HEART RATE AND INSTANTANEOUS CENTRE FREQUENCY AS A PREDICTOR OF VASOVAGAL SYNCOPE DURING HEAD-UPRIGHT TILT TABLE TESTS

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Abstract - The author analysed electrocardiograms from 42 patients with suspected syncopal disorders undergoing head-upright tilt table testing (HUT). Carefully preprocessed tachograms were input to a customised Smoothed Pseudo-Wigner Ville Distribution (SPWVD), to calculate instantaneous metrics related to heart rate variability (HRV), including the instantaneous centre frequency (ICF). The aim was to compare the HRV metrics of HUT-negative patients with those from patients who tested positive for vasovagal syndrome - diagnosed when syncope or presyncope occurred from several minutes to an hour after tilt. It was found that the ICF, coupled with observation of heart rate trend, can be used to predict which patients will experience a positive test, and hence shorten testing time for some HUT patients.

I. INTRODUCTION

Syncope is the sudden loss of consciousness resulting from a temporary impairment of cerebral blood flow. Although recovery is always rapid, syncopal attacks are accompanied by a loss of postural tone, and hence present a danger. They account for up to 3% of emergency room visits [1], and patients with recurrent syncope endure a quality of life comparable to sufferers of rheumatoid arthritis or chronic lower back pain. [2]

The most common cause of syncope is vasovagal syndrome, characterised by fainting some minutes (seldomly more than an hour) after standing. The patient population is heterogeneous - i.e., it is believed that more than one cause of vasovagal syncope exists. Unfortunately, details of all of the most plausible mechanisms have yet to be decided upon, so they remain vague. Research is underway worldwide to learn more about vasovagal syncope's pathophysiology. [3]

Head-upright tilt table testing (HUT) is a popular protocol for the reproduction of symptoms in patients with vasovagal syncope. However, the test can be lengthy, rarely lasting less than 45 minutes; for this reason, in Oxfordshire fewer than 10% of patients who should be tested are actually referred. In this study, cardiovascular data from patients undergoing HUT was gathered using the Software Monitor Project (SMP), a patient-monitoring device described elsewhere. [4] One of the aims of the present work was to find a method to shorten the test for tilt-negative patients, by classifying patients based on their cardiovascular response to tilt.

The methodology relied on the use of parameters related to instantaneous heart rate variability (HRV), the tendency of pulse rate to vary over seconds and minutes. To this end, "tachograms" - plots of beat-to-beat intervals *vs* time - were employed, to analyse heart rate and spectral power. This included the instantaneous centre frequency (ICF), i.e., the frequency of the first moment of area of the instantaneous spectrogram at a given time.

II. METHODS AND MATERIALS

A. HEAD-UPRIGHT TILT-TABLE TESTING

The SMP measured the following signals in 70 patients referred to a Falls Clinic in Oxford for unexplained falls:

- ECG (electrocardiogram) using three chest leads
- Blood pressure (continuous, using a Finapres device (Ohmeda Medical) on the finger; and intermittent, using an oscillometric cuff on the contralateral arm)
- Respiration rate, using impedance pneumography
- Oxygen saturation at four points along the arm, using pulse oximeters (Nellcor)
- Cerebral performance, using a NIRO-300 device on the forehead (Hamamatsu).

Patients lay supine for at least ten minutes of baseline recording, before being tilted head-up to about 70 degrees from horizontal. The test was terminated when:

- The patient lost consciousness (syncope occurred),
- The patient felt syncope to be imminent ("presyncope" occurred), or
- The presiding doctor felt confident (usually 30-60 minutes into tilt) that vasovagal syndrome could be ruled out as a diagnosis.

B. DATA PROCESSING

Data analysis is limited here to the ECG, in which the following processing occurred. The raw ECG was filtered and heart beats were detected using an algorithm inspired by Pan and Tompkins [5,6]. The data was further processed using the timing of signals – as opposed to their amplitude – to remove artefacts (e.g. rapid successions of beats) and to insert beats that were missed in peak detection due to their low amplitude or noise masking. Next, cubic spline interpolation converted the unevenly sampled beat-to-beat intervals to a 3-Hz instantaneous heart rate signal. Finally, regions of sudden heart change were marked as specious, to be excluded from analysis.

Time-frequency analysis of the resulting tachogram was facilitated using the Smoothed Pseudo-Wigner Ville Distribution (SPWVD), a popular transform in biosignal analysis:

$$\mathrm{W}\,(\mathrm{n,m}) = \tfrac{1}{2}\,\mathrm{N} \sum_{\mathrm{k}\,=\,\text{-N}+1}^{N+1} |\,\mathrm{h}(k)|^2 \sum_{\mathrm{p}\,=\,\text{-M}\,+1}^{\text{M-1}} \mathrm{g}\,(p)$$

Methods for choosing the two windows g(p) and h(k) have been suggested in the literature [7] but usually involve visual inspection and intuition. The author chose Hamming windows, and a novel optimisation procedure, based on minimising HRV error for a carefully constructed artificial tachogram, selected window sizes of 45 and 57, respectively. The optimised SPWVD was then validated by comparing 5-minute-averaged HRV, using the LF/HF ratio, to the values obtained with the Lomb periodogram, on artificial tacho-grams and two normal subjects' tachograms. The validated SPWVD was finally applied to all of the patients' tachograms to determine the ICF in the first five minutes after the start of tilt. Since tilting took up to 20 s and was often followed by adjustments to the patient, the first minute of the 5 was excluded from analysis.

Heart rate trend was calculated using linear regression of the pulse rate over the same time period as ICF. Statistical comparisons within the heart rate and ICF data were accomplished using the Mann-Whitney U test and the Student's t test, respectively.

III. RESULTS

Twenty-eight patients were excluded from the present study, owing to noisy data or uncertain diagnoses. Of the remaining 42 patients (mean age 72, range 21-90), 30 were diagnosed as negative and 12 as positive for vasovagal syndrome.

The heart rate of all patients increased upon tilting. However, in most non-vasovagal patients, the heart rate thereafter remained steady or continued to climb in the few minutes after tilt, whereas in most vasovagal patients, it fell slightly. (See Table I.) Also shown in Table I is the standard deviation of ICF during the test; this was higher in vasovagal patients than in the tilt-negative patients.

IV. DISCUSSION

The finding that ICF variance was higher in vasovagal patients may be linked to the concept that these patients suffer from weak autonomic nervous systems. Although healthy haemodynamics is characterised by some degree of variability in cardiovascular state, it might be the case that too much variance in ICF represents a lack of control. If a patient is prone to vasovagal syncope, it is conceivable that his or her nervous system struggles to find the "right" ICF for homeostasis. Further studies are required to test this hypothesis.

The finding that vasovagal patients' heart rate fell after the initial post-tilt rise could be indicative of one of two things: it is possible that the heart rate in these patients rose too much upon tilt, and some adjustment was necessary thereafter; alternatively, it may be hypothesised that a fast pulse could not be maintained in these patients, and hence some degree of slowing was required.

TABLE I
DIFFERENTIATING PATIENTS USING HEART RATE AND ICF

Value	Non-vasovagal patients	Vasovagal patients
δ : Heart rate trend over 4 minutes, 1 min after tilt	+0.65 beats/s/min (*)	-1.25 beats/s/min
σ : ICF standard deviation in the same time period	6.4×10^{-3} Hz (*)	8.6×10^{-3} Hz

* - $p < 0.05$, compared with vasovagal patients

Finally, based on the performance of ICF and heart rate, a very simple patient classifier could be established:

$$P = a\,\sigma \,-\, \delta\,,$$

where σ was the standard deviation of ICF in Hz, δ was the trend in heart rate in beats per second per minute, *a* was a coefficient to dictate merely the relative effect of the two parameters, and *P* was the result to be compared with an appropriate threshold, classifying patients as vasovagal or not. The Receiver-Operating Characteristics (ROC) of this classifier were examined for various a, and it was found that a = 250 produced the most accurate classifications. A monoexponential function was fitted to the ROC curve, and this function had an area of 0.90. This is an encouraging finding, being close to unity. Indeed the true positive rate and true negative rate of HUT are themselves comparably less than unity. [8] The integration of the SMP's other parameters in novel ways is the subject of future work which will hopefully increase classification accuracy.

V. CONCLUSION

The present study demonstrated the usefulness of the SPWVD in the time-frequency analysis of tachograms from patients prone to fainting. A steady or increasing heart rate during the few minutes following the initial post-tilt rise, coupled with a low variance in a patient's ICF, could be used to terminate a tilt test earlier than normal. This could save the physician time and possibly enable a greater number of patients to undergo HUT.

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