Special Article

Electrocardiographic Changes Resulting from Peripheral Edema: Theoretical Considerations and Clinical Implications

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The objective of this review article is to familiarize the readers of the Hellenic Journal of Cardiology with a recently described ECG syndrome, characterized by marked attenuation of the potentials of the standard ECG (AECGV), in association with the development of peripheral edema (PERE).[1] A relevant lecture on the topic was delivered in Athens, on November 20, 2004 at the XXV Annual Panhellenic Congress of Cardiology. However, the complexity and wide scope of contemporary meetings with the customary overlapping sessions prevented many of those attending from being exposed to this new development. The initial work,[1] published in 2001, drew attention mainly to the gradual reduction in the QRS potentials noted with fluid retention, and resultant weight gain (Figure 1). A quantitative assessment of the amplitude of QRS potentials from serial standard ECGs employed sums of the QRS complexes from zenith to nadir of all 12 leads (ΣQRS). The patients studied represented a wide range of pathology, including sepsis, pneumonia, exacerbation of chronic obstructive lung disease, congestive heart failure (CHF), acute renal failure, aschites, and other conditions requiring admission to a critical care environment.[1] Thus, it became clear from the outset that the specifics of the pathophysiology for the development of the PERE were not important for the emergence of the LVECG.[1] It should be pointed out that the PERE often reached the point of anasarca, involving all four extremities and the entire torso, particularly of its dorsal plane. The correlation between the changes in the amplitude of ECG potentials and the weight of the patients was good ($r=0.61$, $p=0.0005$). Some patients, who subsequently lost weight after attaining their peak weight, regained some of the lost amplitude of the QRS potentials,[1] and thus the inverse phenomenon (i.e. augmentation of the amplitude of QRS complexes, instead of attenuation) was also documented (Figure 1), further corroborating the dependence of the amplitude of the QRS complexes on the degree of fluid overload and its alleviation. More experience with the latter was also shown in subsequent reports of patients with PERE due to CHF, who showed a gradual increase in their ECG voltage with a gradual loss of weight resulting from diuretic therapy.[2,3] Another clinical implication of the above concept has been reported recently and concerns the masking of the ECG diagnosis of left ventricular hypertrophy (LVH) by PERE. In this scenario a patient is admitted to the hospital with a critical illness and with ECG evidence of LVH employing any of the es-

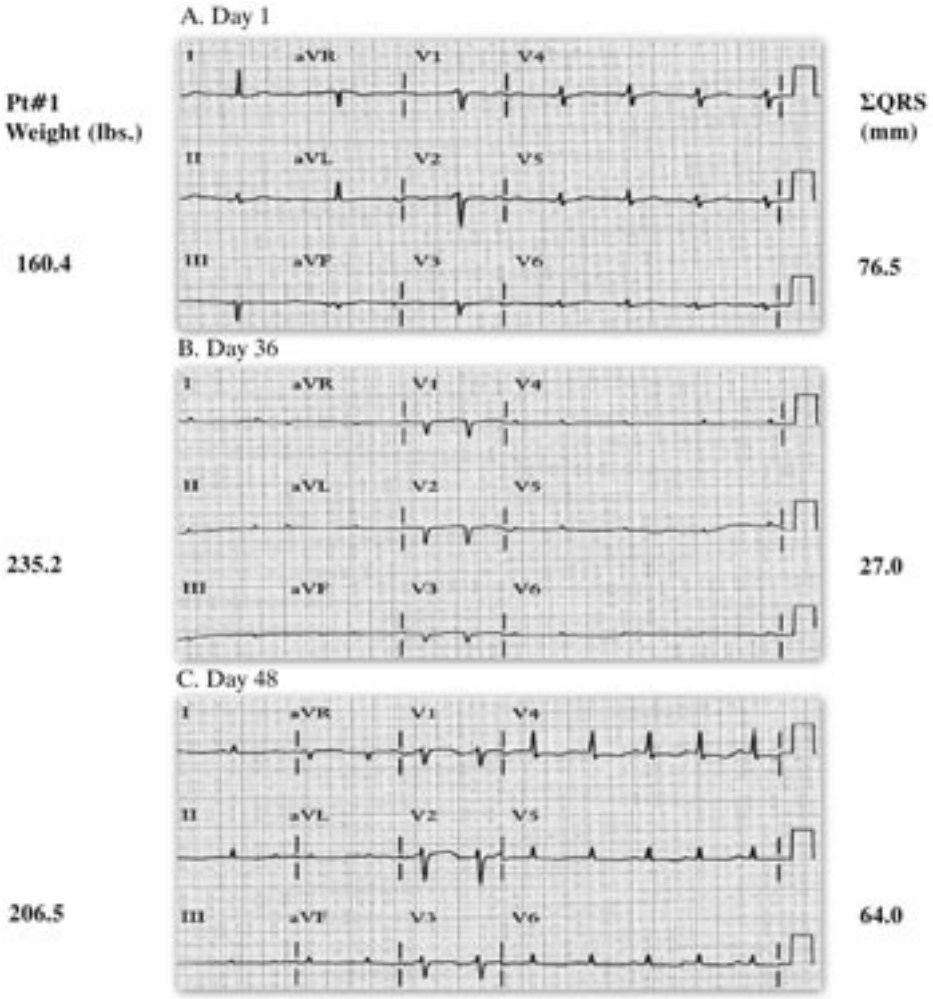

Figure 1. An 80-year-old woman with renal failure, hip fracture, gastrointestinal bleeding and sepsis, who gained 74.8 lbs (34.0 Kg) and in the process showed a reduction of ΣQRS. Subsequent partial loss of the gained weight, 28.7 lbs (13.0 Kg), resulted in augmentation of the ΣQRS. Abbreviations as in the text. (Reproduced by permission of the Journal of the American College of Cardiology, Ref # 1).

tablished sets of criteria, but within a few days, and while fluid overload is developing, his/her ECGs now fail to show LVH (Figure 2).[4] This observation, which has clinical and research implications, suggests that ECG assessment for LVH cannot be reliably carried out in the presence of PERE. Augmentation of QRS voltage in patients following hemodialysis has been appreciated for some time,[5-8] although it was not linked conclusively to PERE, as it has been recently.[9]

The mechanism of these attenuations/augmentations of the QRS voltage and their associations with an increase/decrease in the patient's weight were attributed to the changes in the electrical impedance of the passive body volume conductor enveloping the cardiac generator, as per Ohm's law, which dictates that an attenuation of voltage occurs with a fall in the resistance, when the electrical current is stable. The decrease in the electrical resistance in PERE states is brought about by the increase of the tissue water content, and it is based on the low resistivity (specific resistance) of water.[10] This speculation has been supported by serial body bioimpedance measurements in one patient with CHF,[3] and in one with chronic renal failure undergoing repeated sessions of hemodialysis,[9] obtained via a device employed in nutrition and weight reduction clinics for estimating the body muscle, fat, and water composition (Quantum, Model No. BIA-101Q, RJL Systems, Inc.), by attaching 4 electrodes to the right hand and foot, as per manufacturer's instructions. What is implied by the above, and needs to be clearly stated here, is that these ECG al-

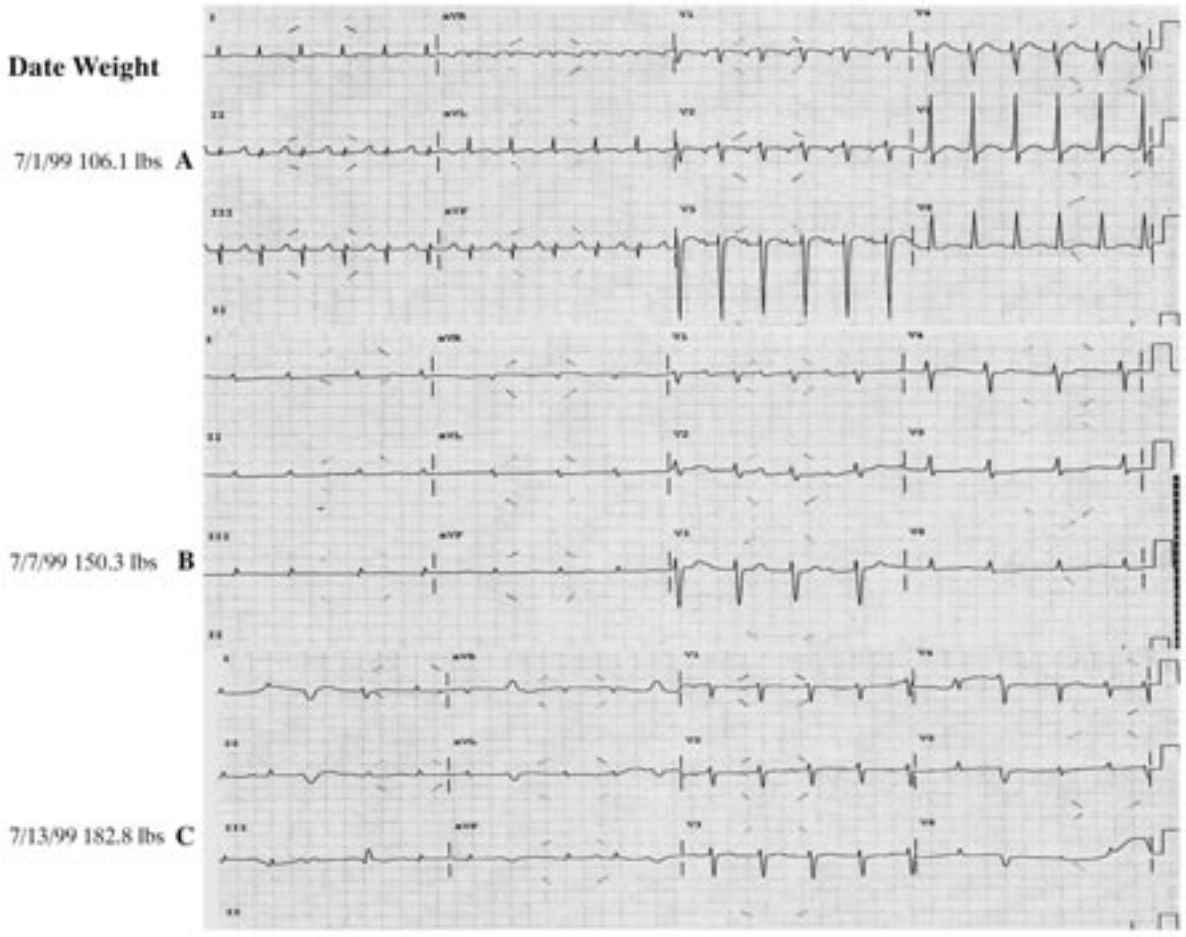

Figure 2. A 53-year-old patient with pneumonia and acute respiratory distress syndrome showed on admission evidence of LVH by both "Romhilt-Estes" and "Cornell" ECG systems (A), but after he gained 44.2 lbs (20.1 Kg) (B), and subsequently another 32.5 lbs (14.8 Kg) (C), LVH could no longer be diagnosed by ECG. In his serial daily ECGs a false negative diagnosis of LVH became first apparent after his gaining 14.9 lbs (6.8 Kg), which represented 14.0% of his admission weight. Abbreviations as in the text. (Reproduced by permission of the American Journal of Hypertension, Ref # 4).

terations are attributed to an extracardiac mechanism, rather than being the result of electrophysiologically-mediated changes.[1] Thus, when PERE develops as a result of any etiological mechanism, attenuation of the ECG potentials takes place, proportional to the resulting fluid accumulation. This of course does not exclude the simultaneous occurrence of electrophysiologically-mediated ECG alterations, which can modulate the ECG voltage, along with the changes imparted by the transfer of potentials through the passive body volume conductor. Proof of the extracardiac nature of the ECG attenuation of voltage with PERE is that veno-venous hemofiltration of patients with PERE led to enormous loss of accumulated weight and marked augmentation of the QRS complexes, while the simultaneously recorded cardiac electrograms, via a catheter in the right atrium, did not reveal any changes (Figure 3).[1] Finally, the attenuation of the amplitude of pacemaker stimulation "spikes" in patients with PERE fitted with pacemakers, simultaneously and proportionally with similar changes in the corresponding paced QRS complexes ($r=0.72$, $p=0.11$, $N=3$), bespeaks of an extracardiac mechanism for these ECG alterations (Figure 4).[11]

The amplitude changes with PERE do not involve only the QRS complexes and, since the phenomenon described herein is extracardiac in nature, it involves the entire "PQRST curve". Accordingly, attenuation of the amplitude of P-waves has been documented, and such changes correlate well with alterations in the cor-

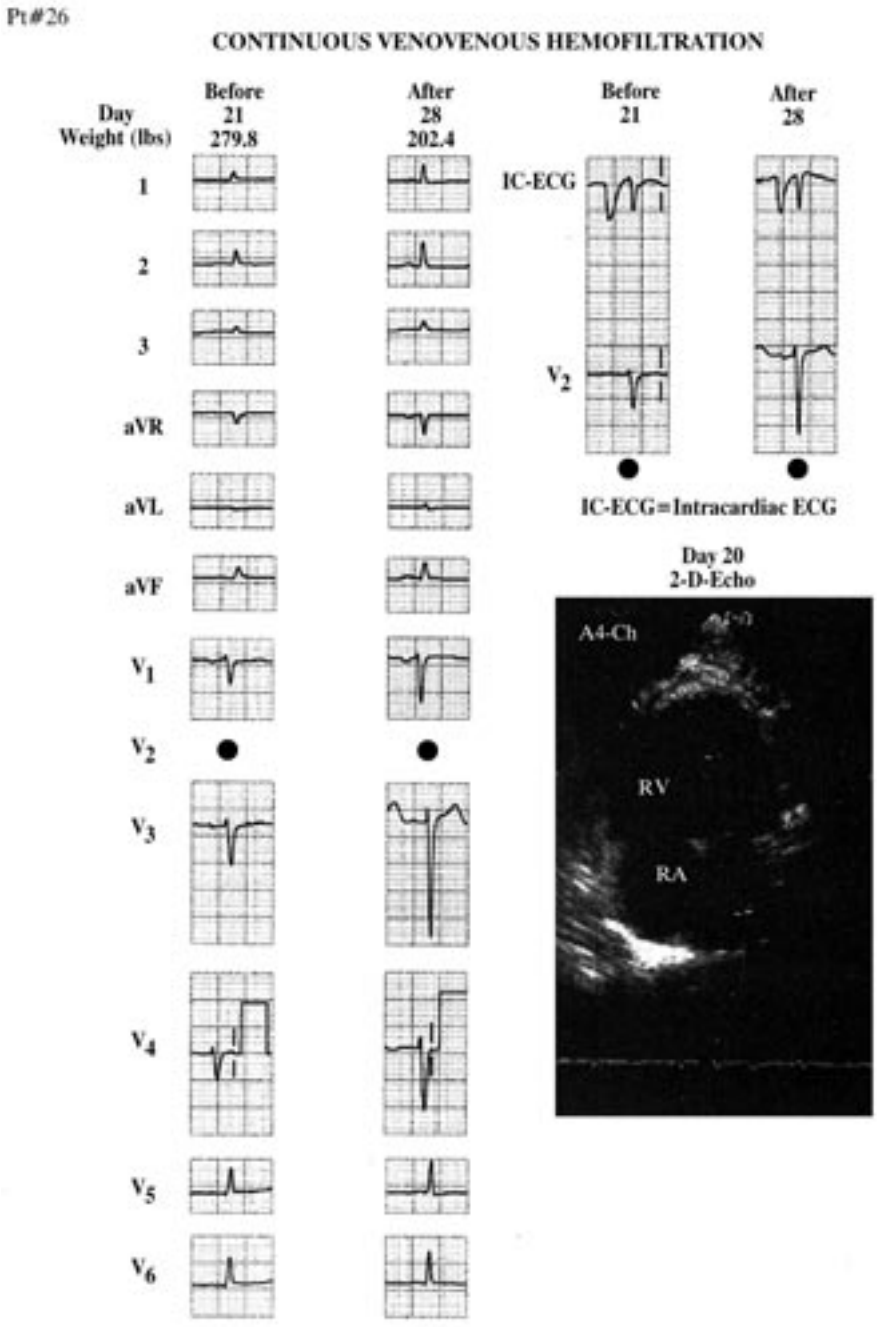

Figure 3. A 31-year-old man with sepsis who had gained weight, lost within 1 week 77.4 lbs (35.2 Kg) employing a veno-venous hemofiltration device. Note the stability of the intracardiac electrogram, while the surface ECG showed marked augmentation as a result of fluid loss (vide V2 lead simultaneously recorded with the intracardiac electrogram). The echocardiogram prior to starting the hemofiltration did not disclose pericardial or pleural effusions. (Reproduced by permission of the Journal of the American College of Cardiology, Ref # 1).

responding QRS complexes (r=0.62, p=0.01) (Figure 5).[12] The reduction of the amplitude of P-waves when PERE supervenes occasionally renders them virtually "invisible", requiring intracardiac ECG recordings for their identification (Figure 6).[13] Due to the marked attenuation of the P-waves with anasarca PERE, these "invisible" P-waves cannot be detected by the automated ECG algorithms, which generate reports of "junc-

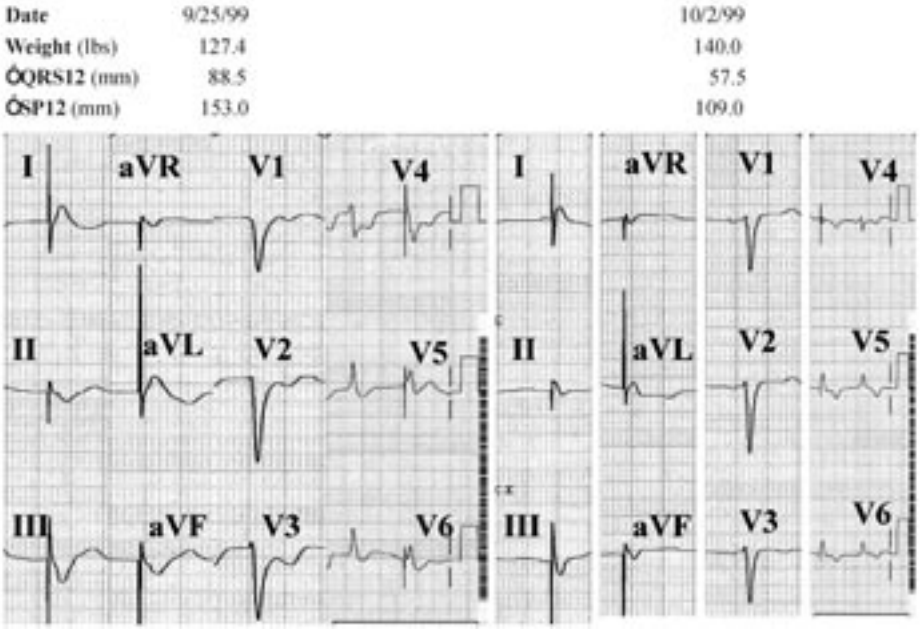

Figure 4. An 85-year-old man with a DDDR permanent pacemaker was admitted with sepsis, gained 12.6 lbs (5.7 kg), and in the process he showed reduction of ΣQRS12 (sum of QRS complexes of all 12 ECG leads) as well as ΣP12 (sum of pacemaker "spikes" from all 12 ECG leads). Abbreviations as in the text. (Reproduced by permission of the Annals of Noninvasive Electrocardiology, Ref # 11).

tional rhythm" or "junctional tachycardia" in the presence of "normal sinus rhythm" and "sinus tachycardia", respectively. Also this attenuation of P-waves in the presence of PERE transiently hinders the diagnosis of "P-mitrale", "P-pulmonale" and "bilateral P-wave abnormality",[14] with obvious clinical implications. As expected, regeneration of the amplitude of P-waves is noted in patients with PERE after they have lost part of the accumulated fluid.[12] Decrease in the amplitude of T-waves has been noted in serial ECGs from patients with PERE. However, the well known volatility of T-waves, which often show abrupt changes in amplitude and polarity that are not always easily explainable, has prevented the study of T-wave amplitudes in connection with the development of PERE.

Another consequence of the attenuation of the amplitudes of QRS complexes is the shortening of the QRS duration (QRSd).[15] This occurrence has nothing to do with changes of the QRSd resulting from electrophysiological causes, and has been attributed to a "measurement error". Accordingly, a loss of detection of a part of the onset and termination of the QRS complexes due to their overall attenuation brings these parts to levels of very low voltages, not different from the voltage of "noise". As a result, part of the onset and termination of the QRS complexes is undetectable, and this applies to both manual measurements and the ECG-based automated measurement and detection algorithms available in most contemporary equipment, which provide instant measurements, calculations and printed reports on numerical data along with the ECG interpretation.[16] There are many clinical implications of this "artifactual" shortening of the QRSd imparted by PERE. One example is the "apparent" conversion of complete right and left bundle branch blocks or nonspecific intraventricular conduction delays to incomplete ones, or even to normal intraventricular conduction, since the above designations are made on the basis of QRSd along with the QRS configuration.[17] A more important consequence of this PERE-mediated shortening of the QRSd is the potential influence it could exert on the patient selection for cardioverter/defibrillator implantation and cardiac resynchronization therapy, since decisions for such procedures are made based on the QRSd, among other clinical and laboratory parameters.[18-22] Furthermore, it could be hypothesized that the suboptimal performance of the QRSd as a measurement predict-

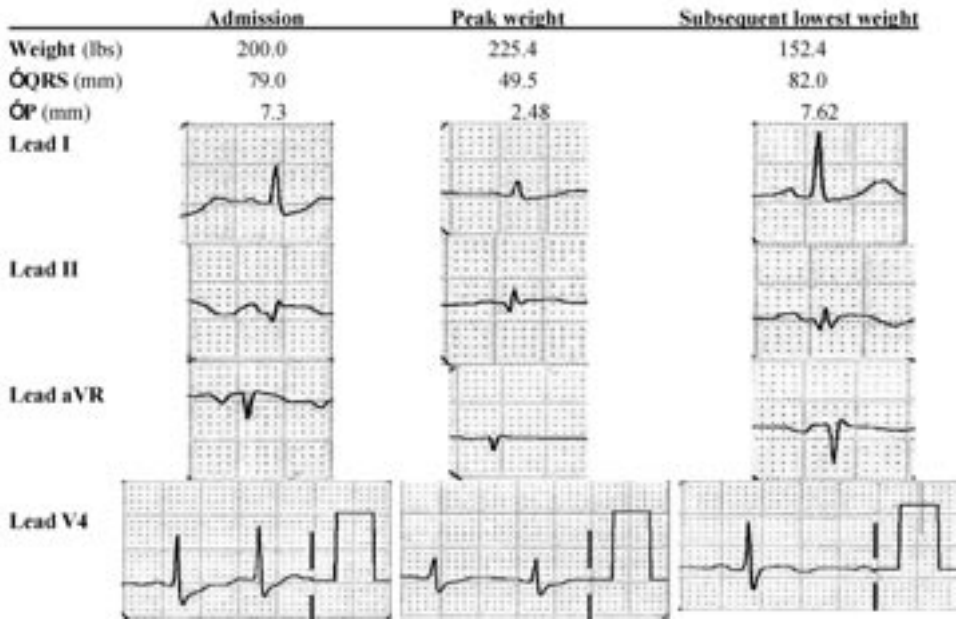

Figure 5. A 47-year-old man who survived cardiac arrest and subsequent anoxic encephalopathy gained 25.4 lbs (11.5 Kg) and showed decrease in the amplitude of the P-waves (ΣP=sum of the amplitude of P-waves of all 12 ECG leads) commensurate with decrease in ΣQRS. Later on, when he lost 73.0 lbs (33.2 Kg), the amplitude of P-waves in his ECGs returned to the level seen on admission. (Reproduced by permission of Pacing and Clinical Electrophysiology, Ref # 12).

ing response to the above two procedures might be due to its compromise by the presence/absence of the confounding factor of intercurrent PERE.[22-24] Although there are no data on patients with CHF, one could envisage that development or alleviation of PERE in such patients could change the QRSd, with resultant placement of a particular patient in a different category than that to which he/she would be assigned prior to the change of edematous state. Specifically, a patient with phases of compensated and uncompensated CHF would be categorized in different groups in a trial of cardiac resynchronization therapy employing specific brackets of QRSd, depending on the particular phase he/she is in at the time of randomization. It is thus advised that many ECGs are taken into consideration and the edematous state of the patient is also considered at the time of a patient's assignment to a particular QRSd group.

It has been reported recently that the QT and QTc intervals are also shortened as a result of PERE development.[25] The specific pathophysiology of the illness that led to the emergence of PERE is irrelevant in the shortening of the QT and QTc. The patients who subsequently experienced some alleviation of their PERE showed re-lengthening of the QT and QTc.[25] Further support of the link between the edematous state of a patient and the recorded QT and QTc was provided by the lengthening of these 2 parameters in a patient with chronic renal failure, who underwent repeated hemodialysis sessions.[9] The mechanism of this shortening of the QT intervals with PERE is the same one that is implicated in the shortening of the QRSd, discussed above, i.e. the "artifactual" loss of measurement of part of the QRS onset and QT termination. Again, this does not imply that such compromises of QT and QTc measurements as described herein (extracardiac) are not associated with electrophysiologically-mediated (cardiac) alterations of the QT and QTc. The voluminous, rapidly expanding literature on the QT interval and its importance in cardiac diagnostics and therapeutic decision-making does not need to be emphasized here. Suffice it to say that among the other many vagaries (drugs, change in clinical condition, electrolytes, etc.), associated with the proven and speculated influences on the QT interval, the edematous state of the patients needs to be considered,[25] particularly when comparisons of serial values of QT intervals are made. These apply to pa-

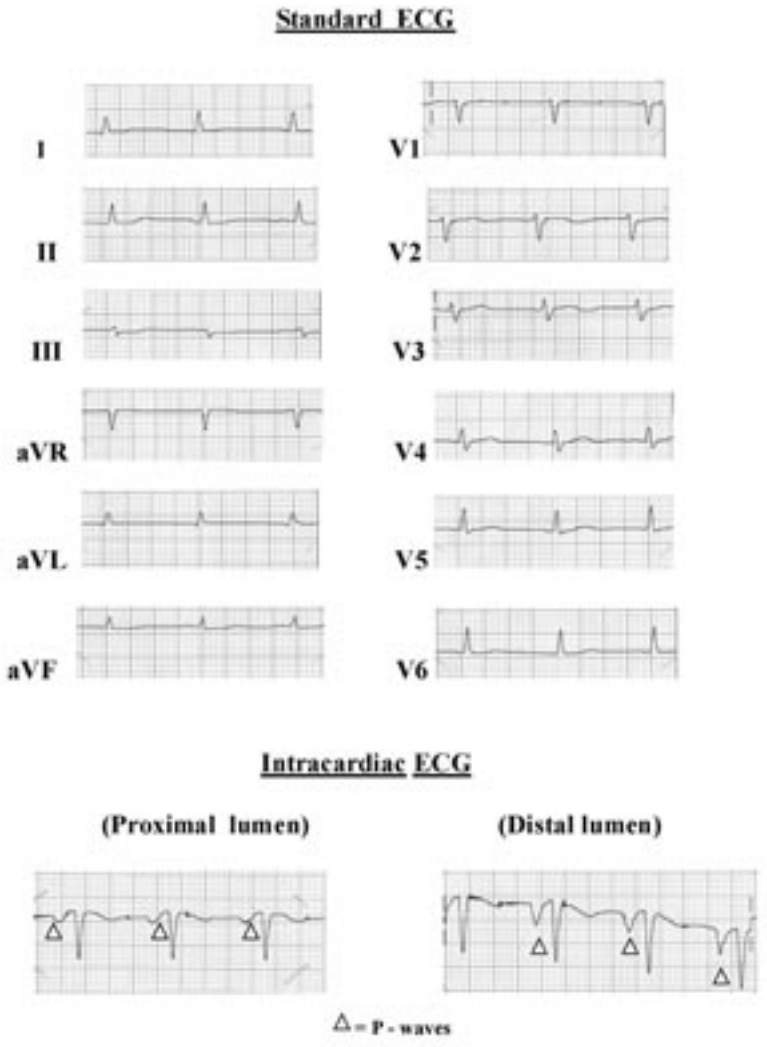

Figure 6. A 68-year-old woman, admitted with asystole, anoxic encephalopathy, and sepsis, gained 30 lbs (13.6 Kg), and in the process showed invisible P-waves on the standard ECG, their detection requiring intracardiac electrograms obtained via a saline-filled central venous catheter. Note the larger amplitude P-waves obtained via the distal port of the catheter (closer to the right atrium) as compared to those recorded via the more proximal port. (more distant from the right atrium). (Reproduced by permission of the American Journal of Cardiology, Ref # 13).

tients in critical care units, or to those under active therapy for CHF, or to subjects undergoing hemodialysis, who experience significant changes in their edematous states.

In the course of the past 6 years it has been observed that changes in all the above ECG measurements occur in connection with a very large array of illnesses.[1] In addition to the pathological entities mentioned above, the presence of chronic and acute cor pulmonale with development of PERE is frequently encountered in the respiratory care unit.[26] Perusal of serial ECGs from patients in such an environment reveals the very frequent AECGV in patients admitted with COPD exacerbation. These patients also display PERE and alleviation of their clinical condition, with partial or complete relief of fluid volume overload, results in dramatic restoration of the ECG voltage.[14] Other patients showing this phenomenon are those experiencing changes in their fluid volume status perioperatively in the setting of cardiac and non-cardiac surgery.[14] Since there is a burgeoning literature on the change in ECG measurements in patients undergoing cardiac surgery, and an effort to use such measurements for prediction of the clinical outcome, one can only imagine how compromised are such ECG parameters rendered by the presence and change of PERE

resulting from large fluid infusions, diuresis, and hemofiltration employed perioperatively. PERE is often experienced in connection with drugs, and such adverse effects often result in discontinuation of the offending agent. Data on this have not yet been published, however transient AECGV has been noted in patients taking drugs known to enhance fluid retention.[14]

In conclusion, PERE of varying pathophysiologic mechanism and in association with a wide range of illnesses results in AECGV. Alleviation of PERE leads to regeneration of the ECG voltage. Since PERE influences the entire ECG curve, the amplitudes of QRS complexes and P-waves are affected. In addition, reversible changes of the QRSd and QT-intervals occur with PERE and its alleviation. The above have important clinical implications, some of which have already been shown while others are currently under evaluation. As this new field of clinical practice and research is evolving, the clinician could start employing these ideas by monitoring "at a glance" and at the bedside the edematous state of his/her patients using the standard leads I and II from serial ECGs, which are a good reflector of changes occurring in the 6 limb leads, as was shown recently.[27]

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