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Cardiac function in Vietnamese patients with different dengue severity grades

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Abstract

Objective—Dengue continues to cause significant global morbidity and mortality. Severe disease is characterized by cardiovascular compromise from capillary leakage. Cardiac involvement in dengue has also been reported, but has not been adequately studied.

Setting—Hospital for Tropical Diseases, Ho Chi Minh City, Viet Nam.

Design—Seventy-nine patients aged 8-46 years with different dengue severity grades were studied using echocardiography including tissue Doppler imaging. The patients were split into severity grades: dengue, dengue with warning signs and severe dengue. Changes in cardiac functional parameters and haemodynamic indices were monitored over the hospital stay.

Measurements and Main Results—Patients with severe dengue had worse cardiac function compared to dengue, in the form of left ventricular (LV) systolic dysfunction with increased Left myocardial performance index (LMPI) (0.58 (0.26-0.80) vs. 0.38 (0.22-0.70), $P=0.006$). Septal myocardial systolic velocities (S') were reduced, (6.4 (4.8-10) vs. 8.1 (6-13) cm/s, $P=0.01$) as well as right ventricular (RV) systolic (11.4 (7.5-17) vs. 13.5 (10-17) cm/s, $P=0.016$), and diastolic (E') velocities (13 (8-23) vs. 17 (12-25) cm/s, $P=0.0026$). In the severe group, these parameters improved from hospital admission to discharge; septal S' to 8.8 (7-11) cm/s ($P=0.002$), RV S' to 15.0 (11.8-23) cm/s, ($P=0.003$) and diastolic velocity E' to 21 (11-25) cm/s ($P=0.002$). Patients with cardiac impairment were more likely to have significant pleural effusions.

Conclusions—Patients with severe dengue have evidence of systolic and diastolic cardiac impairment, with septal and right ventricular wall being predominantly affected.

Keywords

Dengue; cardiac function; Haemodynamics; Vietnam; echocardiography; Tissue Doppler Imaging

Introduction

Dengue is the second most common vector born disease in the world with 50-100 million cases reported annually and 2.5 billion people at risk of the disease [1]. It is also the most rapidly spreading, with a fourfold increase in incidence in the last decade. Dengue causes a spectrum of disease processes ranging from dengue fever, a non-specific viral illness, to severe disease where patients can develop cardiovascular compromise secondary to increased capillary permeability and plasma leak. Cardiac complications have also been reported including; reduced myocardial function, acute myocarditis and conduction disturbances [2,3,4,5]. The nature and mechanism of the cardiac impairment and its contribution to severe disease has not been systematically defined.

Cardiac function as assessed by traditional echocardiographic parameters is dependent on preload. Severe dengue is characterized by reduced intravascular volume making accurate cardiac functional evaluation more difficult. Myocardial tissue Doppler imaging (TDI) is known for its sensitivity in detecting diastolic and early systolic dysfunction, and is considered to be relatively preload independent [6,7,8,9].

In this study we investigated in detail cardiac affection across a spectrum of dengue patients with different disease severities using echocardiographic techniques including TDI, coupled with intravascular volume measurements, and monitoring of any changes throughout the course of the hospital stay.

Patients, Materials and Methods

This observational study was conducted in the Hospital for Tropical Diseases, Ho Chi Minh City, Vietnam, in September and October 2008. Children and adults admitted to the hospital with suspected dengue of any severity were eligible for inclusion in the study. Diagnosis of dengue was confirmed using standard IgM and IgG ELISA and NS1 assays [10]. Seventy nine patients were included in the study, 22 of whom had dengue, 42 dengue with warning signs (box 1) and 15 with severe dengue (box 2), according to the 2009 WHO Dengue Clinical Case definition [11]. Using the previous WHO classification, there was 1 dengue fever, 22 dengue hemorrhagic fever (DHF) grade 1, 43 DHF grade 2, 12 DHF grade 3 and 1 grade 4. Informed consent was obtained from all patients or their guardians. The study was approved by the Scientific and Ethical Committee of the Hospital for Tropical Diseases, Ho Chi Minh City. Clinical and Laboratory parameters were recorded, including, Blood pressure, respiratory rate, haematocrit, platelets, electrolytes and liver enzymes. Troponin I was measured on admission in a sub group of patients. Patients who met the criteria for severe dengue with shock received intravenous fluids, with an initial bolus of 15 ml/kg over 1 hour. Further boluses of 10ml/kg were given if signs of haemodynamic compromise persisted.

Echocardiography

Echocardiographic examinations were performed by two of the investigators (SY and AG), using a Phillips HD11 system with cardiac settings and linear array probe (4 - 2 MHz). In patients with shock the first echocardiogram was performed after initial resuscitation, or as soon as the patient was stable and able to be transferred to the ultrasound department. Echocardiograms were repeated at 24 hours, and before discharge, and included two-dimensional, M-mode, Doppler and tissue Doppler (TD) studies. Measurements were made from 3 consecutive cardiac cycles and the average was calculated. The 2D parasternal long axis view was used to measure the left ventricular end diastolic (LVEDD) and end systolic (LVESD) dimensions just below the tips of the mitral valve leaflets. The ejection fraction was calculated as; $EF = (LVEDD^3 - LVESD^3) / LVEDD^3 \%$. Transmitral pulsed wave Doppler velocities were obtained from the apical four chamber view with the sample volume positioned at the tips of the mitral valve leaflets, and the aortic velocity from the apical five-chamber view with the sample volume positioned just below the aortic valve cusps, and the velocity time Integral (VTI) was measured. Left myocardial performance index (LMPI) was calculated from trans-aortic and trans-mitral pulsed Doppler velocities, and RMPI from tricuspid and pulmonary Doppler, using previously defined method [(isovolumic contraction time + isovolumic relaxation) time/ ejection time] [12]. Stroke volume (SV) was calculated as $VTI \times$ cross sectional area of the aortic valve (CSA), with $(CSA = 0.785 \times \text{aortic diameter}^2)$ and cardiac output (CO) as $SV \times$ Heart Rate. Myocardial TD velocities were obtained in the standard manner, with the sector width and depth optimized to ensure maximum frame rate with optimum gain adjustment. Myocardial velocities were taken at the LV lateral (S'lat), septal (S'sept) and RV walls at the level of the mitral and tricuspid valve annulus, respectively. Peak systolic (S') and early diastolic (E') velocities were taken. Measurements of annular systole excursion at the mitral (MAPSE) and tricuspid (TAPSE) free wall were taken from nadir to peak. The inferior vena cava (IVC) was measured using the subcostal view, below the level of the hepatic veins, 5cm from the IVC-right atrial junction. The maximal diameter during expiration and minimal diameter in inspiration were measured from M-mode recordings and the collapsibility index (IVCCI) calculated using the formula $IVCCI = (IVC_{max} - IVC_{min} / IVC_{max}) \times 100$ [13]. Pericardial effusions were reported using conventional criteria. A left pleural effusion was reported if an echo-free space was seen around the heart and descending aorta, in the sub costal view. And a right pleural effusion was reported if an echo free space was seen posterior to the liver. The pleural effusions were quantified visually as; minimal, small, moderate or large. All images were stored digitally and reviewed by a consultant cardiologist in the UK (MH) independent to the clinical severity of disease. The inter-and intra-user variability was less than 10%.

Statistics

Medians, minimum and maximum values were calculated for continuous variates. Percentages for two groups were compared using a Fisher exact test and continuous variates were compared using a Mann Whitney test. The Wilcoxon signed ranks test was used to compare values at admission and discharge. Associations between continuous variates were measured using Spearman's rank correlation coefficient. Significant evidence of a difference was indicated by $p < 0.05$.

Results

The median age of all the patients was 20 years (range 8 – 46 years) and the male: female ratio was 50:29. Length of hospital stay varied between 2- 7 days (median 3 days). Time from admission to first echo ranged between 2.5-72 hours (median 23 hours). Further admission laboratory parameters are shown in table 1. Fifty-one patients had a 12 lead ECG recorded; of which 18/51 (35%) were abnormal; 3/10 (30%) in dengue, 11/32 (34%) in dengue + and 4/9 (44%) in the severe group. The abnormalities included 1st degree AV block, sinus bradycardia, T wave changes and ST segment abnormalities. There were no deaths in the study group.

Clinical and biochemical findings

Admission clinical and biochemical data are shown in table 1. Platelets decreased parallel to disease severity (dengue: 82.0 (5-223) vs. severe: 28.0 (3-119) /l, $P=0.006$). Troponin I was tested in 17 patients at admission, one severe dengue patient had a borderline raised troponin of 0.31 ng/ml (normal<0.3 ng/ml), and the other 16 in different severity grades were normal. The amount of intravenous fluids received was slightly more in severe dengue compared to dengue +group (2350 (450-4800) vs. 1500 (500-3500)L, $P=0.73$). Dengue patients only received oral rehydration therapy, which was not possible to quantify.

Cardiac function between groups

Heart rate was higher in dengue compared with the dengue + patients (88 (62-110) vs. 80(50-105) b/min, $P=0.001$) (table 2). This could be explained by the higher number of dengue+ patients with ECG abnormalities, particularly bradyarrhythmias. Stroke volume (SV) was lowest in the severe group (table 2). The Inferior vena cava collapsibility index (IVCCI) increased with disease severity, but was not statistically significant (46.8 (27.1-100) vs. 56.3(33.7-100) $P=0.19$). (Fig 1, table 2). More patients in the severe group had pleural effusions compared to the other groups (92% vs. 30% and 5%, $P<0.001$) (table 1). The pleural effusions were larger in the severe group with 8/12 being quantified as moderate and 4/12 as small. In dengue+ 11/12 were small and 1/12 minimal, and dengue 1/1 had a minimal pleural effusion.

Left Ventricular (LV) systolic function in severe dengue was impaired compared to dengue, demonstrated by an increased LMPI (0.58 (0.26-0.8) vs. 0.38 (0.22-0.7), $P=0.006$) (Fig 2), and reduced septal myocardial systolic velocity (S' sept), (6.4 (4.8-10) vs. 8.1(6-13) cm/s, $P=0.01$). Right ventricular (RV) function was also impaired in the severe group with reduced S' RV (11.4 (7.5-17) vs. 13.5 (10-17) cm/s, $P=0.016$). Myocardial diastolic velocity (E') was also reduced in severe dengue, (13 (8-23) vs. 17 (12-25) cm/s, $P=0.003$) (Fig 3) as was E/A ratio (1.33 (0.92-2.11 vs. 1.75 (1.09-2.6), $P=0.002$). LV filling pressures (defined as $E-E' <6$ at the lateral wall) were normal [14,15] and did not alter with disease severity.

Cardiac function over time

SV and CO significantly increased by hospital discharge compared to admission, particularly in severe dengue, 35.7 (25.9-59.5) vs. 49.4 (30.1-69.2) ml, ($P=0.004$) and 3.1(1.9- 5.2) vs. 4.1 (2.7- 5.3) L/min ($P=0.008$) (table 3). In the same group, LV diastolic

dimension (LVDD) increased by an average of 0.21cm (P=0.002). IVCCI decreased in all severity groups by discharge (Table 3).

Using TDI, 42% of patients at admission had evidence of LV systolic impairment (S' lat <13 and S' sept <7.5cm/s) and 45% impaired diastolic function (E' <16 cm/s).

In severe dengue, S' velocities were all depressed on admission, particularly septal S' which increased from 6.4 (4.8-8.8) to 8.8 (7-11) cm/s (P=0.002) by discharge (fig 4). In the same group RV S' increased from 11.4 (7.5-17.0) to 15 (11.8-23.0) cm/s, (P=0.003) (Table 3). E' also increased by an average of 8 cm/s (P=0.002) (Fig 3).

At admission, patients with pleural effusions had worse cardiac function with higher LMPI (0.48 (0.26-0.8) vs. 0.39 (0.21-0.74), P=0.01) and lower LV lateral S' (10.8 (7-16) vs. 12.0 (7-18) cm/s, P=0.02) and RV S' (12.2 (7.5-17) vs. 13.5 (9.3-22) cm/s, P=0.04) (table 4). Also, patients with pleural effusions were more likely to have abnormal septal S' (<7.5cm/s) (P=0.04). Haematocrit and IVCCI at admission inversely correlated with ejection fraction ($r=-0.39$, P<0.001 and $r=-0.24$, P=0.04). None of the TDI parameters (S' lat, sept and RV) correlated with IVCCI. There was no association between the amount of IV fluid given and cardiac function parameters, specifically S' lat, S' sept, S' RV, EF and LMPI. Nor was there any association between CO and systolic ($r=0.082$, P=0.49) or diastolic blood pressure ($r=-0.086$, P=0.47).

Discussion

We have shown that particularly in severe dengue, systolic and diastolic, left and right ventricular function was reduced. Patients with cardiac impairment were more likely to have pleural effusions. The cardiac dysfunction appeared to be transient, with significant improvements seen by the time of hospital discharge (2-7 days). These results could have therapeutic implications, as the current treatment of severe dengue is judicious replacement of intravenous fluids and careful fluid balance.[16] The severe dengue cases had been fluid resuscitated prior to the first echocardiogram, but still showed more signs of intravascular volume depletion than the other grades, likely representing ongoing vascular leakage. This made cardiac functional assessment in this group more challenging and hence our use of TDI parameters, some of which have been shown to be relatively load independent [15,17,18,19]. E' was significantly reduced in the severe dengue group, suggesting impaired LV relaxation, and diastolic impairment [8,15]. The average E/E' in the severe group was similar to the other grades, which may be due to the systolic dysfunction counteracting the reduced preload, thereby increasing LV pressures.

Systolic function was also impaired particularly in severe dengue, which confirms previous findings [2,3]. One study demonstrated 36% of dengue shock patients had reduced systolic function with an EF<50% [2]. We have demonstrated that myocardial velocities of the septal and right ventricular (RV) wall were predominantly affected. The exact cause for these regional wall differences requires further investigation. One possible mechanism could be differential regional myocardium vulnerability to coronary hypoperfusion [20].

Diastolic TDI parameters have been shown to correlate with outcome in a range of cardiovascular diseases, [6] and have prognostic value in previously healthy patients admitted to Intensive Care Units (ICU) [21,22]. Non-survivors of sepsis had significantly lower septal systolic velocities than survivors, with no difference on conventional echo parameters[23]. Although dengue and septic shock are different entities, there are several overlapping features, including increased capillary permeability and vascular leakage [24,25,26,27]. In sepsis a circulating myocardial depressant factor has been suggested as the cause [28], including pro-inflammatory cytokines [29,30,31,32,33]. The pathogenesis of severe dengue is poorly understood, but is thought to involve an overactive immune response[34], particularly in secondary infections, with a cytokine ‘storm’ being associated with the capillary permeability [35,36,37,38]. Our observed cardiac dysfunction may share the same underlying mechanism, with high circulating proinflammatory cytokines causing myocardial depression as well as the capillary permeability, particularly as they occur simultaneously. Other potential mechanisms may include altered intracellular calcium homeostasis [38] and coronary hypoperfusion. Direct viral invasion of the myocytes may be a possibility, but there was no evidence of myocardial injury, with no elevation of serum troponin I and little evidence from autopsy data [39]. There was electrical evidence of myocarditis with a third of patients having abnormal ECGs, which may have contributed to the functional impairment. This is consistent with previous findings where 70% of severe dengue patients had global hypokinesia using radionuclide ventriculography but no myocardial necrosis using 99m Tc-pyrophosphate imaging [40].

The clinical implications of these findings are potentially very important. Although the cardiac impairment is transient, it does occur at the same time as the vascular leakage, when the patients are most likely to be haemodynamically unstable. Patients with severe dengue are likely to have a degree of cardiac impairment in addition to intravascular volume loss, which combine to worsen cardiovascular instability and increase the risk of iatrogenic fluid overload [41]. The IVCCI used in our study has been shown to be a useful non-invasive method of volume assessment and determining preload [42]. It correlates well with CVP (a risky procedure in dengue patients with thrombocytopenia) and is useful in predicting fluid responsiveness [43,44]. Echocardiography, particularly portable machines are becoming more widely available worldwide, along with trained staff. We would therefore recommend severe dengue patients to have cardiac functional assessment particularly using the TDI parameters; S' lat, sept and RV and IVCCI for intravascular volume evaluation and to estimate fluid responsiveness. This could guide fluid resuscitation and identify early, patients at risk of iatrogenic fluid overload and allow the use of alternative therapies including inotropes.

Limitations

The limitations include small patient numbers when separated into severity groups. The unstable cases were fluid resuscitated prior to first echo, so as not to interfere in the emergency management of the patients. This delayed time to first echo, which could have underestimated the cardiac involvement in this critical phase. Ideally the patients would have been recalled several months after discharge to check all parameters had normalized and investigate any long-term cardiac sequelae.

Conclusion

Dengue patients have evidence of systolic and diastolic myocardial impairment, with septal and right ventricular wall being predominantly affected. These changes are more common and pronounced in severe dengue and are associated with more pleural effusions. Echo screening should be considered for all severe dengue cases, to assess cardiac function and intravascular volume evaluation to tailor their management.

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Box 1**Dengue warning signs**

- Abdominal pain or tenderness
- Persistent vomiting
- Clinical fluid accumulation
- Mucosal bleed
- Lethargy/ restlessness
- Liver enlargement >2 cm
- Increase in HCT concurrent with rapid decrease in platelet count

Box 2**Severe Dengue**

- Evidence of plasma leakage
 - High or progressively rising HCT
 - Pleural effusions or ascites
 - Circulatory compromise or shock (tachycardia, cold extremities, pulse pressure <20 mmHg or unrecordable blood pressure)
- Significant bleeding
- Altered consciousness
- Severe gastrointestinal involvement (persistent vomiting, increasing abdominal pain or jaundice)
- Severe organ impairment

Taken from WHO 2009 dengue case classification

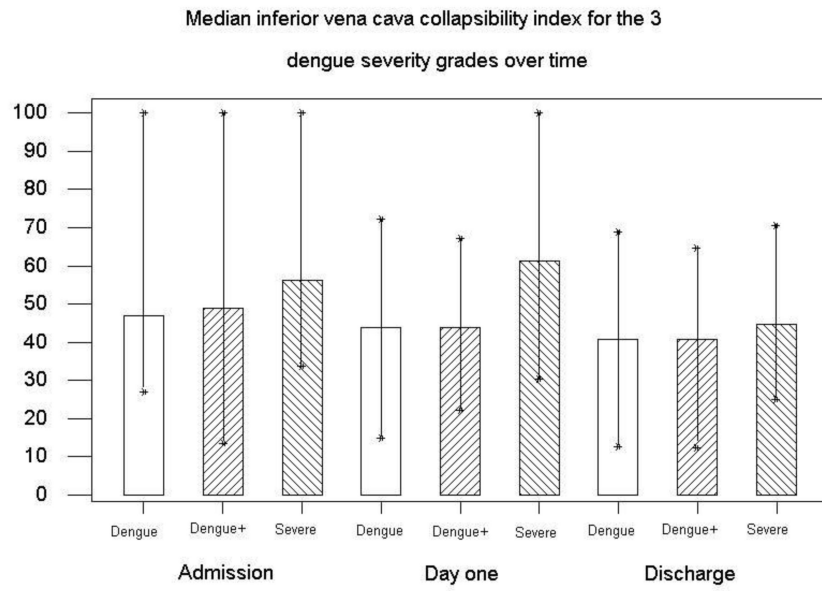


Figure 1. The Inferior vena cava collapsibility index decreased significantly from admission to discharge in all groups, particularly severe dengue (P=0.03).

Median LMPI for 3 dengue severity grades over time

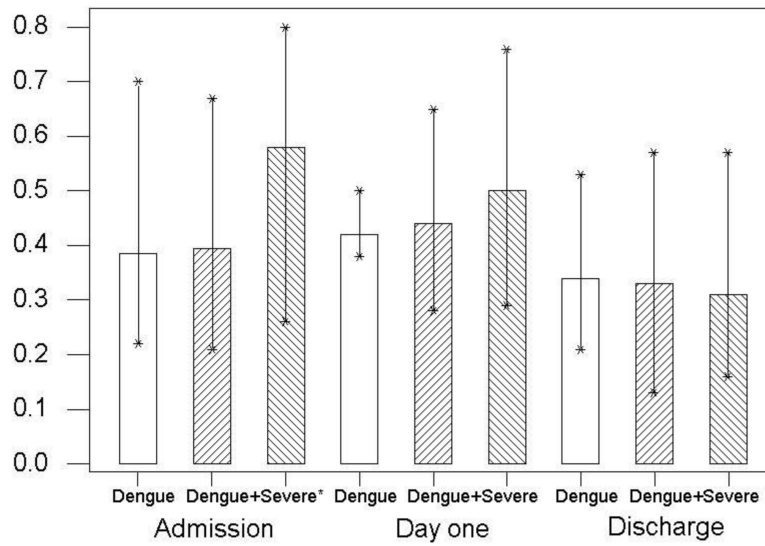


Figure 2. The left myocardial performance Index was increased in severe dengue compared with dengue (P=0.006), and improved significantly by hospital discharge in this group (P=0.002). *indicates a significant difference from dengue patients.

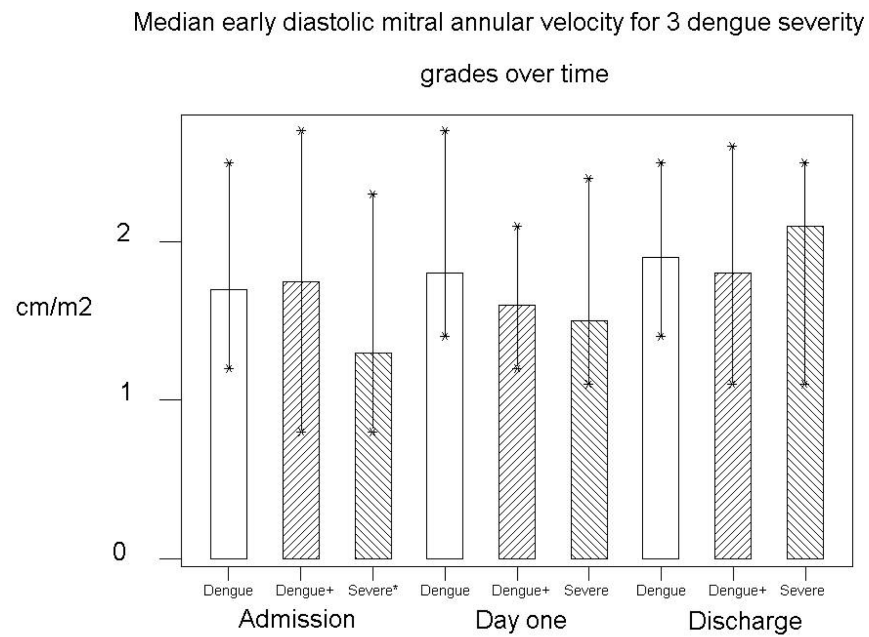


Figure 3. The early mitral annular velocity (E') was decreased in severe dengue compared to dengue ($P=0.003$), increasing significantly by hospital discharge ($P=0.002$).

*indicates a significant difference from dengue patients.

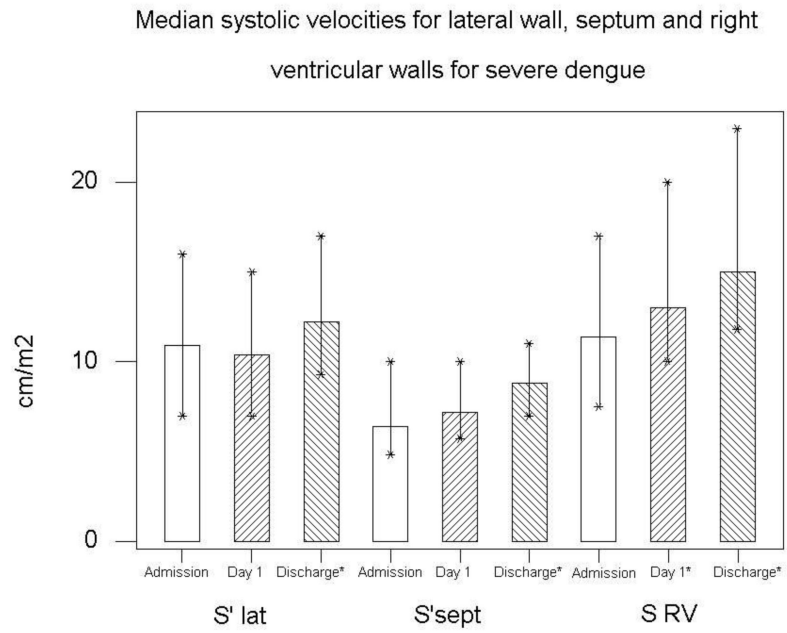


Figure 4. In severe dengue, systolic velocities were reduced at admission compared to discharge, most marked at the septal wall, (P=0.002).

* Indicates a significant difference between admission and the other time points.

Table 1
Admission characteristics for patients with different dengue severity grades

	Dengue 22	Dengue+ 42	p-value	Severe dengue 15	p-value
Age (yrs)	18.5 (8 - 33)	21.5 (14 - 46)	0.007	18.0 (11 - 36)	0.70
Illness day	6.0 (2 - 9)	6.0 (4 - 8)	0.13	5.0 (3 - 8)	0.78
Temp (°C)	37.5 (37 - 40)	37.2 (37 - 40)	0.22	37.2 (36 - 39)	0.22
Resp rate(b/min)	20.0 (18 - 28)	20.0 (18 - 24)	0.98	22.0 (20 - 24)	0.11
Creat (µmol/l)	89.5 (58 - 142)	80.0 (42 - 112)	0.32	79.0 (42 - 109)	0.36
ALT (mg/dl)	62.0 (19 - 76)	83.0 (14 - 331)	0.056	73.0 (7 - 298)	0.066
K (mmol/l)	3.5 (2.9 - 3.8)	3.7 (3.1 - 5.1)	0.053	3.7 (3.1 - 4.5)	0.099
HCT (%)	43.8 (35 - 50)	44.6 (36 - 56)	0.13	44.0 (36 - 61)	0.40
WBC (g/dl)	2.96 (1.6 - 5.4)	3.18 (1.1 - 5.6)	0.89	3.90 (1.7 - 7.1)	0.24
Platelets (/l)	82.0 (5 - 233)	36.0 (9 - 177)	0.017	28.0 (3 - 119)	0.006
Pericardial effusion	1	0		1	
Pleural effusion	1/20	12/40	0.043	12/13	<0.0001

Data are presented as median (minimum - maximum). The p-values refer to a test of dengue against dengue+ and dengue against severe dengue. They are obtained using Mann-Whitney (non-parametric) tests, except for pleural effusion where Fisher exact tests are used.

Table 2
Echocardiographic parameters by dengue grade at admission

n	Dengue 22	Dengue + 42	p-value	Severe dengue 15	p-value
HR (b/min)	88 (62 - 110)	80 (50 - 105)	0.001	88 (58 - 115)	0.92
PP (mmHg)	40 (30 - 50)	40 (20 - 50)	0.99	30 (20 - 40)	0.011
SV (ml)	42.6 (23.2 - 61.5)	46.6 (19.0 - 75.1)	0.12	35.7 (25.9 - 59.5)	0.19
CO (l/min)	3.81 (2.15 - 5.39)	3.47 (1.98 - 6.76)	0.46	3.11 (1.87 - 5.21)	0.16
LVDd (cm)	4.17 (3.39 - 5.03)	4.29 (3.25 - 5.22)	0.28	4.10 (2.97 - 4.87)	1.00
EF (%)	68.8 (57.8 - 80.2)	67.8 (54.6 - 79.1)	0.60	66.0 (48.0 - 75.9)	0.095
S' lat (cm/s)	12.0 (9.0 - 16.5)	11.2 (7.0 - 18.0)	0.32	10.9 (7.0 - 16.0)	0.11
S' sept (cm/s)	8.1 (6.0 - 13.0)	8.0 (6.0 - 12.2)	0.43	6.4 (4.8 - 10.0)	0.010
S' RV (cm/s)	13.5 (10.0 - 17.0)	13.0 (9.0 - 22.0)	0.65	11.4 (7.5 - 17.0)	0.016
RMPI	0.14 (0.06 - 0.38)	0.23 (0.03 - 0.42)	0.006	0.17 (0.04 - 0.43)	0.18
L MPI	0.38 (0.22 - 0.70)	0.39 (0.21 - 0.67)	0.94	0.58 (0.26 - 0.80)	0.006
E' (cm/s)	17 (12 - 25)	17 (8 - 27)	0.33	13 (8 - 23)	0.0026
MAPSE(cm/s)	14.0 (11.0 - 18.9)	16.0 (10.0 - 20.0)	0.096	12.8 (9.0 - 17.0)	0.026
TAPSE (cm/s)	20.0 (14.0 - 26.0)	19.7 (13.0 - 29.0)	0.62	16.3 (10.5 - 24.0)	0.0089
IVCCI	46.79(27.10-100)	49.03(13.60-100)	0.86	56.25 (33.70 - 100)	0.19

Data is presented as median (minimum - maximum). P values correspond to differences between dengue with dengue +, and dengue with severe dengue using Mann-Whitney (non-parametric) tests.

HR- heart rate, PP-pulse pressure, CO- Cardiac Output, SV- stroke volume, LVDd- Left ventricular diastolic dimension, EF- Ejection fraction, L MPI and RMPI- Left and right myocardial performance index, S' lat, Sept, RV - myocardial systolic velocity of lateral wall, septum and right ventricle, MAPSE, TAPSE- Mitral, tricuspid annulus plane excursion, E'- Early diastolic mitral annular velocity, IVCCI- Inferior vena cava collapsibility Index.

Table 3
Haemodynamic and cardiac parameters in different dengue severity grades at hospital admission compared to discharge

N	Dengue and Dengue+			Severe dengue		
	Admission 64	Discharge 11	p-value	Admission 15	Discharge 14	p-value
HR (b/min)	82 (50 – 110)	78 (52 – 94)	0.46	88 (58 – 115)	80 (58-110)	0.005
SV (ml)	44.2 (19.0–75.1)	51.3 (31.8–67.6)	0.001	35.7 (25.9-59.5)	49.4 (30.1-69.2)	0.004
CO (L/min)	3.5 (2.0 – 6.8)	4.0 (2.4-5.3)	0.074	3.1 (1.9 – 5.2)	4.1 (2.7-5.3)	0.008
LVDd (cm)	4.24 (3.25-5.22)	4.32 (3.74-5.44)	0.60	4.10 (2.97-4.87)	4.31 (3.64-5.05)	0.002
EF (%)	68.4 (54.6-80.2)	68.5 (57.3-79.2)	0.27	66.0 (48.0-75.9)	71.7 (56.9-78.8)	0.033
LMPI	0.39 (0.21-0.70)	0.33 (0.13-0.57)	0.002	0.58 (0.26-0.80)	0.31 (0.16-0.57)	0.002
RMPI	0.21 (0.03-0.42)	0.19 (0.06-0.46)	0.91	0.17 (0.04-0.43)	0.17 (0.03-0.40)	0.54
S' lat (cm/s)	11.3 (7.0-18.0)	11.2 (7.8-16.9)	0.75	10.9 (7.0-16.0)	12.2 (9.3-17.0)	0.047
S' Sept (cm/s)	8.0 (6.0-13.0)	8.0 (6.3-15.0)	0.89	6.4 (4.8-10.0)	8.8 (7.0-11.0)	0.002
S' RV (cm/s)	13.2 (9.0-22.0)	13.0 (8.2-25.0)	0.62	11.4 (7.5-17.0)	15.0 (11.8-23.0)	0.003
MAPSE (cm/s)	15.0 (10.0-20.0)	16.0 (12.3-20.0)	0.008	12.8 (9.0-17.0)	16.0 (13.0-18.1)	0.003
TAPSE (cm/s)	20.0 (13.0-29.0)	21.0 (17.0-27.0)	0.003	16.3 (10.5-24.0)	22.5 (17.7-25.0)	0.002
E' (cm/s)	17 (8-27)	18 (11-26)	0.074	13 (8-23)	21 (11-25)	0.002
IVCCI	47.9 (13.6-100)	40.7 (12.5-68.7)	0.001	56.2 (33.7-100)	44.6 (25.0-70.6)	0.058

The p-value relates to a (non-parametric) Wilcoxon test of zero median difference between admission and discharge.

Table 4
Cardiac function in patients with and without pleural effusions

	Without Pleural Effusion	With Pleural effusion	p-value
n	48	25	
EF %	68.32 (57.78 – 79.10)	67.38 (49.80 – 80.23)	0.63
L MPI	0.39 (0.21 – 0.74)	0.48 (0.26 – 0.80)	0.012
S'lat cm/s	12.0 (7.0 – 18.0)	10.80 (7.0 – 16.0)	0.023
S'sept cm/s	8.0 (6.0 – 13.0)	7.0 (4.8 – 12.0)	0.047
S'RV cm/s	13.5 (9.3 – 22.0)	12.2 (7.5 – 17.0)	0.036

The data are presented as median (minimum - maximum). The p-values refer to a test of without pleural effusion against with pleural effusion.