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Prediction of Ventricular Fibrillation based on the ST-segment deviation: Allometric Model

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Abstract— **Based on some reported clinical data, we attempt to apply the allometric law for evaluating the probability of ventricular fibrillation when electrocardiographic ST-segment deviations are determined. The deviation is measured in millimeters at the standard calibration of 1mV = 10mm and the probability in percent. Using the equation $VF_P = \delta + \beta\,(ST)$ in log-log representation, the fitting procedure produced the following overall coefficients: Average β = 1.11, with a maximum = 1.65 and a minimum = 0.78; Average δ = 0.83, with a maximum = 1.39 and a minimum = 0.41. For a 2mm ST-deviation, the full range of predicted ventricular fibrillation probability extended from about 6% at 1 month up to 47% at 4 years after the original cardiac event. These results, at least preliminarily, appear acceptable and still call for full clinical test. The model seems promising if other parameters were taken into account, such as cardiac enzyme concentration, ischemic or infarcted epicardial areas or ejection fraction. It is concluded, considering these results and a few references found in the literature, that the allometric model shows promising features in cardiology.**

I. Introduction

VENTRICULAR fibrillation (VF) is intrinsically a probabilistic event that can be biased under certain pathophysiological and daily life situations. Physicians, in their practice, try to predict as close as possible how high such probability is, since most of cardiac deaths are due to this lethal arrhythmia. Empirical tests, as possible quantitative criteria to screen out patients of high risk (that is, searching for a better answer to the question shall we confine the patient to the coronary unit?) have been attempted with moderate success, but always the degree of uncertainty is rather large. In such endeavor, we might try an appealing and old universal scaling, the allometric law, although in principle not directly related to the fibrillation-defibrillation overall phenomenon, it might find a place in it and at least deserves to be recalled bringing about first a nice and well carried out paper by Noujaim *et al.*, in 2004 [1]. In it, it is recalled that from mouse to whale, the PR interval increases 10^1 times whereas body mass (B_M) augments 10^6. Scaling of many biological processes can be described by the allometric equation $Y = a(B_M)^b$ where Y is the biological process and a and b are scaling constants, with b smaller than 1. These authors assumed that the heart behaves as a set of "fractal-like" networks tending to minimize propagation time across the conducting system while ensuring a hemodynamically optimal atrioventricular activation sequence. With the potential relationship given above and, subsequently, based on previously published values of PR interval, heart rate, and body masses of 541 mammals, they reported as best fit the equation $PR = 53(B_M)^{0.24}$.

Inspired in the latter report, the following question seems pertinent: Would a relationship similar to the allometric equation be conceivable, say, between the probability of fibrillation and heart weight, or perhaps other parameter somehow related to the latter, as for example, the number of cardiac diseased fibers or the ST-electrocardiographic deviation? The objective of this communication tries to find an answer to such question.

II. Materials and Methods

A. Theoretical background

Allometry, in general biology, measures the relative growth of a part in relation to the whole living organism. The term was first used by Snell in 1891 [2] to express the mass of a mammal's brain as a function of the body mass. The growth velocity of a component *'y'* is related to the growth velocity of another component (or the whole organism) *'x'* in a constant way. This was clearly described by von Bertalanffy in 1957 [3]. Thus, the relative rate of change of a given event *'y'* is proportional to the relative rate of change of body mass or body weight *'x'*, i.e.,

$$\frac{dy/dt}{y} = B\frac{dx/dt}{x} \qquad (1)$$

After integration and some easy algebraic manipulation, equation (1) becomes $\ln y = A + B\ln x$, or

$$y = Ax^B \qquad (2)$$

Originally, *'y'* was the weight of an organ (heart, stomach, other) and *'x'* was body weight or mass. The parameters A and B require numerical estimation by an appropriate procedure usually using empirical information. By the same token, let us say that the probability of fibrillation (P_F)

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follows a relationship with the number of ventricular diseased fibers (N_{DF}) formally equal to (2), i.d.,

$$P_F = \alpha(N_{DF})^{\beta} \quad (3)$$

Hence, *'y'* in equation (2) is replaced by P_F in (3), and N_{DF} in the latter takes the place of *'x'* in the former. After all, the number of diseased cardiac fibers (ischemic or infarcted or both) are part of the cardiac mass. Besides, since the electrocardiographic ST-segment deviation (Δ_{ST}) is a traditional estimator of cardiac injury, it sounds sensible to state that,

$$N_{DF} = \gamma\Delta_{ST} \quad (4)$$

or in words, the number of diseased ventricular fibers is proportional to the ST-deviation (Δ indicating precisely "deviation"). Hence,

$$P_F = \alpha(\gamma\Delta_{ST})^{\beta} \quad (5)$$

After taking logarithms of both sides, the latter equation becomes $\ln P_F = (\ln\alpha + \beta\ln\gamma) + \beta(\ln\Delta_{ST})$, which can be reduced to

$$VF_P = \delta + \beta(ST) \quad (6)$$

We define VF_P as ventricular fibrillation probability, where $\delta = \ln\alpha + \beta\ln\gamma$, $ST = \ln\Delta_{ST}$ and $VF_P = \ln P_F$. The straight line, equation (6), in log-log paper with the parameters β and δ would represent the probability of fibrillation as function of the ECG ST-depression or elevation. However, keep in mind that ST is a logarithm, meaning that an actual zero deviation (that is, the normal situation) is not logarithmically defined and, as a consequence, equation (6) does not hold for Δ_{ST} values smaller than 1.

B. Numerical procedure

To calculate the two constants δ and β of equation (6) and later on apply the mathematical expression for predictive purposes, the probability of the data having occurred can be estimated by, (a) simply assuming an arbitrary and theoretical set of coupled pairs of numbers, or (b) using a particular hypothesis, say, based on clinical data.

Let us explain both approaches:

(a) Assuming a quadratic law of the type $w = K z^2$, that is, the VF_P is accepted as being proportional to the square of the *ST*. If that deviation is measured in millimeters (with the standard calibration of 1mV = 10mm), the curve shown in Figure 1 can be easily graphed. Such curve can be taken as a reference where, for example, an ST-deviation of 2mm would predict a 4% of VF_P.

(b) Clinical data, criteria and procedure.

Medical experience is obviously the best and reliable source of information where from an idea of the probability of fibrillation based on ECG evidence can supply an excellent lead. For that matter, three sets (*i*, *ii* and *iii*) were used to fit the allometric equation, two from Hyde *et al*. [4] and another from Kaul *et al.* [5], as follows:

(*i*) In the first one, 642 patients had been admitted to coronary care unit with prolonged chest pain. Due to the exclusion criteria applied by these authors, 469 were removed leaving a net number of 173 for their study. Besides, they reported survival rates at 1 and 4 years after the first admission.

(*ii*) In the second paper (PARAGON-A trial), out of 2,282 patients with chest discomfort within the previous 12 hours, there was a screen out of 694 due to either missing or not clear enough records leaving a net of 1,588 cases. They were evaluated at 1 month, 6 months and 1 year.

(*iii*) Besides, the latter authors had 8,001 patients (GUSTO-IIb trial) comparing hirudin and heparin therapy when unstable angina or acute myocardial infarction was present without ST-segment. Out of this total, only 6,301 were evaluated at 1 month, 6 months and 1 year, i.e., 1,700 were removed.

In Hyde *et al.* [4], patients with ≥ 0.5mm ST-segment depression were classified as "true depression". This deviation was subclassified as 0.5mm, 1mm or ≥ 2mm. The ST-segment criteria in Kaul *et al.* [5], instead, rounded out the depression of 0.5 mm to 1mm, of 1.5mm to 2mm, and so on, which is a traditional arithmetic rule of thumb. These authors distinguished three groups: No ST-segment depression, 1mm ST-segment depression in two contiguous leads, and ST-segment depression of 2mm in two contiguous leads. Curves presented herein were constructed after the numerical values given in [4][5], including the arbitrary theoretical set (a) that may be used tentatively as reference (Figure 1). All were adjusted to a linear quadratic equation of the type $y = ax^2 + bx + c$ while simultaneously resampling them in steps of 0.025mm to improve the resolution. Thereafter, a log-log algorithm was applied to the ventricular fibrillation probability *versus* the ST-segment deviation (see equation 6). The parameters β and δ were computed by linear regression. All quadratic fits used values within the 0-2mm range, however, the logarithmic transformation, because of its very nature, forced to leave out the 0-1mm interval retaining only the 1-2mm deviations.

III. RESULTS

Figure 2 displays all 8 curves, where there are three clearly distinguishable groups: The lower one corresponds to 1 month after confinement, as reported by the PARAGON-A study (open circles) and by the GUSTO-IIb data (dark circles), both in the same paper [5]. For 1.5mm shift, the predicted probability is slightly below 5%. The middle group refers to the same above-mentioned studies but after 6 months (dark triangle, GUSTO-IIb; open triangle, PARAGON-A) and 12 months (dark squares, GUSTO-IIb; open squares, PARAGON-A). For the same shift selected above, the probability values predict 11% or somewhat below it down to about 8%. Finally, the upper two curves describe the behavior at 1 (slanted crosses) and 4 years (vertical crosses) after the event, according to Hyde *et al.* [4]. For the same previous deviation, the foreseen probability range goes from 25 to about 36%. The fitted adjustments pass essentially through the depicted points those curves

were not shown because the graph would have become too confused (see Table 1).

In Figure 3, instead, we collect the results after averaging out PARAGON's and GUSTO's data, as reported by Kaul *et al.* [5], respectively, at 1, 6 and 12 months, from bottom to top, showing also the standard deviation for each data point. Notice the spread increase in the bottom curve as opposed to the practically zero dispersion in the two upper sets as the ST-deviaton augments.

TABLE I
COEFFICIENTS β AND δ, IN EQUATION (6), FOR ALL 12 CURVES AND THE THEORETICAL ONE

	months	β	δ
Theoretic (corresponding to Fig. 1)	-	2	3.10^{-5}
PARAGON-A (Kaul *et al.*) (corresponding to Fig. 2)	1 6 12	1.18 0.96 0.78	0.44 0.79 0.89
GUSTO-IIB (Kaul *et al.*) (corresponding to Fig. 2)	1 6 12	1.65 1.13 1.05	0.41 0.73 0.82
Mean PARAGON-A and GUSTO II-B (Kaul *et al.*) (corresponding to Fig. 3)	1 6 12	1.43 1.04 0.91	0.42 0.76 0.86
Hyde *at al.* (corresponding to Fig. 2)	12 48	1.24 0.91	1.17 1.39
Average curve (corresponding to Fig. 4)	-	1.11	0.83

Figure 4 is an attempt to reach a single equation for all the data presented in Figure 2. For that matter, an average value curve is depicted along with its Standard Error of the Mean (SEM). Dispersion here covers the full time range, i.e., from 1 month to 4 years.

Table 1 summarizes the numerical values for the two parameters characterizing equation (6).

IV. DISCUSSION

This preliminary report has developed an allometric equation simply based on the electrocardiographic ST-segment deviation. The calculated coefficients permit predictions at different times after the first cardiac episode or, with a much wider spread, as an overall quantitative evaluation applying the relationship given in Figure 4. Obviously, the model must be tested in the clinical environment to better assess its accuracy and predictive power. In Figure 3, dispersion increases at 1 month after the cardiac episode, which might be interpreted as the patient still traversing a period of dangerous instability. Conversely, the upper two curves, after a longer time, show a marked spread decrease to essentially zero. We read this fact as a stable condition because of compensation. An interesting numerical observation calls our attention: Hyde *et al.* [4] report values approximately twice as big as those given by Kaul *et al.* [5], both at one year after. Is it a chance phenomenon or is it due to some constant factor introduced by the used methodology?

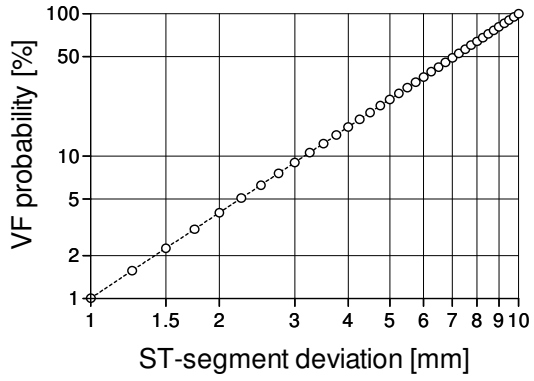

Fig. 1. Theoretical curve

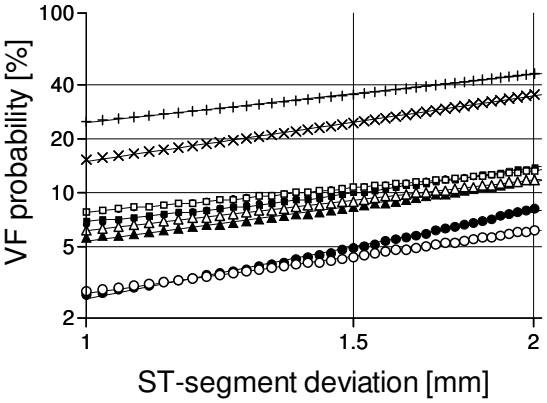

Fig. 2. All 8 curves drawn after data from references [4] and [5], at 1, 6, 12 and 48 months (see text for details). For a 2mm ST-deviation, the full range of predicted VF probability extends from about 6% at 1 month up to 47% at 48 months after the original cardiac event. 1 month: PARAGON-A (open circles) and GUSTO-IIb (dark circles). 6 months: GUSTO-IIb (dark triangles) and PARAGON-A (open triangles). 12 months: PARAGON-A (open squares) and GUSTO-IIb (dark squares). Hyde: 1 year (slanted crosses) and 4 years (vertical crosses).

Besides, the arbitrary reference curve seems to offer a minimum expectation for any given ST-shift. Thus, it should be well taken.

This model uses only the ST-segment as criterion, which obviously leaves out other possible parameters, such as myocardial enzymes (CPK, for example), quantitatively obtainable by blood sample analysis, or ischemic or infarcted epicardial surface, obtainable by an appropriate imaging procedure, or ejection fraction as evaluated by echocardiography. Any of these criteria would lead to allometric equations as the one herein reported. One

tempting and difficult approach would try to combine all the mentioned parameters in a single mathematical model.

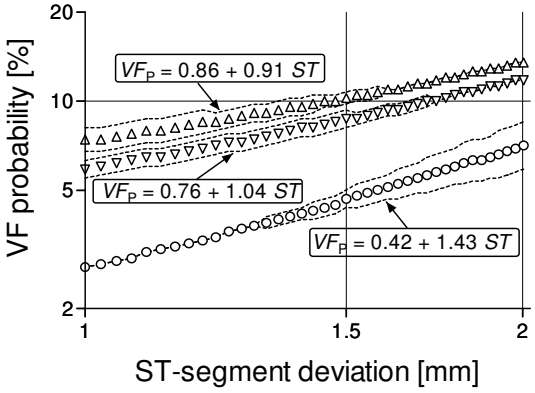

Fig. 3. Average results, obtained from mean PARAGON-A and GUSTO-IIB, at 1 (open circles), 6 (inverted open triangles) and 12 (open triangles) months. The standard deviation increases in the short term (lower curve) but decreases to essentially zero in the longer term (two upper sets).

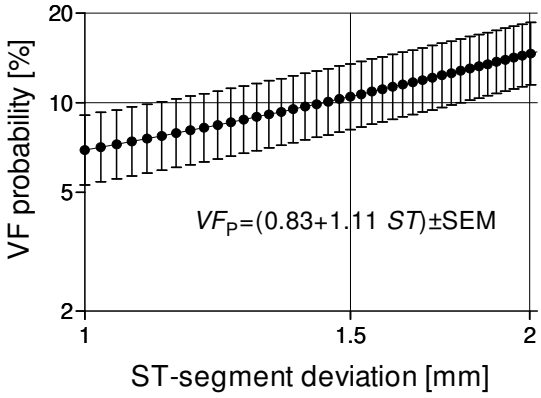

Fig. 4. Overall average curve covering all the reported data of the above-mentioned literature. The upper and lower dashed lines bound the SEM so giving an idea of the possible error in the prediction. Say, for 1.5mm ST-segment shift, the VF probability would go from 8% to 13.5%.

The allometric statement seems to maintain interest, especially in general mammalian biology [7] and the results reported here would indicate an attractive line of research with their consequent clinical tests. The results herein presented foresees a direct application in the clinical environment to better predict the evaluation of a cardiac patient. However, this kind of validation remains to be carried out.

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