Changes in plasma free fatty acid levels in septic patients are associated with cardiac damage and reduction in heart rate variability

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INTRODUCTION

The clinical syndrome sepsis results from a host inflammatory response to infection via innate immune system activation. When this immune response progresses uncontrollably, it can ultimately result in cardiovascular collapse and death. Depressed cardiac performance is a hallmark of septic cardiovascular alterations and may contribute to the high mortality of the disease (1, 2). Cardiodepressive substances produced in the septic state have been investigated by several groups (3–6). Recently, we showed poly(adenosine diphosphate ribosyl) polymerase (PARP) activation by oxidative stress in the hearts of septic patients (7). Poly(adenosine diphosphate ribosyl) polymerase activation was positively correlated with plasma troponin I levels and negatively correlated with left ventricular stroke work. In sepsis, PARP is activated by single-strand DNA breakage caused by oxidative stress. Thus, PARP activation represents a new cardiodepressive pathway (7).

In addition to elevated levels of cardiodepressive cytokines, such as TNF-α and IL-1β (1), there is growing evidence that impairment of cardiac perfusion at the microcirculatory level may hamper cardiac function in septic patients (7). During ischemia, when part of the myocardium becomes anaerobic, the balance of substrates is disturbed, and oxidized products of fatty acids (FAs) accumulate locally (8).

Higher concentrations of certain FAs, particularly polyunsaturated FAs and volatile FAs, can cause cell death via apoptosis or, when concentrations are even greater, necrosis (9–13). Cell death occurs by apoptosis at doses close to the physiological free FA (FFA) concentrations, as assessed by the induction of internucleosomal DNA cleavage, chromatin condensation, and nuclear breakdown (9–13). High doses of FFA generally cause necrosis, with rapid loss of membrane integrity, lysosomal mediator leakage, and cell swelling. These effects seem to be associated with oxidative stress because they can be partially prevented by antioxidants, such as tocopherol (9–13).

A role of plasma FFAs for cardiac alterations has been highlighted (8). In fact, elevated plasma FFA levels may disrupt cardiac plasma membrane structure and function and raise intracellular calcium concentration, thereby affecting cardiac activity. Some studies have shown that FFA might exaggerate cardiac sympathetic nervous system activity in healthy subjects (14, 15). Thus, elevated plasma FFA concentration may be responsible for cardiac sympathetic nervous system overactivity found in septic patients.

Heart rate variability (HRV) is a sensitive and reproducible test that allows investigation of cardiac responsiveness and autonomic tone over time (15, 16). Reduced HRV, which is

ABSTRACT—Free fatty acids (FFAs) have been shown to produce alteration of heart rate variability (HRV) in healthy and diabetic individuals. Changes in HRV have been described in septic patients and in those with hyperglycemia and elevated plasma FFA levels. We studied if sepsis-induced heart damage and HRV alteration are associated with plasma FFA levels in patients. Thirty-one patients with sepsis were included. The patients were divided into two groups: survivors (n = 12) and nonsurvivors (n = 19). The following associations were investigated: (a) troponin I elevation and HRV reduction and (b) clinical evolution and HRV index, plasma troponin, and plasma FFA levels. Initial measurements of C-reactive protein and gravity Acute Physiology and Chronic Health Evaluation scores were similar in both groups. Overall, an increase in plasma troponin level was related to increased mortality risk. From the first day of study, the nonsurvivor group presented a reduced left ventricular stroke work systolic index and a reduced low frequency (LF) that is one of HRV indexes. The correlation coefficient for LF values and troponin was r² = 0.75 (P < 0.05). All patients presented elevated plasma FFA levels on the first day of the study (5.11 ± 0.53 mg/mL), and this elevation was even greater in the nonsurvivor group compared with the survivors (6.88 ± 0.13 vs. 3.85 ± 0.46 mg/mL, respectively; P < 0.05). Cardiac damage was confirmed by measurement of plasma troponin I and histological analysis. Heart dysfunction was determined by left ventricular stroke work systolic index and HRV index in nonsurvivor patients. A relationship was found between plasma FFA levels, LFnu index, troponin levels, and histological changes. Plasma FFA levels emerged as possible cause of heart damage in sepsis.

KEYWORDS—Shock, sepsis, inflammation, cytokines, glucose

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CHANGES IN PLASMA FREE FATTY ACID LEVELS IN SEPTIC PATIENTS ARE ASSOCIATED WITH CARDIAC DAMAGE AND REDUCTION IN HEART RATE VARIABILITY


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indictive of exaggerated cardiac sympathetic nervous system firing, is associated with increased cardiovascular mortality (15). To the best of our knowledge, no studies have yet to evaluate the possible relationship between plasma FFA concentration and cardiac autonomic tone in septic patients.

The aim of this study was to determine if HRV alteration in septic patients is determined or correlated to secondary cardiac damage from inflammation or metabolic changes. The following cardiac functions and biochemical markers were analyzed: hemodynamic parameters, serum cardiac lesion markers (troponin and creatine phosphokinase [CPK]), lipoproteins, and FFA. We also evaluated HRV and survival in septic patients.

METHODS

All adults presenting severe sepsis or septic shock and admitted to the intensive care unit (ICU) of the São Paulo University Hospital between November 2003 and July 2005 were eligible for enrollment in this study. Written informed consent was obtained from the closest family member of each patient. Ethical permission to conduct this study was obtained from the ethics committee of São Paulo University Hospital. The study was approved as a minimal risk protocol.

Study design

Observational and prospective analysis of cardiac alterations in 31 septic patients was conducted. Inclusion criteria were the following: severe sepsis or septic shock (17, 18) (i.e., the finding of temperature of >38°C or <36°C centigrade, pulse rate of >90/min, respiratory rate of >20 breath/min [or PacO2, 32 mmHg], leukocytes of >12,000 cells/μL or <4,000 cells/μL [or more than 10% band forms]); in the presence of infection focus, severe sepsis was defined as all previous characteristics and organ failure associated; and the presence of systolic arterial pressure of less than 90 mmHg or a drop of 40 mmHg characterized as septic shock. Exclusion criteria were the following: acute or previous myocardial infarction, nonsinusual rhythm, use of a permanent pacemaker, chronic heart failure of functional class III or IV, or diabetes.

Data collection

Demographic and clinical information was first obtained, including the information required to determine illness severity and the need for intensive care (Table 1). Scores were calculated for the Acute Physiology and Chronic Health Evaluation (APACHE II) (19). Higher scores indicate greater illness severity.

Blood samples were collected. Hemodynamic parameters were measured, and Holter analysis was performed on days 1, 3, and 6. Serum troponin I, CPK, creatine kinase isoenzyme MB (CKMB), C-reactive protein (CRP), glucose, lipoproteins, and FFA levels were determined. Hemodynamic parameters were determined using a pulmonary catheter on days 1, 3, and 6.

Measurements

Plasma levels of TNF-α, interferon gamma, and IL-10—Plasma concentrations of immunoreactive murine TNF-α, IL-6, and IL-10 were determined by using commercially available enzyme-linked immunosorbent assay. Protocols are available from the manufacturer (R & D Systems, Minneapolis, Minn).

Determination of plasma FFA composition as measured by high-performance liquid chromatography

Total lipids were extracted from plasma as previously described (20). Briefly, lipids were saponified using 2 mL of an alkaline methanol solution (1 mol/mL NaOH in 90% methanol) at 37°C for 2 h in a shaking water bath. Then, FAs were derivatized with 4-bromomethyl-7 coumarin and analyzed in a liquid chromatographer (Shimadzu model LC-10A; Shimadzu, Kyoto, Japan). Samples were eluted using a C8 column (25 × 4.6 cm inner diameter, 5 μm of particles), with a fluorescence detector (325 nm excitation and 395 emission). Fatty acid standards were obtained from Sigma-Aldrich Co (St Louis, Mo). Margaric acid (C17:0) was used to calculate recovery. The minimum concentration of FAs ranged from 1 to 10 ng.

Determination of plasma FFA levels

Plasma FFA concentration was determined by the enzymatic colorimetric method (10) as protocols are available from the manufacturer. Ten microliters of plasma (adenosine triphosphate, 4-aminoantipyrine, phosphate buffer, and magnesium chloride; Wako Chemical, Neuss, Germany) were added to samples and incubated at 37°C for 10 minutes. The amount of total FFA can be determined from the optical density measured at 550 nm (Spectra MAX plus; Molecular Devices). The concentration of each FA was calculated using the values of the proportion of each FA detected by the high-performance liquid chromatography analysis and the concentration of total FA in plasma.

Data acquisition and signal processing

A 30-min record of cardiac rhythm was obtained on the mornings of the days 1, 3, and 6. Heart rate variability data were derived from continuous digitized electrocardiogram recordings. The power spectrum analysis of heart rate includes three peaks (i.e., vasomotor low frequency, low frequency [LF], and high frequency [HF]). These indexes were used to interpret autonomic modulation of heart rate and heart capability to answer autonomic action (14, 15, 21). All patients were observed at bedside in supine position. All patients were under mechanical ventilation, with parameters completely controlled by the ventilator. Respiratory rate was maintained between 12 and 14 breaths/min, and the end-tidal volume was between 7 and 8 mL/kg.

For data acquisition and analysis, CardioFlash Digital Holter and CardioSmart Professional CSK 540 Holter software were used (Carioequipo eletromedica commercial Ltda, São Paulo, Brazil). Briefly, electrocardiographic recording tapes were analyzed using the software. The computer program automatically calculates the autoregressive coefficients necessary to define power spectral density estimates and determines the power and frequency of every spectral component. Two major oscillatory components are usually detectable. One synchronous with respiration is described as HF (approximately 0.25 Hz and varying with respiration). The other corresponds to the slow waves of arterial pressure, described as LF (approximately 0.1 Hz). Each spectral component is presented in normalized form (units) by dividing it by the total power minus the direct current component, if present. Only components greater than 5% of the total power was considered significant. This LF/HF ratio is considered an index of cardiac sympathetic/parasympathetic tone balance (14, 22).

![Fig. 1. Increased levels of glucose are associated with mortality (A).](image-url)
Plasma determinations

Plasma glucose concentration was determined by glucose oxidative methods using a Glucose autoanalyzer (Beckman Coulter, Inc, Fullerton, Calif) or ADVIA Chemistry Systems (Bayer). Total cholesterol, high-density lipoprotein (HDL) cholesterol, and CPK were determined using an autoanalyzer (ADVIAChemistry Systems). When triglyceride (TG) was lower than 4.52 mM, the low-density lipoprotein (LDL) cholesterol was calculated using the Friedwald equation. Plasma troponin I levels and CKMB activity were determined using a solid-phase chemiluminescent immunometric assay (Immulite 1000 System); CRP (high sensitive-protein C reactive) was detected using a Behring Nephelometer 100 Analyser (Behring, Newark, NJ).

Histology studies

Light microscopy—Heart tissues from nonsurvivors were fixed with 4% paraformaldehyde for 6 h at room temperature, dehydrated in graded concentrations of alcohol, embedded in paraffin, and sectioned into 5 μm. Hematoxylin and eosin were used to evaluate the myocardial architecture and infiltration of inflammatory cells.

Electron microscopy—Samples of 1-mm myocardium were fixed in 2% glutaraldehyde dissolved in 0.15 M of phosphate buffer at pH 7.2. This was followed by 1% osmium tetroxide post fixation and block staining in 1% aqueous uranyl acetate. The samples were embedded in a polyester resin, sectioned with an LKB ultratome, double-stained by uranyl acetate and lead citrate, and examined in a Jeol 1010 electron microscope for mitochondrial ultrastructure.

Follow-up

All enrolled patients were followed until hospital discharge. The following variables were recorded daily: mechanical ventilation, use of sedation (midazolan or fentanyl), and catecholamines (dopamine, epinephrine, or norepinephrine). We prospectively followed the evaluation of these patients during their ICU stay and compared HRV indexes, troponin, and echocardiograph (not shown) for survivors and nonsurvivors. There was no difference between hospital discharge or a period of 28 days as criteria for nonsurvivors from sepsis.

Statistical analyses

Results are presented as means and the SDs. For further analyses, a post hoc patients’ separation into survivors and nonsurvivors was performed. Analysis of variance was used for repeated measurements in continuous variables, and correlation coefficients were determined according to multiple-level regression analysis. A $P < 0.05$ was considered significant.

RESULTS

Study population

Thirty-one patients were enrolled in the study. Clinical and demographic characteristics of the treated groups were similar at the beginning of the study (Table 1), and there was no significant difference with respect to the delay in admission to the ICU. Six patients died within the first 24 h after admission. The mortality rate was 61% in the study group.

Glycemia

Septic patients presented elevated plasma glucose levels. The nonsurvivor group had higher plasma glucose levels on the first day of study (nonsurvivors vs. survivors, 167.7 ± 20.0 vs.161 ± 14.5, not significant; Fig. 1A). A marked improvement of blood glucose levels was observed in survivors, whereas nonsurvivors presented a continuous increase ($P < 0.05$).
Lipoprotein levels

Plasma cholesterol profiles showed a typical pattern described for critically ill patients, with the reduction of total cholesterol and HDL and LDL cholesterol levels. Nonsurvivor patients showed the lowest lipoprotein plasma levels (Fig. 1, B and C).

TG and plasma FFA levels

Measurements of plasma TGs and FFA showed an inverse pattern to that observed for cholesterol lipoproteins (Fig. 2). Septic patients presented a rise of 4 times in plasma FFA levels compared with healthy individuals. Also, TGs were elevated in septic patients.

Systemic inflammatory makers (cytokines and CRP)

The TNF-α and CRP levels were not significantly different between survivors and nonsurvivors (data not shown). However, IL-10 was more elevated in nonsurvivor patients (58.9 ± 12.5 pg/mL) than in survivors (7.7 ± 2.5 pg/mL) (P < 0.05).

Heart damage

All patients were mechanically ventilated and received catecholamines. Respiratory frequency and tidal volume parameters for mechanical ventilation were maintained in a small range: 12 to 15 breath/min and 6 to 9 mL/kg, respectively. Catecholamines were infused as necessary to stabilize blood pressure, reach adequate cardiac output, and maintain oxygen delivery. The two groups had similar APACHE II scores (nonsurvivors, 25.8 ± 2.7; survivors, 25.2 ± 5.5; not significant).

Creatine phosphokinase, CKMB, and cardiac output were not significantly different between groups at any time during the study period. Troponin I was significantly lower from the first day of the study in the survivor group (0.58 ± 0.11 mg/mL) compared with the nonsurvivor group (2.42 ± 1.08 mg/mL; P < 0.05). The difference remained on days 3 and 6.

Cellular damage was correlated with cardiac dysfunction as detected by the left ventricular stroke work index. Nonsurvivors presented a significantly depressed stroke index compared with survivors (35.0 ± 5.7 g-m/m² for nonsurvivors, vs. 48.9 ± 6.3 g-m/m² for survivors; P < 0.05).

Histological myocardial damage

Hematoxylin-eosin staining, conducted in the hearts of nonsurviving patients, demonstrated more inflammatory cells in the heart tissue. Also, there was an increase in the proportion of picnotic cells indicative of cell death (Fig. 3A). These histological findings may be related to cardiac rigidity and the inability to dilate in response to sepsis. Electron microscopy analysis showed marked lipidic corpuscula and mitochondrial agglomeration (Fig. 3B).

Holter analysis

Arrhythmias—The 24 h of electrocardiography records showed more patients presenting arrhythmias (Table 2). Supraventricular extrasystoles (SVES) paired and supraventricular tachyarrhythmia were significantly more frequent in nonsurvivors.

HRV and heart dysfunction—The HRV showed significant differences in maximal and minimal LF and HF (Fig. 4). Only LF as an independent variable was a predictor of patient outcome. The amount of injected catecholamine and the type of bacteria present in the infected site were determined to investigate if HRV changes were directly associated with sepsis. The origin of sepsis and the type of bacteria present are shown in Table 3. The quantity of catecholamine given and sedative drugs used in 24 h were not different between groups in the 6 days of study (data not shown). Differences in PR and corrected QT intervals between survivors and nonsurvivors are shown in Figure 4, A and B.

Correlations between LF and plasma troponin levels and of LF and CRP levels were determined to find out whether the HRV alteration in nonsurvivors is associated with heart damage and/or systemic inflammation, or for autonomic imbalance only. The significant correlation between LF and

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**Table 2. Incidence of arrhythmias in patients**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Survivor (n = 12)</th>
<th>Nonsurvivor (n = 19)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SVES, n (%)</td>
<td>12 (95)</td>
<td>17 (95)</td>
</tr>
<tr>
<td>SVES paired, n (%)</td>
<td>6 (46)</td>
<td>14 (78)*</td>
</tr>
<tr>
<td>Supraventricular, n (%)</td>
<td>5 (40)</td>
<td>12 (67)*</td>
</tr>
</tbody>
</table>

*P < 0.05 comparing both groups.

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**Fig. 4.** The indices LF and HF in maximal LF/HF ratio were reduced in nonsurvivors, indicating lessened ability to regulate HRV. PR and corrected QT intervals were increased in nonsurvivors compared with those in survivors. The data presented are mean ± SEM. *P < 0.05.
troponin levels in nonsurvivors is shown (Fig. 5). However, LF and plasma CRP levels presented a weak correlation.

**DISCUSSION**

Nonsurvivor septic patients presented higher plasma FFA and glucose levels, as well myocardial cell damage demonstrated by serum biomarker troponin I levels and microscopic analysis. Cell damage culminated in heart dysfunction, which resulted in impaired cardiac rate regulation, as detected by LF reduction in septic patients.

Plasma lipid composition was markedly changed in septic patients, as shown by lower HDL and LDL plasma levels and increased levels of TGs and FFA. The nonsurvivor group presented higher plasma FFA levels on day 1. The FFA composition analysis showed an increased proportion of saturated FFA (lauric and palmitic). These two FFA, are the constituents of lipid A of lipopolysaccharide from gram-negative bacteria. Cell culture studies have shown that palmitic and lauric acids stimulate TLR-4 as lipopolysaccharide of beta-negative bacteria. Cell culture studies have shown that palmitic and lauric acids stimulate TLR-4 as lipopolysaccharide does and induces macrophages to release cytokines (23–26). Release of these cytokines may lead to increased permeability of the cardiomyocyte membrane, resulting in the release of cardiac enzymes (27). Circulating myocardial depressant agents have been implicated as endotoxin and cytokines, such as TNF-α, IL-1β, and IL-6 (27, 28). Plasma cytokine levels were elevated in all septic patients in this study—plasma levels of TNF-α and interferon-gamma inflammatory cytokines, and CRP, without difference between survivors and nonsurvivors. Only IL-10 level was significantly higher in nonsurvivor patients. It is unlikely that inflammatory alterations were involved in the different septic patients’ outcome in our study. Increased catabolism in heart tissue, cardiac output, and oxygen demand; decreased coronary perfusion; and impairment of oxygen delivery and extraction are all likely to play important roles during sepsis or systemic inflammatory response syndrome (27, 28). Histological heart tissue analysis from patients who died of sepsis in our study revealed cells with picnotic nuclei, characteristic of cell death. Conglomerates of mitochondria, an alteration found in the course of ischemia, were observed using electron microscopy analysis (29).

Evidence for the use of substrates by the ischemic myocardium and its dependence for viability on a critical supply of glucose were established in 1994 (8). An excess of FFAs could increase the severity of ischemic damage and possibly be arrhythmogenic. In severe ischemia and shock, exogenous factors can affect FFA. These include rises in plasma catecholamine concentrations, leading to increased FFA release from adipose tissue stores and decreased secretion of insulin by pancreatic beta cells, which is necessary for glucose uptake by the myocardium. Circulating FFA elicit systemic insulin resistance (8). Oxygen-wasting effects of increased FFA provision to the acutely ischemic myocardium could be augmented by impairment of glucose uptake or use (8).

Hyperglycemia has been highlighted as an important factor in the prognosis of septic patients (30, 31). High plasma glucose levels reflect the relative insulin deficiency being associated with an increase in plasma FFA level concentration that is secondary to increased lipolysis (15). Thus, hyperglycemia associated with low insulinemia may have a negative impact on cardiac activity through changes in plasma FFA levels. The toxic effect of FFA on cardiac cell membranes has been previously highlighted (14, 15). In isolated rat hearts, FFA has arrhythmogenic properties, even in the absence of ischemia, if the molar ratio of FFA to albumin is sufficiently high (8). The analysis of arrhythmia incidence in the nonsurvivor group also showed an elevated number of supraventricular tachycardia and SVES paired events in nonsurvivors on the first day. During ischemia, beta-oxidation of FA in mitochondria is inhibited, and there is accumulation of intracellular acylcarnitine and acyl–coenzyme A. Electron microscopic analysis of the patients’ hearts showed lipidic corpuscles inside cells. This is produced by the accumulation of lipids because of inhibition of beta-oxidation as previously reported (4). This finding is

**TABLE 3. Septic focus and bacteria in patients**

<table>
<thead>
<tr>
<th>Focus of infection</th>
<th>Survivor, n (%)</th>
<th>Nonsurvivor, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pneumonia</td>
<td>7 (54)</td>
<td>6 (50)</td>
</tr>
<tr>
<td>Abdomen</td>
<td>6 (46)</td>
<td>3 (25)</td>
</tr>
<tr>
<td>Osteomyelitis</td>
<td>2 (17)</td>
<td>1 (8)</td>
</tr>
<tr>
<td>Endocarditis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bacteria</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gram-negative</td>
<td>7 (54)</td>
<td>8 (67)</td>
</tr>
<tr>
<td>Gram-positive</td>
<td>4 (31)</td>
<td>5 (42)</td>
</tr>
<tr>
<td>Not identified*</td>
<td>3 (24)</td>
<td>2 (17)</td>
</tr>
</tbody>
</table>

*No bacterial growth from the cultures.
corroborated by the fact that those patients presented high plasma FFA levels, which causes the formation of lipidic corpules.

Free fatty acids in excess may have a detergent effect on plasma membranes (8). In addition, arrhythmogenic effects of lyso phospholipids, derived from the breakdown of membrane lipids during ischemia and of acyl carnitine, have been reported (8). Acylcarnitine inhibits the Ca pump of the sarcoplasmic reticulum, and the sarcolemmal Na\(^+-\)Ca\(^{++}\) exchanger and Na\(^+\) pump; acylcarnitine can also activate Ca\(^{++}\) channels, producing arrhythmias via Ca\(^{++}\) overload. Fatty acids also cause an increase in tissue cyclic adenosine monophosphate levels, which in turn promotes Ca\(^{++}\)-dependent repertussion arrhythmias (8). Furthermore, an accumulation of tissue FFA late in ischemia can open an abnormal K\(^+\) channel (8) that shortens the action-potential duration. Ionic cell changes induced by high plasma FFA levels may explain the increased incidence of arrhythmias in nonsurvivors. Indeed, high concentrations of FFA during myocardial ischemia increase myocardial oxygen demands and reduce myocardial contractility in dogs (32). The latter effect, confirmed in the present study with septic patients, provides a further pathophysiological mechanism for the relationship between poor metabolic control and death, or arrhythmias.

In healthy individuals and diabetic patients, the elevation of plasma FFA levels has been reported to produce an important alteration in HRV as indicated by a reduced LF value (14, 15). Godin et al. (33) suggested that HRV reduction in critically ill patients, caused by exaggerated immunoinflammatory response and subsequent uncoupling of organ systems, is the cause of multiple-organ dysfunction syndrome. These studies also demonstrated a positive correlation between LF reduction and ICU mortality, and LF reduction as a risk for the development of multiple-organ dysfunction syndrome (33). In our study, HRV impairment was observed in all patients (Fig. 4). Multivariate analysis showed that LF is an independent variable that can be used to predict patient outcome. Our results showed a good correlation \(r^2 = 0.75\%; P < 0.05\) between LF and troponin on the first day of sepsis. Exogenous catecholamines were continuously provided in excess to all patients to sustain arterial blood pressure; the amount of catecholamines did not present difference between both groups. In our patients, exogenous catecholamines overcome autonomic nervous system and overfeed heart receptors; in that way, the problem is the capacity of heart to respond properly. We raised the hypothesis that the heart response to autonomic control is impaired in the damaged septic heart, and one possible cause for the cardiac alteration in sepsis is the elevation in plasma FFA levels. Plasma FFA levels were elevated in septic patients and were even higher in nonsurvivors as previously mentioned; FFA causes cell death through oxidative stress (9–13). Free FAs can be the cause of the myocardial damage, arrhythmias, and reduction in HRV as observed in nonsurvivors.

In conclusion, evidence for heart dysfunction in septic patients is presented. Parameters indicative of heart damage in septic patients were the following: plasma troponin levels, left ventricular stroke work systolic index, and HRV analysis. Low-frequency index was correlated with plasma troponin level \(r^2 = 0.58\) for all patients; and \(r^2 = 0.75\) for nonsurvivors) and LF with plasma FFA levels \(r^2 = 0.2\) all patients; and \(r^2 = 0.78\) for nonsurvivors). Heart rate variability is indicative of a direct heart dysfunction due to oxidative stress and another associated cause, which is most likely due to the high plasma FFA levels. Heart rate variability analysis enables the study of the interaction of the autonomic nervous system control and heart response ability. High plasma FFA levels may affect both end points: autonomic nervous firing and heart response ability. Interventions that improve perfusion may thus reduce lipolysis and plasma FFA levels, decrease systemic inflammation, and thereby lead to heart damage and mortality.

REFERENCES


