Decrease/Disappearance of Pacemaker Stimulus “Spikes” Due to Anasarca: Further Proof that the Mechanism of Attenuation of ECG Voltage with Anasarca Is Extracardiac in Origin

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Background: Recent work showed that AN leads to a decrement of the potentials of QRS complexes. Although the mechanism has been thought to be extracardiac in origin, and due to a decrease of the electrical impedance of the volume conductor from water overload, more proof on this will be welcome. It is hypothesized that the pacemaker “spikes” (PS) are independent of heart depolarization, and thus their change at the body surface with AN would be reflective of extracardiac influences. This study was designed to explore the impact of anasarca (AN) on the amplitude of PSs, and to further delineate the mechanism of ECG attenuation with AN.

Methods: The sum of PS measurements in millimeters in the 6 limb leads (ΣPS_6), and 12 ECG leads (ΣPS_{12}), and the sum of QRS complexes in the 6 limb leads (ΣQRS_6), and 12 ECG leads (ΣQRS_{12}) were computed in six patients fitted with a pacemaker (3 with AN and 3 “controls”), and these variables were correlated with weight change.

Results: Correlation of percentage change in weight and ΣPS_{12} was excellent ($r = -0.88$, $P = 0.02$), but not for ΣPS_6 ($r = -0.73$, $P = 0.1$). Also, the percentage weight correlated well with ΣQRS_6 ($r = -0.82$, $P = 0.046$), but not ΣQRS_{12} ($r = -0.61$, $P = 0.2$). Correlation of percentage change in ΣQRS_6 and ΣPS_6 was excellent ($r = 0.91$, $P = 0.01$), but not the percentage change in ΣQRS_{12} and ΣPS_{12} ($r = 0.72$, $P = 0.11$).

Conclusions: PSs undergo amplitude attenuation in patients developing AN, similar to the one noted in the QRS complexes. Since these changes are independent of the cardiac activation, and are similar in extent to those impacting the QRS complexes, the attenuation of the voltage of the entire ECG curve in AN appears to be extracardiac in origin.

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Anasarca peripheral edema (AN) leads to a decrease in the amplitude of the ECG QRS complexes; such change occurs gradually as the patients gain weight, and partial reconstitution of the QRS amplitude is noted in patients who subsequently lose some of the weight they had gained.¹ Attenuation of the QRS complexes is independent of the QRS morphologies, and thus it was noted in all 28 patients with AN (17 with normal intraventricular conduction, 3 with complete left bundle branch block, 1 with incomplete left bundle branch block, 2 with right bundle branch block, 2 with intraventricular conduction delay, and 3 with left bun-

dle branch block-like pattern due to right intracardiac pacemaking). Due to space limitations, these details were not included in the original article.¹ Intuitively, the variety of intraventricular ECG patterns and their uniform behavior during AN suggests that a mechanism unrelated to cardiac activation must be at play for QRS attenuation. Correlation of the percentage reduction in the QRS complexes and the percentage increase in weight from admission to the point of peak weight was good ($r = 0.61$, $P = 0.0005$), and this change in the amplitude of the QRS complexes was attributed to extracardiac mechanisms (alterations in the body volume

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conductor electrical properties, resulting from its increase in the water content with AN).¹ Mechanistically, this attribution also was supported by the stability of the amplitude of intracardiac electrograms in patients with changes in their edematous states, while the voltage of the corresponding surface ECGs changed drastically; this suggested that the change was not due to alterations of the heart *per se*, but of the conducting medium interspersed between it and the body surface.¹

The pacemaker stimulus artifacts or pacemaker "blips" or "spikes" (PS) are stable deflections of fixed amplitude and polarity in each of the 12 ECG leads in repeat tracings of an individual patient, barring change in the pulse generator's energy output, position of the pacing lead, or thoracic landmarks of recording V1-V6 leads.²⁻⁵ It was hypothesized that since PS precedes the QRS complex formation, it can be considered an independent parameter whose change in the surface ECG could be attributed to influences unrelated to the heart's activation. Accordingly, a change in the extracardiac conducting medium enveloping the heart would be expected to alter the PS's potential. Thus this study was set up to evaluate the change in the amplitude of PSs in patients with AN, and to correlate it with the corresponding voltage alteration in the QRS complexes, as the patients developed fluid overload.

METHODS

Study Patients

From 28 patients with AN and the corresponding 28 "controls," who had a cardiovascular illness but did not gain weight during hospitalization,¹ six were fit with a temporary (TPM) or permanent pacemaker (PPM) (3 in each patient subgroup), and they constitute the study group.

Measurements and Variables

Data used in this study were suitable ECGs as early and as late as possible in the clinical course of these patients, and corresponding weights. Since TPM and PPM in these patients were functioning on the "demand" mode, paced activity was not present in all ECG leads, or all tracings of these

six patients who had at least 1 ECG recorded daily, and daily measurement of their weight. No changes in the pulse generators' output or position in the pacing leads of the TPM were made during the patients' hospitalization. Since chest wall marking was not used for the recording of precordial ECGs, data from both the entire ECG, and only the 6 limb leads, were analyzed to adjust for inherent variation in repeat ECGs recorded without such marking. The PS and QRS in each lead were measured in complexes with a stable baseline, and in portions of the tracing showing at least two adjacent complexes with similar measurements. PSs of PPMs were much larger than the ones of TPMs; however, occasionally for both systems no PS was inscribed in a particular lead, a normal phenomenon based on the vectorial relationship of the PS and lead axes.²⁻⁵ Only paced beats were analyzed; PS not followed by QRS complexes (noncapture) were not considered. Also, fusion beats, pseudofusion beats, or paced beats with the PS superimposed on a P-wave, a T-wave, or ST-segment of a preceding beat, were excluded; the reason for the latter was that the deflection (positive or negative) of a superimposed wave alters the amplitude of the PS by simple algebraic addition of the two signals. The "overshoot" of the pacemaker stimulus was not considered in the measurement, since it was not present always, or consecutive paced beats bore "overshoot" signals only in some of the beats. Measurements of PS (baseline to peak, positive, or negative) and QRS (zenith to nadir) to the nearest 0.5 mm were made using calipers and a magnifying glass under strong overhead light. The intraobserver variability of measurements of Σ QRS in 10 randomly used ECGs was $0.41 \pm 3.34\%$ in a previous study.¹ The sums of the PSs from the 6 limb leads (Σ PS6), 12 ECG leads (Σ PS12), and the corresponding sums of QRSs from the 6 limb leads (Σ QRS6) and the 12 ECG leads (Σ QRS12) were calculated. Calibration of the ECG recordings was 10 mm = 1.0 mV, and the paper ECG speed was 25 mm/s. No changes in the filters of the ECG recorders (HP, now Philips M1700A PageWriter model) were made during the study.⁶ Although the number of patients was small, a correlation analysis was attempted, taking all six patients together, and including as variables the percentage change in weight, Σ PS6, Σ PS12, Σ QRS6, and Σ QRS12. All statistical operations were 2-tailed,⁷ the SPSS/PC+ 4.0.1 statistical package was used,⁸ and $P < 0.05$ was taken as statistically significant.

RESULTS

Patients

Patient 1

This was patient 14 of the original article,¹ an 82-year-old man with a past history of myocardial infarction; he was admitted with pneumonia, bradycardia, and junctional rhythm and received a TPM, which provided stimulation intermittently, since the patient was off and on tachycardic. Between April 24, 1999 and April 30, 1999 he gained 16.0 lbs, 13.7% of his weight. Figure 1 reveals that the Σ PS12 was decreased by 26.2%, while the corresponding Σ QRS12 dropped by 35.8%. The drop of Σ PS6 was 66.7% and of the corresponding Σ QRS6 was 55.9%. In this case the drop of the amplitudes of the PS noted in the limb leads was not matched by the corresponding drop in the precordial leads, most probably due to variation in the precordial lead placement.

Patient 2

This was patient 16 of the original article,¹ a 97-year-old woman with a past history of myocardial infarction; she developed sepsis had right bundle branch block, left posterior hemiblock intermittent complete heart block, junctional rhythm, for which she received a TPM, which provided stimulation intermittently, since the patient was off and on tachycardic. Between May 20, 1999 and June 6 1999 she gained 24.6 lbs, 15.9% of her weight. Figure 2 reveals that the Σ PS12 was decreased by 55.7% while the corresponding Σ QRS12 dropped by 37.5%. The drop of Σ PS6 was 38.3% and the corresponding Σ QRS6 drop was 38.2%.

Patient 3

This was patient 22 of the original article,¹ an 85-year-old man with a past history of hypertension, diabetes mellitus, and a PPM (DDDR) implantation,

Figure 1. Changes in weight, Σ RS12, Σ P12, 12-lead ECGs (A, B), and enlarged leads I, II, and III (C, D) between the indicated dates. Note the attenuated amplitude of PSs (C, D) at the point of increased weight. Calibration signals are noted on ECGs A, and B. Abbreviations as in the text.

Figure 2. Changes in weight, $\Sigma RS12$, $\Sigma P12$, 12-lead ECGs (A, B), and enlarged leads I, II, and III (C, D) between the indicated dates. Note the attenuated amplitude of PSs (C, D) at the point of increased weight. Calibration signals are noted on ECGs A, and B. Abbreviations as in the text.

who was admitted with sepsis. He showed mostly normal sinus rhythm, sinus tachycardia, and atrial fibrillation, overdriving his PPM most of the time with rare exceptions when a few of his ECG leads showed some paced QRS complexes in the midst of intrinsic beats. Atrial PSs, noted only rarely could not be studied, since they were not present in the ECGs chosen for analysis. Between September 25, 1999 and October 2, 1999 he gained 12.6 lbs, 9.0% of his weight. Figure 3 reveals that the $\Sigma PS12$ was decreased by 28.8% whereas the corresponding $\Sigma QRS12$ dropped by 35.0%. The drop of $\Sigma PS6$ was 22.4% and the corresponding $\Sigma QRS6$ drop was 35.9%. In this patient data from leads V1–V3 were not available. Also, the lower drop of $\Sigma PS6$ noted is due to its underestimation since at baseline the PSs in leads III and aVF were truncated (Fig. 3).

“Controls”

Patient 4

This was “control” patient 1 of the original article,¹ a 62-year-old man admitted for a battery change of his PPM. During hospitalization he had an increase of 1.7% of his weight. Over the course of 11 days the $\Sigma PS12$ and $\Sigma QRS12$ of his ECGs were not appreciably changed. Due to an intermittent function of his PPM only some of the 12 ECG leads (the same for both ECGs) were available for the calculation of the above variables (Fig. 4); also, a truncated portion of the PSs could not be accounted for. Nevertheless, the stability of the $\Sigma PS12$ and $\Sigma QRS12$ over a course of 11 days is apparent. $\Sigma PS12$ decreased by 9.4%, and $\Sigma QRS12$ increased by 5.8%. $\Sigma PS6$ decreased by 17% and the $\Sigma QRS6$ increased by 1.4%.

Figure 3. Changes in weight, $\Sigma QRS12$, $\Sigma PS12$, and enlarged 12-lead ECGs corresponding to the indicated dates. Note the attenuated amplitude of PSs (left vs right panel ECGs). Calibration signals are noted in conjunction with leads V4–V6. Abbreviations as in the text.

Patient 5

This was “control” patient 14 of the original article,¹ a 59-year-old man admitted with syncope, bradycardia, and a third-degree AV block. A TPM was inserted. During hospitalization he had a decrease of 6.2% of his weight. Over the course of 5 days the $\Sigma PS12$ increased by 1.2%, and the $\Sigma QRS12$ decreased by 24.1% (Fig. 5). However, major changes in the QRS amplitude of the precordial leads suggested significant variation in the sites of chest lead placement. This was corroborated by the $\Sigma PS6$ and $\Sigma QRS6$, which decreased by 13.0% and 6.3%, respectively.

Patient 6

This was “control” patient 28 of the original article,¹ a 72-year-old man admitted with syncope, atrial fibrillation, and bradycardia, and a third-degree AV block. A TPM was inserted. During

hospitalization he had an increase of 1.1% of his weight. Over the course of 2 days the $\Sigma PM12$ increased by 7.0%, and the $\Sigma QRS12$ increased by 1.9% (Fig. 6). $\Sigma PM6$ increased by 9.1% and $\Sigma QRS6$ increased by 11.6%.

Correlation of the percentage change in weight and $\Sigma PS12$ during the observation period of all six patients was excellent ($r = -0.88$, $P = 0.02$), but not for $\Sigma PS6$ ($r = -0.73$, $P = 0.1$). Also, weight correlated well with $\Sigma QRS6$ ($r = -0.82$, $P = 0.046$), but not with $\Sigma QRS12$ ($r = -0.61$, $P = 0.2$). Finally, while the correlation of $\Sigma PS6$ with $\Sigma QRS6$ was excellent ($r = 0.91$, $P = 0.01$), it was poor for $\Sigma PS12$ and $\Sigma QRS12$ ($r = 0.72$, $P = 0.11$).

DISCUSSION

This study showed that AN led to the attenuation of PSs, comparable to the one noted in the corresponding QRS complexes, and that both these variables correlated well with the weights of the

Figure 4. Changes in weight, Σ RS12, Σ P12, and enlarged 12-lead ECGs corresponding to the indicated dates. Note the stability of PSs (left vs right panel ECGs) in this patient without change in weight. Abbreviations as in the text.

patients; moreover, the good correlation of PSs and QRSs provided further support that changes in the amplitude of these two parameters must be due to the same kind of influences. PS, independent of the ventricular activation parameter, showed reduction of amplitude with the ensuing fluid overload, the explanation of which should be sought in extracardiac mechanisms. That PS is independent of the ensuing atrial or ventricular depolarization can be supported by the facts that PSs precede such activations and the amplitude of PSs is identical in paced beats and on occasions of failure to capture, or when the PSs occur during the refractory period of these two chambers. Consequently, changes of PSs must be related to alterations in the body volume conductor, and a similar mechanism must be also responsible for the attenuation of the QRSs during AN, since these two ECG variables showed parallel and comparable changes. Although reference is made to extracardiac mechanisms influenc-

ing the change in PSs, one should still account for the influence of the right ventricular wall, since the pacemaker lead is inside this chamber. However, it is unlikely that the change in the PSs was due to alterations in the thin walled right ventricle, separating the pacing lead from the conductive medium surrounding the heart, alterations that would have been taking place during the process of fluid accumulation in the patients with AN. Some of the correlations in the analysis did not reach statistical significance; this could be due to the small number of patients analyzed, and the unavoidable lumping of the patients with AN and the “controls” who did not experience weight changes. Due to the above, it is more important to evaluate the six presented cases in qualitative or quasi-quantitative terms, instead of strictly quantitative/statistical ones, since the results of statistical analyses with such a small study cohort may reflect the presence of either type I or type II errors.^{7,8} This, of course, does not

Figure 5. Changes in weight, Σ RS12, Σ P12, and enlarged 12-lead ECGs corresponding to the indicated dates. Note the stability of PSs (left vs right panel ECGs) in this patient without change in weight. Abbreviations as in the text.

mitigate the importance of this study, since the changes noted in PSs were marked, were seen in association with similar changes in the corresponding QRS complexes (Figs. 1–3), and were absent in the patients who had a stable weight during the observation period (Figs. 4–6).

Scrutiny of the ECG tracings of paced patients and of the figures in published studies or in ECG textbooks reveals that atrial or ventricular PSs are reproducible in polarity and voltage, except when distorting influences are at play; also, they retain their stability regardless of whether they result in capture or not, suggesting that PSs are not influenced by the heart's subsequent activation, or the atrial and ventricular refractoriness.

Theoretical modeling and clinical work by Rudy et al. have established an important role for the altered geometry and composite impedance of the volume conductor on the recorded ECG signals at the body surface.^{9–11} This “operational” or “aggregate” impedance depends on the different resistiv-

ities of the composite tissues and organs (“inhomogeneities”) comprising the volume conductor.^{4,9–11} Water, a constituent with the lowest resistivity in the body,¹² which is in excess in both intracellular and extracellular spaces when AN develops, imparts a reduction in the composite impedance, thus leading to an attenuation of ECG signals at the surface of the body, according to Ohm's law. Such an extracardiac influence is expected to cause a decrease in the potential of the entire ECG curve, and thus in both PSs and QRSs, and this was observed in this study. In fact, even the P waves are influenced in this process, to the point that rarely they become undetectable, requiring intracardiac recordings for their identification.¹³

Although the main objective of the present study was to explore the thesis that PSs would show proportionally similar changes to QRSs in the process of AN development, and thus provide further support for the extracardiac origin

Figure 6. Changes in weight, ΣR_{S12} , ΣP_{12} , and enlarged 12-lead ECGs corresponding to the indicated dates. Note the stability of PSs (left vs right panel ECGs) in this patient without change in weight. Calibration signals are noted in conjunction with leads V4–V6. Abbreviations as in the text.

of the attenuating mechanism for both, some practical implications nevertheless emanate from these findings. These pertain to the understanding of the nature of QRS complexes of attenuated amplitude due to AN with regular or irregular rhythm, not preceded by PSs in patients with TPM and PPM and critical illnesses; such rhythms are often misdiagnosed by both cardiologists and automated interpretation algorithms as "junctional rhythm with an intraventricular conduction delay" or "rhythm cannot be determined." In reality, these represent paced activity with or without interspersed intrinsic complexes, and "invisible" PSs, a situation similar to the one just described with P waves.¹³

REFERENCES

- Madias JE, Bazaz R, Agarwal H, et al. Anasarca-mediated attenuation of the amplitude of ECG complexes: A description of a heretofore unrecognized phenomenon. *J Am Coll Cardiol* 2001;38:756–764.
- Wagner GS. *Marriott's Practical Electrocardiography*, 9th Edition. Baltimore, Williams & Wilkins, 1994, pp. 263, 265, 398, 407, 408.
- Goldberger A, Goldberger E. *Clinical electrocardiography. A Simplified Approach*, 5th Edition, St. Louis, Mosby, 1994, p. 239.
- Macfarlane PW, Vetch Lawrie TD. *Comprehensive Electrocardiology*. New York, Pergamon Press, 1989, pp. 1177.
- Boudreau Conover M. *Understanding Electrocardiography*, 7th Edition. St. Louis, Mosby, 1996, p. 492.
- Hewlett-Packard Interpretive Cardiograph. Physician's Guide. HP Part No. M1700–92908, Edition 4, Printed in USA September 1994, p. 7–12.
- Colton T. *Statistics in Medicine*, 1st Edition. Boston, Little, Brown and Company, 1974, pp. 120, 124, 131, 136, 163, 174, 189, 202.
- Norusis MJ. *The SPSS Guide to Data Analysis for PDD/PC+*, 2nd Edition, 1991, Chicago, IL, pp. 218, 230, 244, 311, 362, 374, 390.
- Rudy Y. The effects of the thoracic volume conductor (inhomogeneities) on the electrocardiogram. In Lieberman J, Plonsey R, Rudy Y (eds): *Pediatric and Fundamental Electrocardiography*. Dordrecht, Martinus Nijhoff Publishing, 1987, p. 49.
- Rudy Y, Plonsey R, Lieberman J. The effects of variations in conductivity and geometrical parameters on the electrocardiogram, using an eccentric spheres model. *Circ Res* 1979;44:104.

11. Rudy Y. The electrocardiogram and its relationship to excitation of the heart. In Sperelakis N (ed), *Physiology and Pathophysiology of the Heart*, 3rd Edition. Amsterdam, Kluwer Academic Publishers, 1995, p. 201.
12. Geddes LA, Baker LE. The specific resistance of biological material—A compendium of data for the biomedical engineer and physiologist. *Med Biol Engng* 1967;5:271–293.
13. Madias JE, Narayan V, Attari M. Detection of P waves via a “saline-filled central venous catheter electrocardiographic lead” in patients with low electrocardiographic voltage due to anasarca. *Am J Cardiol* 2003;91:910–914.