patient is tilted. In individuals with short neck in whom the sternocleidomastoid muscle may be partially interposed between the arterial pulse and the transducer, a slight pressure should be applied to the belt holding the transducer over the carotid pulse. Once these recommendations were considered, it was possible to measure the parameter in all the cases. The availability of a computer-based digital measurement system that stores the information in its memory allows a retrospective beat-to-beat analysis of the changes occurring during the study. So far, patients with atrial fibrillation have been excluded from the study due to permanent changes in the cardiac cycle which turn the parameter measurement unstable. Therefore, our current purpose is to incorporate the parameter during decision-making in patients with reflex syncope in a multicenter prospective study with a control group. Finally, as we have shown in the results of the fifth stage, three volunteers without history of syncope presented delay of the carotid pulse wave. This may be interpreted as a group that has not developed syncope yet or as false positive results due to an imperfection of a method still under development.

CONCLUSIONS

The "time delay of the carotid pulse wave" showed a close correlation with the result of the head-up TT in different scenarios and identified more than 80% of the patients who will present syncope and volunteers without history of syncope who developed syncope during TT. The parameter, which is related with the ejection period and linked to changes in vascular compliance, may help to make rapid diagnostic decisions in patients with syncope, to understand pathophysiological aspects and to evaluate therapeutic interventions.

RESUMEN

Fast tilt test: tras un nuevo paradigma en el manejo del síncope reflejo

Introducción

El 20% a 30% de la población presenta episodios sincopales a lo largo de la vida y el mecanismo reflejo representa la causa más común. Su diagnóstico diferencial se basa en el interrogatorio de las características del episodio y en la reproducibilidad de los síntomas con el tilt test. Sin embargo, este último tiene limitaciones importantes, lo que nos ha llevado a explorar en sucesivas etapas de investigación un nuevo parámetro, al que denominamos "retraso de la onda de pulso carotídeo".

Objetivos
Presentar los resultados de la investigación sobre el descubrimiento, el desarrollo y la aplicación clínica del parámetro "retraso de la onda de pulso carotídeo", capaz de identificar a pacientes con síncope reflejo.

Material y métodos
Se describen el nacimiento de la idea, los resultados del análisis de la correlación entre el parámetro con el tilt test mediante un estudio piloto en 43 pacientes con síncope, la confirmación de su correlación en 100 pacientes con síncope y grupo control, el estudio del mecanismo fisiopatológico del parámetro, el diseño y la validación de un equipo de adquisición automática en un estudio multicéntrico sobre 100 pacientes con historia de síncope mediante tilt test sensibilizado y la búsqueda de un nuevo patrón oro del síncope reflejo.

Resultados
El análisis estadístico mediante modelos univariados y multivariados y la construcción de curvas ROC sobre 243 pacientes sometidos a tilt test mostró que, a pesar de diferentes edades o métodos empleados, el parámetro clasificó correctamente a más del 80% de los pacientes con historia de síncope y tilt test positivos y al 100% de los voluntarios (2/30) sin historia de síncope que presentaron tilt test positivo. La medición del parámetro prescindiendo de la camilla basculante identificó al 100% de los voluntarios que refirieron historia de síncope (7/30).

Conclusiones
Desarrollamos un parámetro de medición simple y no invasiva capaz de predecir en 5 minutos el resultado del tilt test en pacientes con síncope e identificar a personas con historia de síncope reflejo prescindiendo de la camilla basculante. El parámetro podría ayudar a la rápida toma de decisión diagnóstica en pacientes con síncope, a comprender aspectos fisiopatológicos y a evaluar intervenciones terapéuticas.

Palabras clave > Síncope vasovagal - Diagnóstico - Técnicas electrofisiológicas cardíacas - Tilt-table test

Conflicts of interest
None declared.

REFERENCES

1. Ganzeboom KS, Colman N, Reitsma JB, Wieling W . Prevalence and triggers of syncope in medical students. Am J Cardiol 2003; 1006-8.

2. Tambussi A, Kochen S. Estudio diagnóstico del síncope en pacientes de consultorio externo de un hospital general. Rev Latinoam Cardiol 1996; 7:6.

3. Sheldon R, Rose S, Connolly S, Ritchie D, Koshman ML, Frenneaux M. For the syncope Symptom Study Investigators. Diagnostic Criteria for vasovagal syncope based on quantitative history. Eur Heart J 2006;27:344-50. http://doi.org/d8ttn9

4. Sheldon R, Rose S, Ritchie D, Connolly SJ, Koshman ML, Lee MA et al. Historical criteria that distinguish syncope from seizures. J Am Coll Cardiol 2002;40:142-8. http://doi.org/cnmg25

5. Benditt DG, Ferguson DW, Grubb BP, Kapoor WN, Kugler J, Lerman BB, et al. Tilt table testing for assessing syncope. American College of Cardiology. J Am Coll Cardiol. 1996;28:263-75. http://doi.org/dnjzv7

7. Nyman JA, Krahn, AD, Bland PC, Griffiths S, Manda V. The costs of recurrent syncope of unknown origin in elderly patients. Pacing Clin. Electrophysiology. 1999;22,1386-94. http://doi.org/dfnf4q

8. Calkins H, Byrne M, el-Atassi R, Kalbfleisch S, Langberg JJ, Morady F. The economic burden of unrecognized vasodepressor syncope. Am J Med. 1992;95,473-9. http://doi.org/ffggz6

9. Strickberger SA, Benson W, Biaggoni I, Callans DJ, Cohen MI, Ellenbogen KA . AHA/ACC Scientific Statement on the evaluation of Syncope. From the American Heart Association Council on Clinical Cardiology, Cardiovascular Nursing, Cardiovascular Disease in the Young and Stroke, and the Quality of Care and Outcomes Research Interdisciplinary Working Group; and the American College of Cardiology Foundation in Collaboration with the Heart Rhytm Society. Endorsed by the American Autonomic Society. Circulation 2006;113:316-27. http://doi.org/bt3zjb

10. Gulli G, Cooper VL., Claydon V, Hainsworth R. Cross-spectral analysis of cardiovascular parameters whilst supine may identify subjects with poor orthostatic tolerance. Clin. Sci. 2003;105,119-26. http://doi.org/bx8wq8

11. Bellard E, Fortrat JO, Schang D, Dupuis JM, Victor J, Leftheriotis G. Changes in the transthoracic impedance signal predict the outcome of a 70 head-up tilt test. Clin. Sci. 2003;104,119-26. http://doi.org/bsstz9

12. Simek J, Wichterle D, Melenovsky V, Malik J, Svobodova J, Svacina S. Pulse wave analysis during supine rest may identify subjects with recurrent vasovagal syncope. Clin Sci (Lond). 2005;109:165-70. http://doi.org/d4vmms

13. Majul CR, Paez OB, De María M, Manzur P, Prieto N. Arterial compliance in pregnancies with and without risk of preeclampsia. Rev Argent Cardiol 2004; 72:21-4.

14. Villamil AM, Perona C, Carnero GS, Torres Y, Mariani JA, Tajer CD y col. Evaluación del comportamiento del intervalo desde el inicio del QRS al inicio de la onda de pulso radial y carotidea con el resultado del tilt test. Tema libre oral, Jornadas de los Consejos Científicos de la SAC 2008. Rev Argent Cardiol 2008; 76 (Supl. 1): 136 (resumen)

15. Villamil AM, Perona C, Carnero GS, Torres Y, Mariani JA, Tajer CD, y cols. Evaluation of the Behavior of the Time Interval from the Onset of the QRS Complex to the Onset of Radial and Carotid Pulse Waves with the Result of the Tilt Test. Rev Argent Cardiol. 2009;77:347-53.

16. Paolasso MF, Estévez AO, Terragno AL, Torres P, Torrejón N, Villamil AM y cols. Evaluación del comportamiento del intervalo desde el qrs al inicio de la onda de pulso carotídea con el resultado del tilt test en 100 pacientes y grupo control. Abs 49. XXII Jornadas Nacionales de los Distritos Regionales. Rev Argent Cardiol 2011; 79(Supl 1):49 (resumen)

17. Natale A, Akhtar M, Jazayeri M, Dhala A, Blanck Z, Deshpande S, et al. Provocation of hypotension during head-up tilt testing in subjects with no history of syncope or presyncope. Circulation 1995;92:54-8. http://doi.org/pvq

18. Villamil AM, Torres Y, Perona C, Mariani J, Tajer CD, Fiamengo J. "Valor del intervalo desde el inicio del QRS al inicio de la onda de pulso carotidea con el resultado del Tilt Test para distintas edades". Abs 197. XXXVI Congreso Argentino de Cardiología. Rev Argent Cardiol 2010; 78 (Supl. 2):124

19. Paolasso MF, Pezzati L, Villamil AM, Perona C, Fiamengo JM, Becillia L y cols. Correlación del intervalo entre el inicio del qrs y la onda de pulso carotídea, durante el tilt test con ecodoppler. Aproximación del síncope neurocardiogénico. Abs 14 XXII Jornadas Nacionales de los Distritos Regionales. Rev Argent Cardiol. 2011;79 (Supl. 1): 14 (resumen)

20. Villamil AM, Torres Y, Estepo J, Cáceres M.C, Tello IA, Mariani J, Tajer CD, Perona C. Evaluación del comportamiento del retraso de la onda de pulso carotidea con el resultado del Tilt Test sensibilizado en 100 pacientes. Abs 085.XXXVIII Congreso Argentino de Cardiología; Rev Argent Cardiol 2012; 80(Supl. 3):85 (resumen)

21. Villamil AM, Torres Y, Mariani J, Estepo J, Cáceres MC, Tello IA. Relación entre la medición manual y automática del retraso de la onda de pulso carotidea durante el tilt test en 100 pacientes con síncope. Tema libre oral: I Congreso Argentino de Arritmias 2011

22. Villamil AM, Torres Y, Mariani J, Di Leva A, Ríos L, Cáceres M.C. Hosp. Santojanni, Gedic, SAC DC. Norte. Fast Tilt Test, un nuevo paradigma en el estudio del síncope vasovagal. Poster: II Congreso Argentino de Arritmias 2012.

23. Villamil A, Sánchez R, Baglivo H. En: "Hipertensión Arterial, de la Investigación a la Práctica Clínica": Cap. 2. 1a ed; Buenos Aires,2013