The Egyptian Journal of Hospital Medicine (January 2023) Vol. 90 (2), Page 2379-2384

Relation between Net Atrioventricular Compliance and In-Hospital Outcome in Patients with Acute Coronary Syndrome

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ABSTRACT
Background: The leading cause of death in the world is coronary heart disease. Acute coronary syndrome (ACS) patients can have their in-hospital outcomes evaluated using the tissue Doppler imaging metric known as net atrioventricular compliance. **Objective:** The aim of the current study is to assess relation between net atrioventricular compliance and in hospital outcome in ACS patients. **Patients and methods:** A cross sectional study was conducted in Zagazig University Hospital, Cardiology Department on patients with ACS. Patients with atrial fibrillation, a history of moderate or severe valve stenosis or regurgitation, and myocardial infarction, poor echocardiographic picture quality, and refusal to participate to the study, significant congenital heart disease or left ventricular hypertrophy were excluded from the study. Detection of outcome of patients (arrhythmia, death, improvement) was assessed through their hospital stay.
Results: Multivariate logistic regression predictors, in hospital complications among patients with ACS, showed that Cn level ≥11.65 and decrease EF% were significantly independent predictors in hospital complications among ACS patients. **Conclusion:** Net atrioventricular compliance can be used as independent predictors in hospital complications among patients with ACS.
Keywords: Net Atrioventricular Compliance, Coronary artery disease, In-Hospital, Acute coronary syndrome, Cross sectional study, Zagazig University.

INTRODUCTION
Despite significant advancements in management, coronary artery disease (CAD) remains the most prevalent kind the primary cause of cardiac disease of mortality globally **(1).** The identification and risk classification of acute coronary syndrome (ACS) patients are greatly aided by non-invasive imaging procedures like echocardiographic evaluation of the systolic and diastolic activities of the left ventricle, which are frequently used in clinical practice for the detection and evaluation of CAD (2). By using hydrodynamic analysis, it is possible to quantitatively estimate a measurement of the left atrium and left ventricle's net compliance is called net atrioventricular compliance (Cn). Doppler mitral flow can be used to compute a measure of the potential value of the net atrioventricular compliance an accurate representation of the left atrial and ventricle's net compliance (3).

According to earlier research, Cn was very useful for risk stratifying individuals with mitral stenosis. It was discovered to be a reliable predictor of cardiovascular death in patients with mitral stenosis and to be a predictor of successful mitral valvuloplasty (4), improvement or persistence of pulmonary after successful mitral valvuloplasty (5), considerable impact on outcome (6,7).

The aim of the current study is to assess relation between net atrioventricular compliance and in hospital outcome in acute coronary syndrome patients.

PATIENTS AND METHODS
A cross sectional study was conducted in Zagazig University Hospital, Cardiology Department on ACS patients. Patients with atrial fibrillation, a history of moderate or severe valve stenosis or regurgitation, and myocardial infarction, poor echocardiographic picture quality, and refusal to participate to the study, significant congenital heart disease or left ventricular hypertrophy were excluded from the study.

All study participants underwent a thorough history and physical examination, as well as routine laboratory investigations such as cardiac biomarkers, lipid profiles, and routine lab investigations required for preoperative assessment such as CBC, ECG, serum electrolytes, and evaluations of liver and kidney functions.

Echocardiographic examination: Transthoracic echocardiography was conducted on all patients by the same operator who will be blind to the patient groups.
During end diastole, the internal diameter of the left ventricle (LV), from the parasternal short-axis view, the septal thickness and posterior wall thickness of the LV were measured. The American Society of Echocardiography formula was used to calculate LV mass, which was then indexed for body surface area. In both the parasternal long-axis and apical four-chamber perspectives, the LA volume was computed using the prolate ellipse method, and it was indexed for body surface area. Using two-dimensional planimetry, the mitral valve area was determined (MVA).

The estimated SPAP was defined as 4 × (maximum tricuspid regurgitant jet velocity) 2 + right atrial pressure. The diameter of the inferior vena cava and its response to inspiration were utilized to compute right atrial pressure. On echocardiography, PHT was classified as an SPAP of 35 mmHg. The mean trans-mitral pressure gradient was

Received:30/08/2022
Accepted:3/11/2022

determined by following the envelope of a continuous-wave Doppler signal through the mitral valve. To calculate this, MVA was determined by pressure half time using the formula 220/pressure half time. Cn was computed using the formula: Cn (mL/mmHg) = 1270 (downslope of the planimetric MVA/E-wave).
Figure 1 depicts a representation of a Cn measurement. The Cn value was hidden from the attending physician and measured and estimated by an experienced echocardiographer without access to the patient's medical information. The average echocardiographic values for three beats in patients with SR and five beats in patients with AF were calculated.

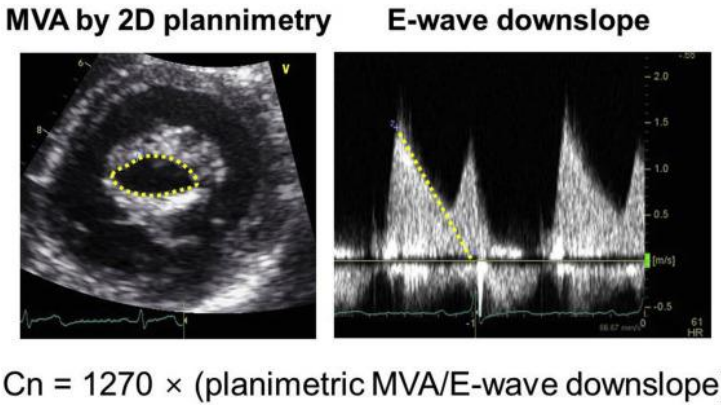

Figure 9: 2D, two-dimensional, representative image of Cn measurement.

The degrees of Cn readings' intra- and interobserver variability were assessed. One observer took measurements based on the study of 10 random SR and AF images. The observer then performed the examination at least once per month while staying blind to the previous findings. A second observer performed additional image analysis without knowledge of the first observer's measurements. During the same cardiac cycle, measurements were obtained and the values for each image were averaged 5 times.

We applied this equation to all patients: C_n = 1270 x (MVA/E-wave downslope)
The following items were assessed:

1. 2D and M- mode echocardiography;
- Left ventricular end-systolic and end-diastolic diameters.
- Left ventricle ejection fraction.

2. Doppler echocardiography;
- Mitral valve flow velocities, for assessment of E-wave, A-wave, E/A ratio, and E-wave deceleration time (LV diastolic function).

3. Tissue Doppler echocardiography;

From the apical 4-chamber view, we will study the MV ring segments of left ventricle. Calculation of parameters:
- Septal e`.
- Lateral e`.
- E/e`.

Follow up: Detection of outcome of patients (arrhythmia, death, improvement), through their hospital stay.

Ethical Approval:

This study was ethically approved by the Institutional Review Board of the Faculty of Medicine, Zagazig University. Written informed consent was obtained from all participants. This study was executed according to the code of ethics of the World Medical Association (Declaration of Helsinki) for studies on humans.

Statistical Analysis

The collected data were introduced and statistically analyzed by utilizing SPSS (Statistical Package for Social Sciences. Armonk, New York-based IBM Corp.) version 23.0 for windows. Qualitative data were defined as numbers and percentages. Chi-Square test/Fisher's exact test was used for comparison between categorical variables as appropriate. Quantitative data were tested for normality by Kolmogorov-Smirnov test. Normal distribution of variables was described as mean and standard deviation (SD), and independent sample t-test/ Mann-Whitney U test was used for comparison between groups. Performance net atrioventricular compliance was evaluated as a predictor in-hospital outcome with patients suffering from acute coronary syndrome using the receiver operating characteristic (ROC) curve. P value ≤0.05 was considered to be statistically significant.

RESULTS

Table 1 summarizes demographic characteristics of the studied patients.

Table (1): Frequency and percentage distribution of the studied patients, according to baseline characteristics (n. 60)

Personal Characteristics	Patients (n= 60)	
Sex:		
○ Males	44	73.3
○ Females	16	36.7
Age per years:		
○ Mean ± SD	58.7±8.1	
○ (Range)	(40-81)	
Net atrioventricular compliance:		
○ Mean ± SD	14.4± 8.6	

Table 2 showed the serum Cn sensitivity, Specificity, positive predictive value, negative predictive value, and accuracy. At the cut off value given in the preceding table, Cn was an excellent predictor of in-hospital prognosis in individuals with ACS.

Table (2): Performance net atrioventricular compliance as predictor in-hospital outcome with patients suffering from acute coronary syndrome.

Cut off level	In-hospital outcome		Sensitivity	Specificity	PPV	NPV	Accuracy
	Bad outcome (N=20)	Good Outcome (N=40)					
Cn							
≥11.65	16	14	80%	65%	53.3%	86.7%	70%
<11.65	4	26					

Cn: net atrioventricular compliance.

There was no significant difference between ACS patients of Cn ≥11.65 group and Cn <11.65 group regarding age, gender and presence of CAD risk factors (**Table 3**).

Table 3: Relation between Net Atrioventricular Compliance and age, gender and presence of CAD risk factors, in acute coronary syndrome patients (n. 60).

Variables	Cn level						t-test	P-value
	Group 1 (Cn ≥11.65), N= 30			Group 2 (Cn<11.65), N=30				
Age	Mean ± SD	57.3 ± 7.3		60.1 ± 8.7			1.3	0.19
HR	Mean ± SD	79.6 ± 12.8		78.4 ± 14.1			0.746	0.614
Systolic blood pressure	Mean ± SD	131.3 ± 15.02		136 ± 10.7			1.38	0.17
Diastolic blood pressure	Mean ± SD	78 ± 11.3		82 ± 67			1.79	0.078
		n.	%	n.	%	Total	χ^2	P –value
Sex	Males	26	59.1	18	40.9	44	f	0.22
	Females	4	25.0	12	75.0	16		
D M	Yes	10	45.5	12	54.5	22	0.29	0.59
	No	20	52.6	18	47.4	38		
HTN	Yes	16	44.4	20	55.6	36	1.1	0.29
	No	14	58.3	10	41.7	24		
IHD	Yes	8	42.1	11	57.9	19	0.69	0.41
	No	22	53.7	19	46.3	41		
Smoking	Yes	13	56.5	10	43.5	23	0.64	0.43
	No	17	45.9	20	54.1	37		

Data expressed as mean ± SD, SD: Standard deviation, t: student t-test, $\chi 2$: Chi-square test of significant, P>0.05 insignificant.

All Cn ≥11.65 group had ECG abnormalities, compared to 80% in Cn <11.65 group the difference being statistically significant (**Table 4**).

Table 4: Relation between Net Atrioventricular Compliance and Troponin, ECG and diagnosis, in acute coronary syndrome patients (n. 60).

Variables		Cn level				χ^2	P-value
		Group (Cn ≥11.65) N= 30		Group (Cn <11.65) N=30			
		No.	%	No.	%		
Killip class	- Killip class I	18	60	22	73.3	1.2	0.27
	- Killip class II	12	40	8	26.7		
Troponin	- Positive	20	66.7	16	53.3	1.1	0.29
	- Negative	10	33.3	14	46.7		
ECG	- Abnormalities	30	100	24	80		
	- Not significant changes	0	0.0	6	20	F	0.023*
Diagnosis	- Anterior STEMI	4	13.3	4	13.3		
	- Inferior STEMI	6	20	4	13.3	3.1	0.55
	- Infero-posterior STEMI	2	6.7	0	0.0		
	- N-STEMI	8	26.7	8	26.7		
	- Unstable angina	10	33.3	14	46.7		

There was significant, lower value of EF%, E-Deceleration slope, E/e in Cn ≥11.65 group, compared to Cn <11.65 group. While, there was significant higher value of DT in Cn ≥11.65 group, compared to Cn <11.65 group (**Table 5**).

Table 5: Relation between Net Atrioventricular Compliance and echocardiography, in acute coronary syndrome patients (n. 60).

Variables	Cn level			t/u	P-value
		Group (Cn ≥11.65) n. 30	Group (Cn<11.65) n. 30		
2D and M- mode echocardiography					
EF%	Mean ± SD	40.8 ± 11.1	50 ± 11.8	3.1	0.003*
LVEDD	Mean ± SD	5.95 ± 0.77	5.94 ± 0.72	0.069	0.945
LVESD	Mean ± SD	4.6 ± 0.97	4.32 ± 0.82	1.497	0.140
Doppler echocardiography;					
MVA	Median (range)	4 (1.6-7.4)	3.9 (2.7-7.6)	U 0.18	0.859
E-Deceleration slope	Median (range)	2.8 (0.8-7.1)	7.7 (3.2-14.6)	U 5.7	0.0001*
E/A ratio	Median (range)	0.9 (0.6-2.7)	1.5 (0.7-3)	U 1.93	0.054
DT	Median (range)	268 (133-544)	164 (87-310)	U 4.46	0.0001*
Tissue Doppler echocardiography;					
Lateral e`	Mean ± SD	7.4 ± 2.3	6.7 ± 2.2	1.202	0.234
septal e`	Mean ± SD	6 ± 1.7	5.7 ± 1.6	0.92	0.36
E/e	Median (range)	10 (6-30)	15 (9-50)	U 2.6	0.008*

There was significant, higher percent of in hospital complications, arrhythmia among Cn ≥11.65 group compared to Cn <11.65 group (**Table 6**).

Table 6: Relation between Net Atrioventricular Compliance and acute coronary syndrome Patients' In-Hospital Outcome.

Variables		Cn level				χ^2	P-value
		Group (Cn ≥11.65) n.30		Group(Cn<11.65) n.30			
		No.	%	No.	%		
Complications	Yes	16	53.3	4	13.3		
	No	14	46.7	26	86.7	10.8	0.001*
Thrombolysis in STEMI patients	Failed	4	13.3	2	6.7	F	0.99
	Succeed	8	26.7	6	20.0		
Heart Failure	Yes	6	20.0	4	13.3	0.48	0.49
	No	24	80.0	26	86.7		
Arrhythmia(VT)	Yes	8	26.7	0	.0	F	0.005*
	No	22	73.3	30	100.0		

Multivariate logistic regression predictors, in hospital complications among patients with ACS, showed that Cn level ≥11.65 and decrease EF% were significantly independent predictors in hospital complications among ACS patients (**Table 7**).

Table 7: Multivariate logistic regression analysis for significant predictors in hospital complications among patients with acute coronary syndrome.

Variables	**B**	**S.E.**	**Wald**	**Sig.**	**Exp (B)**	**95% CI for EXP(B)**	
						Lower	Upper
Cn level ≥11.65	2.36	1.07	4.71	0.03	10.6	1.26	88.9
EF%	-0.257	.074	12.02	.001	0.77	0.67	0.89

DISCUSSION

Demographic data shows that sex of studied patients was 44 (73.3%) males and 16 (36.7%) females. All patients had aged ranged from 38 to 81 years old, with mean of 57.3.

Nunes *et al.* [6] aimed to ascertain how Cn affects clinical outcomes and how much it contributes to pulmonary hypertension in mitral stenosis; 116 (90.6%) patients were female, with a mean age of 42.6 years.

Regarding AV compliance shows that all patients had net atrioventricular compliance from 3.7 to 30.7, with mean of 14.4 (SD 8.6).

Nunes *et al.* [6] conducted their study on 128 rheumatic mitral stenosis patients without additional substantial patients with valve disease. In the study, extensive echocardiography was performed, and a previously validated algorithm was utilized to calculate Doppler-derived Cn. All patients had net atrioventricular compliance with mean of 5.1 (SD 1.1).

Cn power sensitivity, specificity, positive predictive value, negative predictive value, and accuracy to serum Cn were achieved. At cut off value of 11.65, Cn was good marker to detect acute coronary syndrome patients' in-hospital outcomes.

Schwammenthal *et al*. [8]**,** reported low Cn patients were more symptomatic, with a criterion value of 4 mL/mm Hg (lowest third of values): When compared to 0% with levels below 6 mL/mm Hg and 29% with values between 4 and 6 mL/mm Hg, 71% were in functional class III (P=0.025).

Nunes *et al.* [7] also found that Cn does not just reflect the severity of symptoms; it also identifies individuals who are likely to need intervention at some point during an intermediate follow-up period. Cn evaluations in patients with modest exercise intolerance or mostly asymptomatic baseline conditions (NYHA classes I or II) showed prognostic significance, demonstrating that pathophysiologic markers of poor outcome exist in addition to symptoms and valve area reduction.

Kim *et al.* [9] reported that, A Cn of less than 4 mL/mm Hg was independently predictive of the incidence of either PMC or MV replacement throughout a mean follow-up of 24 months in individuals with mild MS, demonstrating the therapeutic relevance of Cn. The sensitivity for predicting PMC or MV replacement success was greatly enhanced using Cn less than 4 mL/mm Hg as an additional new discriminator for future events. These results demonstrate the significance of Cn as a prognosticator and a marker of hemodynamic MS severity beyond a simple physiological modulator of pulmonary artery pressure.

Nunes et al [10] reported that by echocardiography, those who met the goal had more severe MS than those who had just received medicinal treatment and displayed a more advanced functional class. It should be noted that only 24% of patients who reached the endpoint had functional status in the NYHA classes III-IV at the beginning. The baseline characteristics predicting valve intervention are determined using multivariable analysis.

Hrabia *et al.* [11] discovered that Cn expresses the location of the left heart on its pressure-volume curve in addition to reflecting intrinsic compliance. Atrial fibrillation can potentially have an impact on LA compliance.

Al Rawahi *et al.* [12-14] examined how AF affected LA compliance in patients with moderate to severe mitral stenosis. A higher Cn was seen in atrial fibrillation.

In this study, we did not find significant difference regarding age, gender and presence of CAD risk factors between the two groups of ACS. All Cn ≥11.65 group had ECG abnormalities, compared to 80% in Cn <11.65 group the statistically significant difference $p<0.05$. There was significantly lower value of EF%, E-Deceleration slope, E/e in Cn ≥11.65 group, compared to Cn <11.65 group $p<0.05$. While, there was significant higher value of DT in Cn ≥11.65 group, compared to Cn <11.65 group $p<0.05$. There was also significantly higher percent of in hospital complications, Arrhythmia among Cn ≥11.65 group, compared to Cn <11.65 group $p<0.05$.

Regarding significant predictors in ACS patients' hospital complications, Cn level ≥ 11.65, Killip class II, significantly associated with occurrence in hospital complications among ACS patients. Also increase HB, Platelet, LVEDD, LVESD, Lateral e; significantly associated with its occurrence, while decreasing K, E deceleration slope, and EF% were strongly linked with the occurrence of hospital complications among patients with ACS, the opposite was also true.

Multivariate logistic regression predictors in ACS patients' hospital complications showed that, Cn level≥ 11.65 and decrease EF% was significantly independent predictors ACS patients' hospital complications ($P<0.05$).

Despite Cn was originally described as a noninvasive method to evaluate left ventricular diastolic function and filling patterns [3]**,** its dependency on mitral valve area made it mainly a suitable method to assess patients with mitral stenosis as shown by the previously mentioned studies, in which, all authors excluded patients with any conditions that may affect LV CAD and hypertension as they relate to diastolic function. So, we thought that if we excluded mitral stenosis patients to eliminate the effect of MV area on the equation, Cn may be a useful way that may give us an idea about LV diastolic function and filling pattern, which in turn, may be reflected on the hospital outcome in ACS patients.

The fact that all previous studies used Cn to assess patients with mitral stenosis in contrast to our study may

explain the major difference between the cut off in our study and other cut off points.
To the best of our knowledge, this was the first study that used Cn to assess the hospital outcome in ACS patients.

CONCLUSION

Net atrioventricular compliance can be used as independent predictors in hospital complications among patients with ACS.

Conflict of interest: The authors say they have no competing interests.
Sources of funding: Funding organisations in the public, private, or nonprofit sectors did not provide a specific grant for this research.

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