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The European Journal of Heart Failure 5 (2003) 443–451

The European Journal of Heart Failure

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The role of cardiac power and systemic vascular resistance in the pathophysiology and diagnosis of patients with acute congestive heart failure

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Received 16 August 2002; received in revised form 6 January 2003; accepted 21 January 2003

Abstract

Objective: Conventional hemodynamic indexes (cardiac index (CI), and pulmonary capillary wedge pressure) are of limited value in the diagnosis and treatment of patients with acute congestive heart failure (CHF). *Patients and methods:* We measured CI, wedge pressure, right atrial pressure (RAP) and mean arterial blood pressure (MAP) in 89 consecutive patients admitted due to acute CHF (exacerbated systolic CHF, $n=56$; hypertensive crisis, $n=5$; pulmonary edema, $n=11$; and cardiogenic shock, $n=17$) and in two control groups. The two control groups were 11 patients with septic shock and 20 healthy volunteers. Systemic vascular resistance index (SVRi) was calculated as $SVRi=(MAP-RAP)/CI$. Cardiac contractility was estimated by the cardiac power index (Cpi), calculated as $CI\times MAP$. *Results and discussion:* We found that $CI<2.7$ l/min/m^2 and wedge pressure >12 mmHg are found consistently in patients with acute CHF. However, these measures often overlapped in patients with different acute CHF syndromes, while Cpi and SVRi permitted more accurate differentiation. Cpi was low in patients with exacerbated systolic CHF and extremely low in patients with cardiogenic shock, while SVRi was increased in patients with exacerbated systolic CHF and extremely high in patients with pulmonary edema. By using a two-dimensional presentation of Cpi vs. SVRi we found that these clinical syndromes can be accurately characterized hemodynamically. The paired measurements of each clinical group segregated into a specific region on the Cpi/SVRi diagnostic graph, that could be mathematically defined by a statistically significant line (Lambda = 0.95). Therefore, measurement of SVRi and Cpi and their two-dimensional graphic representation enables accurate hemodynamic diagnosis and follow-up of individual patients with acute CHF.
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Keywords: Cardiac power; Vascular resistance; Acute congestive heart failure

1. Introduction

Acute congestive heart failure (CHF) is a common disease, accounting for over 700 000 annual admissions to hospitals in the USA alone. We have recently suggested that this disease can be divided into four major clinical syndromes [1]: (1) pulmonary edema, (2) cardiogenic shock, (3) hypertensive (HTN) crisis and (4) exacerbated systolic CHF. However, the diagnosis of these clinical syndromes of acute CHF may be difficult, due to an overlap in symptoms and signs among the different syndromes as well as lack of objective criteria for their diagnosis. For example, both cardiogenic shock and pulmonary edema patients present with severe circulatory and respiratory distress and in both cases CI is low and wedge pressure is high. However, these two clinical syndromes have a completely different course (mortality rates at 1-month in the SHOCK study [2] were approximately 60%, compared with a mortality rate of approximately 10% for pulmonary edema patients during the first 30 days in the RITZ-5 study [3]). In addition, the pathophysiology of the two clinical syn-

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PII: S1388-9842(03)00100-4

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dromes is completely different and their treatment is almost opposite. Moreover, even the diagnosis of acute CHF is sometimes difficult, due to an overlap in signs and symptoms with those of acute exacerbations of obstructive or restrictive lung diseases and the occasional difficulty in differentiation between septic and cardiogenic shock.

Measurement of invasive hemodynamic variables, including CI and pulmonary capillary wedge pressure has been used in patients with acute decompensated and chronic compensated CHF, as well as cardiogenic shock, for more than two decades. However, despite extensive experience and numerous studies, no specific diagnostic criteria or accurate cut-off points have been determined [2,4–6]. In some studies, trends and changes in CI and wedge pressure have been used, however, no reproducible criteria for diagnosis and follow-up could be established.

Cardiac power, an index of cardiac contractility, is calculated based on the classical physical rule of fluids, i.e. power = flow × pressure, hence cardiac power index (Cpi) is the product of simultaneously measured mean arterial blood pressure (MAP) and cardiovascular flow (CI): Cpi = MAP × CI × 0.0022 [1,7–9]. The units are W/m^2. Cpi has been used extensively during recent years to evaluate patients with chronic and acute CHF. In three separate studies, Marmor and Schneeweiss [7], Tan et al. [8] and Cohen-Solal et al. [9] have demonstrated that Cpi increases during exercise (cardiac power reserve) and is the strongest predictor of outcome in patients with chronic CHF, stronger than O_2 consumption and echocardiographic ejection fraction. We have previously demonstrated [1] that in patients with exacerbated systolic CHF, baseline Cpi at admission is the strongest predictor of short- and long-term outcome. On the other hand, the main event preceding recurrent worsening heart failure was a steep increase in SVRi. In a recent analysis, we have also found that Cpi at baseline and during follow-up was the strongest predictor of outcome in a large cohort of cardiogenic shock patients (unpublished data).

The main hypothesis of the present study was that in patients with acute CHF, as Cpi decreases, SVRi should concomitantly increase. Therefore, for each Cpi decrease the SVRi increase may be adequate, too high or too low and, thus, Cpi/SVRi coupling may characterize the clinical-hemodynamic state. Therefore, in the present study, we examined in a two-dimensional representation, the relationship between changes in Cpi (pump work) and SVRi (resistance or work load) in the four clinical syndromes of acute CHF, (i.e. exacerbated systolic CHF, pulmonary edema, cardiogenic shock and HTN crisis), as well as in two control groups: (i.e. septic shock and normal subjects).

2. Methods

2.1. Inclusion criteria

Hemodynamic data was obtained in all patients undergoing right heart catheterization who were diagnosed by the usual clinical criteria as having acute CHF. We also enrolled two control groups: these were 11 patients with septic shock and 20 healthy volunteers.

2.2. Exclusion criteria

Significant valvular disease, significant brady- or tachy-arrhythmias or renal failure (creatinine >2.5 mg/dl).

2.3. Clinical diagnosis criteria

2.3.1. Exacerbated systolic CHF

Patients admitted due to signs and symptoms of worsening CHF, who were in a stable clinical condition; not fulfilling the criteria for cardiogenic shock, pulmonary edema and HTN crisis and who had EF $<35\%$ on echocardiography. (The echocardiographic criteria were used to ensure that the symptoms of dyspnea were indeed due to acute CHF.)

2.3.2. Pulmonary edema

Patients admitted due to clinical symptoms and signs of acute pulmonary congestion accompanied by findings of lung edema on chest X-ray who had severe respiratory distress accompanied by O_2 saturation $<90\%$ in room air by pulse oxymetery during the invasive measurements.

2.3.3. Cardiogenic shock

Systolic blood pressure <100 mmHg for at least 1 h, not responsive to percutaneous revascularization, mechanical ventilation, intra-aortic balloon-pump (IABP), IV fluid administration and dopamine of at least 10 μg/kg/min and accompanied by signs of end organ hypoperfusion but not accompanied by fever $>38°$ or a systemic inflammatory syndrome.

2.3.4. HTN crisis

Patients with signs and symptoms of acute CHF accompanied by high blood pressure (MAP >130 mmHg during invasive measurements); not fulfilling the criteria for pulmonary edema.

2.3.5. Septic shock

Systolic blood pressure <100 mmHg accompanied by fever $>38°$, systemic inflammatory syndrome and signs of end organ hypoperfusion for at least 3 h not responsive to IV fluids and IV dopamine of at least 10 μg/kg/min. No evidence of an acute cardiac event.

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2.4. Assessment of hemodynamic variables

Prior to enrolment in this study all patients gave written informed consent. The study protocol was approved by the local ethics review board. In all patients the hemodynamic variables were obtained during right heart catheterization using a Swan–Ganz catheter placed under fluoroscopic guidance. All measurements were obtained while patients were at least 30 s without IABP while on the same treatment used at the time the clinical diagnosis was made. Measurement of hemodynamic variables was performed at least 6 h after the last intake of an oral drug and 2 h after intravenous drug therapy.

CI was measured by thermodilution, using the mean of at least three consecutive measurements within a range of $<15\%$. In normal subjects, right heart catheterization was not performed for ethical reasons. The values used in this cohort were obtained by standard noninvasive cuff blood pressure measurement and evaluation of CI by the FDA approved NICaS™ 2001, a noninvasive continuous cardiac output monitor [10]. Therefore, wedge pressure was not assessed in normal subjects. Instead, we used standard values documented in the literature [11].

2.5. Calculation of hemodynamic variables

Cpi was determined as $\text{MAP} \times \text{CI} \times 0.0022$ and SVRi was determined as (MAP − right atrial pressure (RAP)/CI. As RAP was not measured in normal subjects, it was estimated to be 10% of MAP [11].

2.6. Echocardiographic evaluation

All patients underwent routine echocardiographic evaluation after initial stabilization. This included visual estimation of cardiac function, evaluation of valvular function and gross estimation of signs of diastolic dysfunction.

2.7. Statistical methods

The five clinical groups were compared with regard to all parameters using a one-way analysis of variance (ANOVA). Therafter, the Ryan–Einot–Gabriel–Welsch Multiple Range Test was used for pair-wise comparisons between the groups, while Dunnett's *t*-test was used to compare all groups to the healthy controls.

A one-sample *t*-test was performed to compare mean wedge pressure in each group to the wedge pressure of normal people (<12 mmHg).

In order to determine the usefulness of the hemodynamic parameters to discriminate between the clinical syndromes, ROC curves, derived from a logistic regression model were applied to the data to determine the best cut-off point for the various parameters, in terms of highest sensitivity and specificity.

2.8. Cpi/SVRi diagnostic graph

A classification rule was developed using second order discriminant analysis. The normality of the distribution of Cpi and SVRi was examined by the Wilk–Shapiro test. Due to the skewness of the data in some groups, both variables (CPi and SVRi) were transformed into log scale for better approximation to normality. Since the number of patients with HT crisis was small they were considered together with the exacerbated systolic CHF group. The classification used two steps. In the first step the rule separated three classes: septic shock, cardiogenic shock and a combined group, which included the normal controls, compensated CHF and pulmonary edema patients (N–C–P). If, after the first step the patient was defined as N–C–P, the second classification was used to differentiate between the normal, exacerbated systolic CHF and pulmonary edema subgroups.

All calculations were performed by SAS 6.12 (SAS Institute Inc., Cary, NC) using procedures FREQ, MEANS, GLM, DISCRIM, GPLOT.

Alfa level: 5%.

3. Results

Eighty-nine consecutive patients admitted due to acute CHF and LV dysfunction (exacerbated systolic CHF, $n=56$; pulmonary edema, $n=11$; cardiogenic shock, $n=17$; and HTN crisis, $n=5$) as well as 11 patients with septic shock and 20 healthy volunteers were enrolled in the study. Baseline characteristics of the different patient groups are presented in Table 1. The mean CI, wedge pressure, MAP, SVRi and Cpi according to clinical diagnosis are presented in Table 2.

3.1. Hemodynamic variables

3.1.1. Cardiac index (*Fig. 1*)

The average values of CI were significantly lower in patients with acute CHF and higher in patients with septic shock. ROC analysis found a cut-off point of $\text{CI} < 2.7$ l/min/m^2 useful for the determination that a patient had acute CHF (sensitivity = 1, specificity = 0.99). However, values between 1.2 and 2.7 l/min/m^2 could be found in all patients with exacerbated systolic CHF and HTN crisis as well as 73% of patients with pulmonary edema and 47% of patients with cardiogenic shock. Moreover, the mean CI of patients with pulmonary edema and cardiogenic shock was found to be almost identical (1.4 ± 0.4 vs. 1.35 ± 0.7 l/min/m^2, P = ns).

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Table 1
Baseline characteristics of the five patient groups

	Normal volunters	Septic shock	Exacerbated systolic CHF	Pulmonary edema	Cardiogenic shock
Sex (male:female)	12:8	7:4	51:10	5:6	11:6
Age (years)	60±8	55±11	69±10	73±12	67±11
Weight (kg)	79±14	77±10	72±8	70±9	80±14
Body surface area (m^2)	1.92±0.22	1.91±0.23	1.88±0.21	1.81±0.24	1.92±0.24
IHD (%)	0	18	79	73	100
Previous MI	0	9	62	55	18
EF (%)	55±3	46±9	27±5	41±10	24±6
Diabetes mellitus (%)	20	73	66	66	53
Current smokers (%)	60	55	36	44	53
Hypertension (%)	50	45	56	88	71
Hyperlipidemia (%)	65	73	66	66	53
Baseline creatinine		135±75	124±55	144±81	110±47
Medications for CHF					
Diuretic (%)	0	0	82	91	6
Digoxin (%)	0	0	33	45	0
ACE inhibitor/AII blocker (%)	0	9	95	91	29
Beta-blocker (%)	0	9	62	55	24
Nitrate (%)	0	0	41	55	0

IHD, ischemic heart disease; MI, myocardial infarction; EF, ejection fraction; CHF, congestive heart failure.

3.1.2. Mean arterial blood pressure

By virtue of their clinical definition, the average values of MAP were higher in patients with HTN crisis and lower in those with septic and cardiogenic shock. However, large areas of overlap were found between pulmonary edema, HTN crisis and exacerbated systolic CHF (MAP > 100 mmHg) and between exacerbated systolic CHF, cardiogenic shock and septic shock (MAP < 100 mmHg).

3.1.3. Pulmonary capillary wedge pressure (*Fig. 2*)

The mean wedge pressure was significantly higher in patients with acute CHF and lower in patients with septic shock. The analysis was based on normal values reported in the literature (< 12 mmHg [8]) ($P = 0.001$). However, the overlap of wedge pressure in the different acute CHF groups was extensive. Values between 12 and 38 mmHg were found in 82, 64, 76 and 18% of patients with exacerbated systolic CHF, pulmonary edema, cardiogenic shock and septic shock, respectively.

3.1.4. Cardiac power index (*Fig. 3*)

Compared with the normal controls, the mean values of Cpi were low in patients with exacerbated systolic CHF and pulmonary edema and extremely low in

Table 2
Baseline distribution of the various hemodynamic parameters in the six diagnosis groups presented as means and S.D.

	Exacerbated systolic CHF	Pulmonary edema	Cardiogenic shock	HTN crisis	Septic shock	Normal
N	56	11	17	5	11	20
SVRi	44.9±8.0	88.2±16.7	55.6±31.1	54.3±3.2	11.8±1.1	25.2±4.1
Cpi	0.47±0.13	0.4±0.13	0.22±0.08	0.75±0.04	0.8±0.13	0.62±0.08
Wedge	25.5±7.2	32.7±8.6	23.3±6.5	28.5±4.5	11.4±7.7	–
MAP	101±18	131.4±12.7	72.2±11.3	150±10.5	68.2±5.4	87.9±8.85
CI	2.06±0.33	1.37±0.32	1.42±0.64	2.24±0.37	5.2±0.5	3.2±0.36

The results of the ANOVA for comparisons between exacerbated systolic CHF (CHF), pulmonary edema (edema) and cardiogenic shock (shock) patients

Parameter groups	*P*-value for overall group comparison (ANOVA)	*P*-value for paired comparisons (Ryan–Einot–Gabriel–Welsch multiple range test)		
		CHF-edema	CHF-shock	Edema-shock
CI	0.0001	+	+	
Wedge	0.0037	+		+
SVRi	0.0001	+	+	+
CPi	0.0001		+	+

N, number of patients; SVRi, systemic vascular resistance index (wood m^2); Cpi, cardiac power index (mmHg l/min/m^2); wedge, pulmonary capillary wedge pressure (mmHg); MAP, mean arterial blood pressure (mmHg); CI: cardiac index (l/min/m^2). +, Significant group difference.

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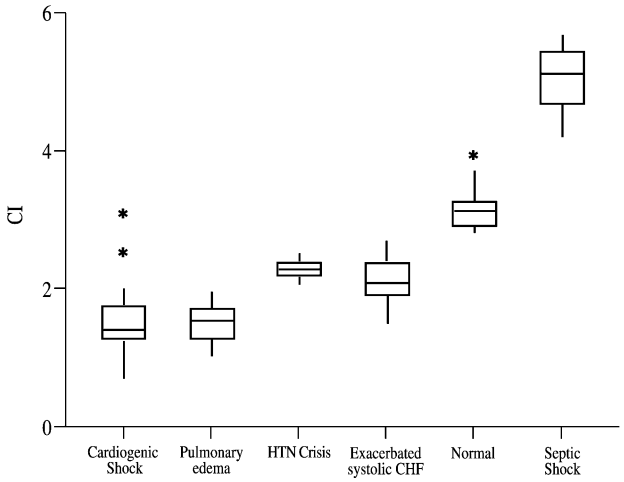

Fig. 1. CI (l/min/m^2) Box-plots (median and 25–75% percentile range) in patients with the different syndromes of acute CHF and patients with septic shock and normal controls.

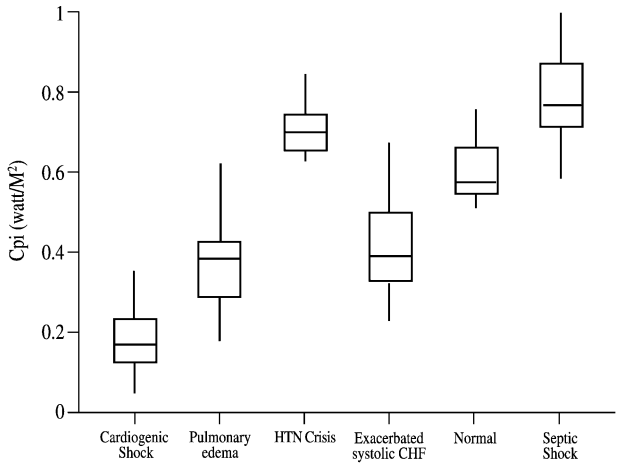

Fig. 3. Cpi (W/m^2) Box-plots (median and 25–75% percentile range) in patients with the different syndromes of acute CHF and patients with septic shock and normal controls.

patients with cardiogenic shock. However, some overlap was encountered among the five groups.

3.1.5. Systemic vascular resistance index (*Fig. 4*)

Average values of SVRi were significantly higher in all patients with exacerbated systolic CHF, HTN crisis and extremely high in patients with pulmonary edema, but were lower in patients with septic shock. SVRi was found to be instrumental in the diagnosis of pulmonary edema. All patients with this clinical syndrome had SVRi $>$ 67 wood m^2, while SVRi values in all other patient groups, as well as in normal subjects, were significantly lower than this value.

3.2. Cpi/SVRi diagnostic graph (*Fig. 5*)

Since the number of patients with HTN crisis was small they were included in the exacerbated systolic CHF group. Distributions of SVRi and Cpi were highly skewed. The normality of the distribution of Cpi and SVRi was assessed by the Wilk–Shapiro test. The results showed that Cpi and SVRi distribution was not normal for the normal volunteers ($P = 0.03$ for Cpi), the exacerbated systolic CHF patients($P = 0.007$ for Cpi and $P = 0.04$ for SVRi) and the cardiogenic shock patients($P = 0.016$ for SVRi).

However, log(SVRi) and log(CPi) were normally distributed ($P =$ ns for both Cpi and SVRi in all patient groups). Therefore, for the analysis we used only log

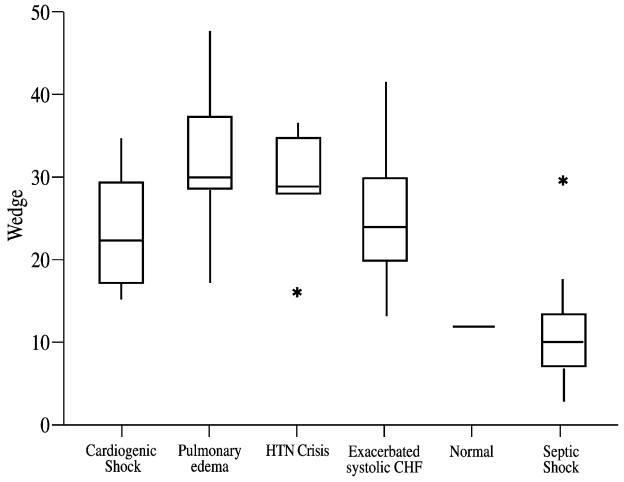

Fig. 2. Pulmonary capillary wedge pressure (mmHg) Box-plots (median and 25–75% percentile range) in patients with the different syndromes of acute CHF and patients with septic shock and normal controls.

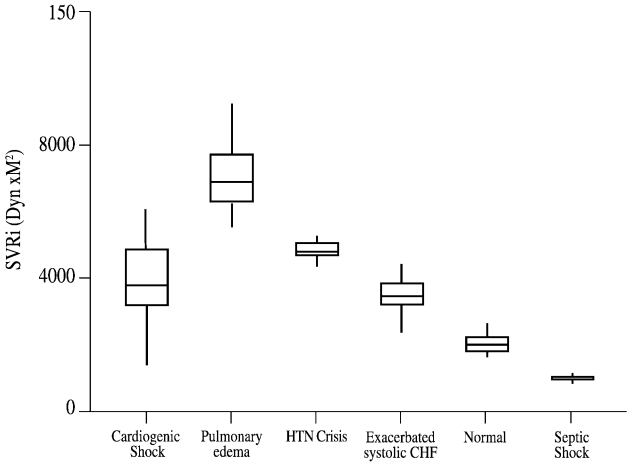

Fig. 4. Systemic vascular resistance index (SVRi) (wood m^2) Box-plots (median and 25–75% percentile range) in patients with the different syndromes of acute CHF and patients with septic shock and normal controls.

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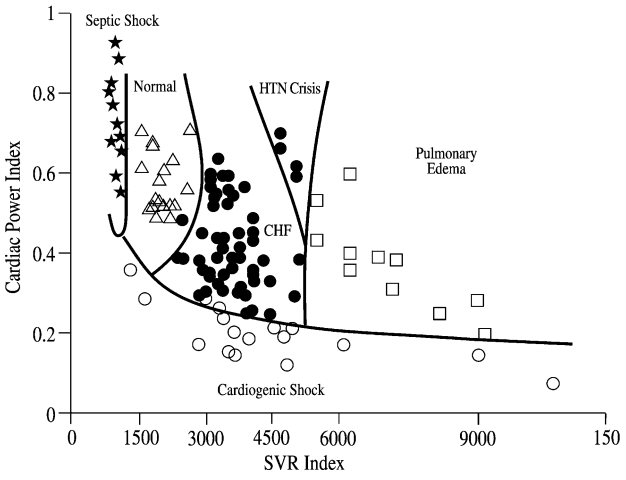

Fig. 5. Diagnostic graph for classification of the hemodynamic status of patients with different syndromes of acute CHF.

values. The distribution of the two log parameters (Cpi and SVRi) was different among the five groups, however, none enabled separation of the groups (Table 3). These data suggested that separation may be possible using two-dimensional discriminant analysis. We used classical discriminant analysis for normal distributions with unequal covariance matrices because the small numbers of observations in two of the groups prevented us from using more flexible kernel functions.

Due to large variability of variances of the parameters in the five groups, we could not suppose equal covariance matrices in the groups. (The test of homogeneity of within covariance matrices gives $P=0$.)

3.2.1. Classification rule

The calculations leading to the classification rule and Cpi/SVRi diagnostic graph are given in Appendix A.

3.2.2. Classification results

The results of the application of the classification rule to the sample are presented in Table 4.

3.2.3. Performance of the classification rule

The performance of a diagnostic procedure with only two possible results and two classes of patients is usually expressed using measures like positive (negative) predictive value [12] or diagnostic odds ratio [13]. For more complex tests with many outcomes and many classes of patients the overall performance may be expressed through the difference between proportion of erroneously classified patients with and without using the test. This measure is usually called Lambda asymmetric (R|C), where R (rows) is the true group and C (column) is the group where the patient was classified.

Table 3
Number of observations classified into the correct clinical group using log(Cpi) or log(SVRi) only

Group	Cardiogenic shock	Exacerbated systolic CHF	Normal	Pulmonary edema	Septic shock	Total
(a) Number of observations classified into appropriate groups: classification using log(CPi) only						
Cardiogenic Shock	13	4	0	0	0	17
Exacerbated systolic CHF	1	44	14	0	2	61
Normal	0	9	8	0	3	20
Pulmonary edema	1	9	1	0	0	11
Septic shock	0	0	3	0	8	11
(b) Number of observations classified into appropriate groups using log(SVRi) only						
Cardiogenic shock	2	12	1	2	0	17
Exacerbated systolic CHF	0	58	3	0	0	61
Normal	0	3	17	0	0	20
Pulmonary edema	2	0	0	9	0	11
Septic shock	0	0	0	0	11	11

Table 4
Number of observations classified into the correct clinical group using log(SVRi) and log(CPi)

Group	Cardiogenic shock	Exacerbated systolic CHF	Normal	Pulmonary edema	Septic shock	Total
Cardiogenic shock	15	2	0	0	0	17
Exacerbated systolic CHF	0	60	1	0	0	61
Normal	0	0	20	0	0	20
Pulmonary edema	2	0	0	11	0	11
Septic shock	0	0	0	0	11	11

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For our data Lambda (R|C)=0.95 (S.D. (Lambda)= 0.03) which corresponds to three errors of classification according to the classification rule, instead of 59 errors of classification according to the prior probabilities.

4. Discussion

During the last decade the pathogenesis of CHF has become clearer. The emphasis on cardiac performance as the sole pathogenic mechanism of CHF has changed to a more comprehensive understanding of the importance of the interaction between cardiac contractility, neurohormonal and inflammatory control mechanisms and vascular resistance. We have recently studied the treatment of the acute CHF syndromes of pulmonary edema and cardiogenic shock and have shown that treatment modalities with significant vascular effect are effective in improving the outcome of these patients [14–16]. These findings substantiated our theory that the SVRi reaction to the decrease in Cpi determines the hemodynamic condition and clinical syndrome of patients with acute CHF.

4.1. Classical hemodynamic monitoring

CI is the most popular parameter used in invasive hemodynamic monitoring of patients with acute CHF. However, the results of the present study as well as previous ones [2,4–6] show that CI measurements are not sufficient for the diagnosis and treatment titration in patients with acute CHF. This might be explained by the fact that CI is actually a measure of cardiovascular flow. Hence, CI (flow) is determined by both cardiac contractility and vascular resistance and, therefore, may change dramatically when Cpi decreases but also with even mild changes in SVRi. Pulmonary capillary wedge pressure is the second most popular hemodynamic variable used in hemodynamic monitoring, since it represents the hydraulic pressure transmitted backwards to the pulmonary circulation, and hence, is an important determinant of pulmonary edema. However, wedge pressure cannot be used for the exact diagnosis of the different clinical syndromes of acute CHF, due to the extent of overlapping values between patients with exacerbated systolic CHF, HTN crisis and even cardiogenic shock.

4.2. Cpi and SVRi and their role in patients with acute CHF

Cpi as measured in the present study [1,8,9] is a simplified version of a previously described method of measuring cardiac contractility [7]. This value is derived from the entire cardiac cycle (instead of instantaneous measurements) and is the product of the mean pressure and flow. Cpi has been shown to be the best predictor of outcome in chronic CHF patients [7–9], exacerbated systolic CHF [1] and cardiogenic shock (unpublished data).

In the present study, we found that in patients with exacerbated systolic CHF either Cpi was decreased or SVRi was increased or both changes occurred. In a previous study, we described the sequence of events leading to acute heart failure [1]. In most patients an acute CHF event starts with a progressive decrease in cardiac contractility and power (Cpi). Thereafter, as Cpi decreases, neurohormonal vascular control mechanisms are activated and SVRi increases [1,17]. This increase is a very important protective mechanism for two reasons:

1. The increase in SVRi in the face of decreased contractility maintains blood pressure and the perfusion of vital organs.
2. This afterload increase (while within certain limits) may improve contractility (possibly through the Gregg phenomenon [18]), which may account for the 'normal' Cpi we observed in some patients with echocardiographically demonstrated systolic dysfunction.

However, SVRi increase in response to Cpi decrease is not uniform. It can be appropriate (thus, leading to a compensated state), inappropriately low (thus, leading to low blood pressure, forward hypoperfusion and cardiogenic shock) or inappropriately high (thus, inducing an extreme afterload mismatch leading to pulmonary edema).

Indeed, in the present study, in patients who were clinically diagnosed as cardiogenic shock, Cpi was found to be extremely low, however, SVRi was only slightly increased. This imbalance between very low Cpi and inadequate increase in SVRi probably resulted in low blood pressure and decreased perfusion pressure of vital organs including the heart. This decrease in coronary perfusion might lead to decreased contractility inducing a vicious cycle of low contractility, low SVRi and reduced perfusion. For this reason, in a previous study [15] we treated patients with cardiogenic shock, by short-term administration of a peripheral vasoconstrictor (L-NMMA) with good clinical response.

On the other hand, in patients diagnosed as pulmonary edema, despite what appears to be a similar clinical presentation (pulmonary congestion, clammy extremities, low CI and high wedge pressure), the pathophysiological findings as well as the treatment, are the complete opposite. In patients with pulmonary edema, we measured Cpi values similar to those in exacerbated systolic CHF, however, SVRi was markedly increased. These findings are collaborated by the study by Gandhi et al. [19] showing a dramatic increase in blood pressure in patients with pulmonary edema. We hypothesize that this increase in SVRi might be an inappropriate

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response, related to neurohormonal, endothelial and perhaps inflammatory activation [20,21]. This remarkable increase in SVRi induces an afterload mismatch, reducing CI and increasing intracardiac pressures, LVEDP and wedge pressure, resulting in the severe congestive symptoms of pulmonary edema. Therefore, as previously suggested [14,16,22,23], vasodilator treatment is effective in the treatment of pulmonary edema.

4.3. Two-dimensional graphic representation of Cpi/SVRi and its use in the treatment of cardiogenic shock and pulmonary edema

In the present study, we found that when plotting on a two-dimensional graph the results of Cpi and SVRi for individual patients, each clinical group of patients could be segregated into a specific area on the graph which could be bound by a mathematically defined line (Fig. 5). This graph enables exact clinical diagnosis of most (95%) patients with exacerbated systolic CHF, pulmonary edema, HTN crisis, cardiogenic shock and septic shock. Of course, the boundaries on the graph are somewhat arbitrary, since the definitions of the syndromes are as used by the medical community, and therefore, arbitrary. However, this two-dimensional representation enables a better understanding of the pathophysiology of the different syndromes of acute CHF.

We believe that this new and simple diagnostic tool may become useful for the initial evaluation of acutely decompensated patients, while the clinical diagnosis has not yet been established and initiation of appropriate disease-specific treatment is crucial. This might become even more important with the advent of new devices that accurately measure CI noninvasively. The combination of noninvasive MAP and CI measurement, Cpi and SVRi calculation and the two-dimensional Cpi/SVRi graph could enable improved diagnosis of patients even in paramedic units and in emergency rooms.

Furthermore, this method may become an important tool for monitoring the patients' response to treatment.

4.4. Limitations

The results of the present study are based on a relatively small number of patients, and therefore, need confirmation by prospectively evaluating a larger group of patients with acute CHF. Also, the measurements in the present study were performed by thermodilution, which has an inherent 10–15% deviation in measuring cardiac output. Finally, cardiac power calculations were performed using whole-cycle measurements (cardiac output and MAP). Although we recognize that the cardiovascular system operates in a pulsatile manner, cardiac power calculated according to the methodology used in the present study has previously been shown to be a useful measure of cardiac contractility and contractility reserve in chronic and acute CHF as well as in cardiogenic shock.

Appendix A: Classification rule

Given a patient with measured values of SVRi and Cpi, the classification may be performed either (A) through special calculations or (B) using the 'Graph for classification of CHF patients (Cpi/SVRi graph)'.

(A) *Classification using calculations*

Step 1. Calculate three values ***v1***, ***v2***, ***v3*** according to the formulas below.

$$\boldsymbol{v1} = \mathrm{LCPi2}\times 21.54 + 2\times \mathrm{LCPi}\times \mathrm{LSVRi}\times 10.61 + \mathrm{LSVRi2}\times 59.44 - \mathrm{LCPi}\times 305.24 - \mathrm{LSVRi}\times 417.70 + 1408.89$$

$$\boldsymbol{v2} = \mathrm{LCPi}^2\times 10.12 + 2\times \mathrm{LCPi}\times \mathrm{LSVRi}\times 5.67 - \mathrm{LSVRi2}\times 4.99 - \mathrm{LCPi}\times 135.81 - \mathrm{LSVRi}\times 90.11 + 482.61$$

$$\boldsymbol{v3} = \mathrm{LCPi2}\times 7.29 + \mathrm{LCPi}\times \mathrm{LSVRi}\times 2.57 + \mathrm{LSVRi2}\times 4.09 - \mathrm{LCPi}\times 97.41 - \mathrm{LSVRi}\times 58.22 + 368.16$$

Classify the patient
into the group 'Septic shock', if ***v1*** is the smallest value
into the group 'Cardiogenic Shock', if ***v2*** is the smallest value
if ***v3*** is the smallest value go to step 2

Step 2. Calculate three values ***v4***, ***v5***, ***v6*** according to the formula below.

$$\boldsymbol{v4} = \mathrm{LCPi2}\times 6.45 - 2\times \mathrm{LCPi}\times \mathrm{LSVRi}\times 0.45 + \mathrm{LSVRi2}\times 16.01 - \mathrm{LCPi}\times 65.16 - \mathrm{LSVRi}\times 116.53 + 391.67$$

$$\boldsymbol{v5} = \mathrm{LCPi2}\times 17.75 + 2\times \mathrm{LCPi}\times \mathrm{LSVRi}\times 26.56 + \mathrm{LSVRi2}\times 54.27 - \mathrm{LCPi}\times 420.26 - \mathrm{SVRi}\times 758.55 + 2775.78$$

$$\boldsymbol{v6} = \mathrm{LCPi2}\times 32.95 + 2\times \mathrm{LCPi}\times \mathrm{LSVRi}\times 3.09 + \mathrm{LSVRi2}\times 19.72 - \mathrm{LCPi}\times 390.74 - \mathrm{LSVRi}\times 161.49 + 1355.57$$

Classify the patient
into the group 'Exacerbated Systolic CHF', if ***v4*** is the smallest value among ***v4***, ***v5***, ***v6*** and $\mathrm{LSVRi} < \log(67)$
into the group 'Pulmonary Edema', if ***v5*** is the smallest value among ***v4***, ***v5***, ***v6*** and $\mathrm{LSVRi} > \log(67)$
into the group 'Normal', if ***v6*** is the smallest value among ***v4***, ***v5***, ***v6***

The value of $\mathrm{SVRi} = 67$ was used to separate patients with exacerbated systolic CHF from patients with pulmonary edema since the group of 'pulmonary edema' was rather small and by classifying these patients according to the usual rule we did not receive a separating line for Cpi measures > 250 W/m^2.

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(B) *Classification using the diagnostic graph*

Put the point (CPi, SVRi) on the diagnostic graph Fig. 5 or point (LCPi, LSVRi) and classify the patient according to the area of the graph, where the point is located.

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