Prognostic Value of Left Ventricular Longitudinal Strain During Sepsis

Valeur Pronostique du Strain Longitudinal Ventriculaire Gauche au Cours du Sepsis

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Summary

Introduction: Sepsis, a severe infection leading to systemic inflammation and multi-organ dysfunction, often includes myocardial dysfunction, which significantly impacts mortality. Doppler-echocardiography is crucial for assessing cardiac function in these patients.

Aim: This study aimed to evaluate the prognostic value of left ventricular (LV) systolic function using global longitudinal strain (GLS) in patients with sepsis.

Methods: This was a prospective study including 30 patients admitted to the intensive care unit (ICU) of military hospital of Tunis within 48 hours of diagnosis of severe sepsis or septic shock. Standard transthoracic echocardiography (TTE) and LV Global Longitudinal Strain (LVGLS) measurements were performed within 48 hours of sepsis onset, then re-evaluated at 72 hours and 7 days.

Results: The mean age of patients was 56 years, with a 60% mortality rate. In the non-survival group, LV end-diastolic (LVEDD), end-systolic (LVESD) diameters, and ejection fraction (LVEF) remained preserved. Survivor patients, however, showed LV dilation early in sepsis. Critically, GLS was significantly better (less impaired) in the survival group compared to non-survivors at both day 3 (-18.44% vs. -14.68%, p=0.013) and day 7 (-17.74% vs. -11.75%, p=0.005). This suggests that GLS is frequently reduced in non-survivors with septic shock within 3 days.

Conclusion: This study concludes that GLS is a significant predictive factor for mortality in patients with septic shock admitted to the ICU.

Keywords

Sepsis, Cardiac function, Echocardiography, Left ventricule, Myocardial deformation, Strain

Résumé

Introduction : Le sepsis, une infection grave entraînant une inflammation systémique et une défaillance multi-organe, inclut souvent une dysfonction myocardique qui impacte significativement la mortalité. L'échocardiographie est cruciale pour évaluer la fonction cardiaque chez ces patients.

Objectif : Cette étude visait à évaluer la valeur pronostique de la fonction systolique du ventricule gauche (VG) en utilisant le strain longitudinal global (SLG) chez les patients atteints de sepsis.

Méthodes : Il s'agissait d'une étude prospective incluant 30 patients admis en unité de soins intensifs (USI) de l'hôpital militaire de Tunis dans les 48 heures suivant le diagnostic de sepsis sévère ou de choc septique. Des mesures standard d'échocardiographie transthoracique (ETT) et de la déformation longitudinale globale (SLG) du VG ont été réalisées dans les 48 heures suivant le début du sepsis, puis réévaluées à 72 heures et à 7 jours.

Résultats : L'âge moyen des patients était de 56 ans, avec un taux de mortalité de 60 %. Dans le groupe des non-survivants, les diamètres télédiastolique (LVEDD) et télésystolique (LVESD) du VG, ainsi que la fraction d'éjection (LVEF), sont restés conservés. Les patients survivants ont cependant montré une dilatation du VG au début du sepsis. De manière critique, le SLG était significativement meilleure (moins altérée) dans le groupe des survivants par rapport aux non-survivants, à la fois au jour 3 (-18,44 % contre -14,68 %, p=0,013) et au jour 7 (-17,74 % contre -11,75 %, p=0,005). Cela suggère que le SLG est fréquemment réduit chez les non-survivants atteints de choc septique dans les 3 jours.

Conclusion : Cette étude conclut que le SLG est un facteur prédictif significatif de la mortalité chez les patients atteints de choc septique admis en USI.

Mots-clés

sepsis; fonction cardiaque ; échocardiographie; ventricule gauche; déformation myocardique ; strain.

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INTRODUCTION

Severe sepsis and septic shock are a major public health problem, due to their high morbidity and mortality. It is one of the most common causes of death in intensive care units all over the world [1]. Sepsis and septic shock are frequently associated with myocardial failure [2]. The incidence of myocardial failure during sepsis varies from study to study depending on evaluation methods and diagnostic criteria [3]. Mortality rises from 20-30% in its absence, to 40-70% in its presence [4].

Two-dimensional echocardiography is a non-invasive, simple imaging technique for assessing heart function in sepsis and septic shock [5]. To access left ventricular (LV) systolic function, traditional echocardiography's LV ejection fraction (LVEF) is most frequently used. It is dependent of fluid state and afterload, and has a poor predictive value in patients with septic shock, among other limitations.

An improved method for assessing intrinsic left ventricular function is LV global longitudinal strain (GLS) mesured by speckle tracking echocardiography (STE), which is a more sensitive, repeatable, and dependable technique for assessing LV systolic function [6] [7]. GLS is a prognostic indicator of mortality and cardiovascular events [5] [8]. Evidence of the prognostic significance of LV GLS for patients with septic shock remains to be proved, despite multiple studies demonstrating the connection of LV GLS with these patients' outcome [9] [10].

Thus, the purpose of this study was to assess the predictive value of an LV systolic function in patients experiencing septic shock using STE. Our hypothesis was that patients suffering from septic shock, lower LV GLS (less negative values, which indicate LV systolic dysfunction) would be linked to a higher death rate.

POPULATION AND METHODS

Study Population

This was a mono-centric, prospective, descriptive and analytical study conducted in the intensive care unit (ICU) of military hospital of Tunis.

All patients who were hospitalized for septic shock that occured within 24 hours prior to ICU admission and who were 18 years of age or older were screened for eligibility over a period of 15 months. The criteria of sepsis, along with persistent hypotension requiring vasopressors to maintain a mean arterial pressure of at least 65 mmHg and a serum lactate level greater than 2 mmol/L despite adequate fluid resuscitation, were combined to define septic shock in accordance with the sepsis-3 definition [11]. The patients were managed in accordance with the 2016 Surviving Sepsis Campaign guidelines [12]. Heart failure, ischemic heart disease, moderate-to-severe valvular disease, valve replacement surgery, cardiac arrhythmia, postcardiac arrest, inadequate echocardiographic image quality, and patient or family refusal to participate were among the exclusion criteria.

Baseline clinical variables include age, gender, comorbidities, hemodynamic parameters, vasopressor dose, and scores for clinico-biological severity, such as the Simplified Acute Physiologic Score (SAPSII), Acute Physiology and Chronic Health Evaluation (APACHE II), and the Sequential Organ Failure Assessment (SOFA) related to sepsis, which is calculated at day 1, day 3, and day 7 of diagnosis. Laboratory findings were collected and then, within 48 hours of the diagnosis, a standard trans-thoracic echocardiography (TTE) was conducted; it was then repeated on days 3 and 7.

Echocardiography and Two-Dimensional Speckle Tracking

Echocardiography was performed by the same operator, using the Vivid 7 echocardiographic device (GE Healthcare) with an M4S probe generating a frequency of 4MHz. Three or more successive cardiac cycles had to be recorded in order to create an echocardiographic cine loop. A frame rate of 50–90 frames per second was used to capture the images.

The entire echocardiographic examination was stored in digital form, enabling images to be analyzed afterwards.

LV diameters were collected using M-mode tracing guided by a two-dimensional (2D) examination: LV end-diastolic diameter (LVEDD), LV end-systolic diameter (LVESD).

LVEF was calculated using the Simpson Biplan method, based on LV end-diastolic volume (LVEDV) and LV end-systolic volume (LVESV) measured in the apical four- and two-chamber views using the guidelines set forth by the American Society of Echocardiography [13].

The apical four-chamber view was used to measure the Doppler mitral valve peak early (E) and late (A) diastolic velocities as well as the E/A velocity ratio. Using tissue Doppler imaging, the mean values of the early diastolic mitral annular tissue velocity (e') and the myocardial systolic excursion velocity (S') were determined.

For every patient, an analysis of speckle tracking echocardiography was conducted using offline software on the EchoPAC workstation (GE-Vingmed Ultrasound AS).

LV GLS was measured in the apical four-chamber, two-chamber, and long-axis views. Using a point-and-click method, the software automatically traced a region of interest that included the entire myocardium.

If necessary, the region-of-interest width was manually changed to achieve the best alignment after the myocardial tracking was confirmed. After that, six standard segments were created from the region of interest of the apical images that outlined the entire left ventricular wall, and six time-strain curves were produced in accordance with those segments. The six segments of the three standard apical views (two- and four-chamber and apical long-axis views) were used to generate the 18 segments' peak systolic values, which were then averaged to determine the GLS [13]. The GLS is represented as a change percentage (%). GLS values that are negative indicate a myocardial contractile capacity.

Statistical Analysis

For analysis, SPSS version 20.0 for Windows was used. For qualitative variables, we determined the relative percentages of each category. For quantitative variables, we calculated means, medians, standard deviations and extremes. Comparisons of the means of quantitative variables were made using Student's t-test. Relationships between 2 quantitative variables were examined using Pearson's correlation coefficients. $P < 0.05$ was considered statistically significant.

Legal and ethical aspects

We obtained the oral consent of all the patients included in our study. Confidentiality of medical records was respected during data collection and analysis. We have no conflict of interest to declare.

RESULTS

General characteristics of the population

During the study period, 34 patients with septic shock were admitted to the intensive care unit over a 15-month period.

Four patients were excluded secondarily due to poor image quality from echocardiography. Thus, 30 patients were analyzed.

The average age was 53 ± 17 years, with 16 patients (53.3%) being male. The SOFA score was 8 ± 4 the first day, the APACHE II score was 19 ± 10, and the SAPS II score was 41 ± 17. Fourteen patients (46.7%) had diabetes. The other comorbidities were dyslipidemia (23.3%), dysthyroidism (13.3%) and renal failure (10%).

The respiratory tract (33.3%), abdomen (23.3%), meningeal (23.3%), soft tissue (10%), urinary tract (6.6%), and multifocal (3.3%), were the sources of infection. ICU and hospital stay duration averaged 22.8 ± 21.7 days. There was a 60% rate of mortality within the hospital.

Table 1 summarizes clinical and biological characteristics of the survival group and non-survival group. There was no significant difference in age, sex, mean duration of mechanical ventilation (MV), SOFA score at D1, Troponin I levels at all 3 measurements and NT-pro BNP at D1 between the two groups. However, APACHE II, SAPS II, SOFA scores at D3 and D7 and catecholamine requirements at D3 and D7 were significantly elevated in the non-survivor group, with a significant difference (p= 0.02, p= 0.02, p =0.001 ,p=0.00, p=0.03 and p= 0.01 respectively).

Table 1. Comparative table of clinical and biological characteristics of the two groups

Variables	Survival group	Non-survival group	p
Age (years)	52 ± 17	55 ± 18	0.69
Sexe (M/F)	8/4	8/10	0.24
Severity score			
APACHE II score	12.83 ± 6.39	23.22 ± 9.85	0.02
SAPS II score	29.67 ± 13.69	48.61 ± 16	0.02
SOFA score D1	6.58 ± 4.4	9.11 ± 4	0.12
SOFA score D3	4.67 ± 3.39	9.81 ± 4.15	0.001
SOFA score D7	3.8 ± 2.82	11.25 ± 5	0,68
Source of infection			
Meningeal	2	5	-
Respiratory tract	4	6	
Abdomen	4	3	
Urinary tract	0	2	
Type of infection (%)			
Community	50 %	33.3%	-
Nosocomial	50 %	66.7%	
Mechanical ventilation			
MV (%)	66.66%	100%	-
Mean duration of MV (days	21.42 ± 27.85	16.39 ± 16.37	0.58
Biology:			
Troponine I D1 (ng/ml)	0.074 ± 0.09	0.083 ± 0.13	0.83
Troponine I D2 (ng/ml)	0.063 ± 0.067	0.22 ± 0.43	0.15
Troponine I D3 (ng/ml)	0.34 ± 0.77	1.72 ± 3.83	0.24
NT-Pro BNP (pg/ml)	2602.08 ± 3727.455	2748.39 ± 2215.699	0.9
Catecholamine requirements			
D1 (%)	75	83.33	0.6
D3 (%)	41.7	87.5	0.03
D7 (%)	40	92.3	0.01

H: Male; F: female; APACHE II : Acute physiology and chronic health evaluation ; SAPS II: Simplified Acute Physiologic Score; SOFA: systemic organ failure score; MV: mechanical ventilation ; D1: day 1; D3: day 3; D7: day 7, p is significant if <0.05.

Echocardiographic variables

Comparison of standard echocardiographic parameters between the two groups (survivors and non-survivors) showed that values for LVEDD, LVESD and LVEF were globally preserved in the non-survivor group. On the other hand, comparison between the two groups enabled us to conclude that the survivors dilated their LV from day 3 of the onset of sepsis and that this dilation persisted on day 7 (survivors vs. non-survivors: LVEDD at D3: 47.63 ± 4.17mm vs 44±3.84 mm with p = 0.031 and LVEDD at D7: 49.6 ± 4.4 mm vs 44.15 ± 4.56 mm, with p = 0.009).

Concerning the study of myocardial deformation, LV GLS was lower in the non-survivors group both on day 3 and day 7 of the onset of the septic episode with a significant difference (survivors vs. non-survivors: LV GLS at D3: -18.44% ± 3.37 vs. -14.68% ± 4.03 with p = 0.013 and LV GLS at D7: -17.74% ± 4.53 vs. -11.75% ± 4.34 with p =0.005).

Table 2. Echocardiographic study

Variables	Survival group	Non-survival group	p-value
LVEDD (mm)			
D1	47.33 ± 5	46.94 ± 4.94	0.83
D3	47.63 ± 4.17	44 ± 3.84	0.031
D7	49.6 ± 4.4	44.15 ± 4.56	0.009
LVESD (mm)			
D1	32.66 ± 4.35	32.44 ± 5.9	0.9
D3	32 ± 4.14	34.12 ± 6.51	0.31
D7	33.8 ± 4.18	37.45 ± 4.78	0.07
LVEF (%)			
D1	64.75 ± 6.67	59.72 ± 16.82	0.26
D3	63.45 ± 7.11	57.18 ± 14.9	0.15
D7	61.7 ± 5.39	52.91 ± 14.1	0.06
S' LV (cm/s)			
D1	9.58 ± 1.67	8.83 ± 2.64	0.35
D3	9.27 ± 1.55	7.81 ± 2.34	0.063
D7	8.8 ± 1.93	7.38 ± 2.32	0.12
E (cm/s)			
D1	109.08 ± 36.62	92.72 ± 24.05	0.19
D3	92.9 ± 30.86	81.68 ± 23.27	0.32
D7	84.7 ± 23.83	66.75 ± 18.28	0.06
E/A			
D1	1.1 ± 0.32	1.26 ± 0.47	0.26
D3	1.05 ± 0.31	1.36 ± 0.47	0.054
D7	1.13 ± 0.22	1.18 ± 0.24	0.64
e' (cm/s)			
D1	10.08 ± 1.97	9.55 ± 2.87	0.55
D3	9.81 ± 2.3	7.75 ± 2.4	0.037
D7	10.5 ± 2.67	6.33 ± 2.57	0.002
E/ e'			
D1	10.42 ± 5.48	9.97 ± 3.71	0.8
D3	8.82 ± 3.69	11.8 ± 3.82	0.054
D7	8.27 ± 3.84	12.06 ± 2.55	0.018
SPAP (mmHg)			
D1	32.5 ± 11.36	40.22 ± 7.88	0.055
D3	38.63 ± 9.64	41.87 ± 9.74	0.4
D7	38.63 ± 9.58	42.91 ± 7.97	0.26
LV GLS (%)			
D1	-18.42 ± 2.8	-17.05 ± 5.05	0.35
D3	-18.44 ± 3.37	-14.68 ± 4.03	0.013
D7	-17.74 ± 4.53	-11.75 ± 4.34	0.005

LVEDD:left ventricular end-diastolic diameter; LVESD: left ventricular end-systolic diameter; LVEF: Left ventricular ejection fraction; S'LV:mitral annular peak systolic velocity; E: transmitral E-wave velocity; A: transmitral A-wave velocity; e': early diastolic peak velocity of mitral valve annulus ; SPAP: Systolic pulmonary artery pressure; LV GLS: Left ventricular global longitudinal strain, p is significant if <0.05.

We found that there was a good correlation between GLS and LVEF within three days of echocardiography (respectively at D1: r = -0.42, p = 0.021; at D3: r = -0.45 , p = 0.017 and at D7 r = -0.75 and p = 0.000 with p<0.05).

As for the seventh day of sepsis, in addition to LVEF, GLS correlated with LV S'wave, E wave, e' wave and E/e' ratio as well as SOFA score.

Table 3. Pearson correlations between LVAS, severity scores, biomarkers and standard ultrasound parameters

Variables	LV GLS D1	LV GLS D3	LV GLS D7
SOFA score	r=0.01, p= 0,91	r=0.04, p=0.82	r=0.49, p=0.024
Troponine I	r=0.05, p=0.78	r=0.005, p=0.98	r=0.53, p=0.013
LVEDD	r=-0.037, p=0.84	r=-0.27, p=0.16	r=-0.087, p=0.7
LVESD	r=0.18, p=0.32	r=0.24, p=0.22	r=0.43, p=0.054
LVEF	r=-0.42, p =0.021	r=-0.45, p = 0.017	r=-0.75, p = 0.000
S'	r=-0.36, p=0.051	r=-0.45, p=0.018	r=-0.52, p=0.015
E	r=-0.14, p=0.44	r=-0.12, p=0.52	r=-0.46, p=0.033
e'	r= -0.097, p=0.61	r=-0.42, p=0.027	r=-0.7, p=0.000
E/e' ratio	r=-0.17, p=0.92	r= 0.38, p=0.05	r=0.56, p=0.008
E/A	r=-0.09, p=0.63	r=0.26, p=0.18	r=-0.072, p=0.758

LVEDD:left ventricular end-diastolic diameter; LVESD: left ventricular end-systolic diameter; LVEF: Left ventricular ejection fraction; S'LV:mitral annular peak systolic velocity; E: transmitral E-wave velocity; A: transmitral A-wave velocity; e': early diastolic peak velocity of mitral valve annulus ; LV GLS: Left ventricular global longitudinal strain, D1: day 1; D3: day 3; D7: day 7; r: Pearson correlation, p is significant if <0.05.

DISCUSSION

This prospective study carried out in the ICU of the military Hospital had enrolled 30 patients admitted for septic shock and aimed to assess the interest of speckle tracking imaging to predict prognosis among patients with severe sepsis or septic shock.

The main finding of this study was a significant association between reduced (less negative) GLS values and mortality. Nevertheless, the most commonly adopted conventional parameter LVEF was preserved. Additionally, we found out that GLS could predict mycoardial dysfunction early on.

Prognostic value of GLS in sepsis and septic shock

One of the common findings in septic shock is myocardial dysfunction, also known as septic cardiomyopathy. The latter occurs in between 40 and 60% within the first 3 days [14].

An increasing number of studies revealed a correlation between myocardial dysfunction and mortality among patients with severe sepsis or septic shock [15] [16] [17]. In the study by Chang et al., there was an increase in ICU and in-hospital mortality among septic shock patients who had decreased LV systolic function assessed by GLS [16]. Consistent with Ricarte-Bratti et al.'s findings [18], nonsurvivors had a significantly lower LV systolic function as determined by STE. Palmieri et al [17] evaluated mortality on days 7 and 28 of hospitalization in patients hospitalized in the ICU for severe sepsis or septic shock who did not require MV, and found that LV GLS was the only parameter correlated with mortality.

According to a meta-analysis by Sanfilippo et al. [9], patients with septic shock or severe sepsis who had a lower GLS value had higher mortality.

The results we found match with previous literature reviews that assessed the prognostic significance of GLS in patients with septic shock.

Our results show that within three days, LV GLS could identify early changes in myocardial function in patients with septic myocardial dysfunction.

De Geer et al. observed that in patients with sepsis, GLS decreased within three days in a study involving fifty-five patients experiencing septic shock [19]. In an experimental research involving septic animals, strain imaging can identify subclinical LV dysfunction. Li et al. demonstrated in a rabbit model that GLS decreased two hours after endotoxin injection before LVEF changes became apparent [20]. Analogous outcomes have been documented in pigs under anesthesia who were given Escherichia coli infusions; in these cases, STE identified cardiac dysfunction prior to notable alterations in left ventricular ejection fraction and cardiac output [21].

Echocardiography evaluation of LVEF is essential for hemodynamically unstable sepsis patients, but it is heavily dependent on the hemodynamic and volume status of the patients.

In fact, since LVEF measures changes in blood pool volume directly, it is based on both volume and the pressure exerted on the myocardium [22] [23], with systolic function rising during vasodilatation and falling during vasoconstriction [23] [24].

For evaluating cardiac systolic function, GLS has been described as a sensitive, repeatable, and dependable modality [25] [26] [27]. However, it is important to remember that GLS is also reliant on LV loading conditions, particularly afterload changes, with longitudinal fibers experiencing higher wall stress because of their orientation [28] [29].

Strain correlations

The SOFA score is widely used to describe organ failure in ICU patients. Although the majority of studies use the SOFA score to predict patient outcome, there is insufficient information regarding its correlation with LV function in patients with sepsis or septic shock. Masaki et al [30] evaluated the correlation between SOFA score and LV function estimated by STE in these patients. The results suggest that a high SOFA score is associated with low LVEF, low LV systolic Strain and high LV filling pressures.

In our study, there was a good correlation between LV GLS and SOFA score at day7 ($p = 0.024$, $r = 0.49$).

Few studies have examined the correlation of LV GLS with standard echocardiographic parameters.

The study by Geer et al [10] included 50 patients admitted to the ICU for septic shock, for whom TTE was performed on day1 and day 3 of admission. They demonstrated that there was a strong correlation between LV GLS , LVEF, e' wave and E/e' ratio at day 1 of diagnosis (with respectively: $p<0.001$ and $r= -0.7$; $p<0.001$ and $r=-0.59$; $p=0.01$ and $r=0.27$), while at day 3, LV GLS correlates only with LVEF and e' wave (with respectively: $p= 0.03$ and $r = -0.44$; $p=0.06$ and $r= -0.59$).

This suggests that LVEF, which appears to reflect systolic dysfunction, is also associated with diastolic dysfunction in patients with septic shock.

The study by Zaky et al [31] found that reduced LV GLS correlated with systolic-diastolic dysfunction in patients with septic shock.

In our study, LV GLS correlated with LVEF at day 1 and day 3 of sepsis diagnosis with respectively ($r = -0.42$; $p<0.05$ and $r =-0.45$; $p=0.017$) but no correlation was found with tissue Doppler parameters at day1. However, at day 3, there was a correlation with two parameters: the LV S'wave and the E' wave.

At day 7 of sepsis diagnosis, LV GLS correlated well with LVEF, LV S'wave, E wave, e' wave and E/e' ratio.

CONCLUSION

icinterestofrightventricularechocardiographicparameters on cardiovascular mortality and rehospitalization for heart failure in acute heart failure with preserved ejection fraction and with mildly reduced ejection fraction could be a good perspective for the future.

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