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Research Article

ECHOCARDIOGRAPHIC AND ANGIOGRAPHIC CHARACTERISTICS OF PATIENTS WITH WELLENS' SYNDROME WHO UNDERWENT PERCUTANEOUS CORONARY INTERVENTIONS

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ABSTRACT

Introduction: Wellens' syndrome is referring to a subtype of unstable angina with specific precordial T-wave changes in ECG (deeply-inverted or biphasic T waves in V₂₋₃, having isoelectric or minimally-elevated ST segment, absence of precordial Q waves and preserved precordial R wave progression) and having a strong likelihood to develop a large anterior myocardial infarction in subsequent clinical course. Hence, the timely diagnosis of this condition is utmost important

Objective: The study was mainly aimed to describe the clinical, echocardiographic and coronary angiographic characteristics of patients with Wellens' syndrome and to follow up the patients who underwent Percutaneous Coronary Interventions (PCI).

Methodology: A descriptive cross-sectional study was conducted on patients with clinical diagnosis of Wellens' syndrome in 2017 at teaching hospital Kandy, Sri Lanka. 2D echocardiogram was carried out in all within 24 hours of admission to evaluate the Regional Wall Motion Abnormalities (RWMA) and Global and Regional Longitudinal Strain (GLS). After the initial assessment, all the patients were subjected for coronary angiogram within 24 hours of admission. Patients who had PCI amenable lesions were treated with angioplasty and stenting. All the patients were reviewed in 30th day and 90th day following PCI for cardiac death, re-infarction or having residual angina following the treatments.

Results: There were 30 patients (Mean age= 56.6±9.3 years) with 60% (n=18) of males. There were 80 % (n=24) of patients with negative cardiac Troponin I. Mean ejection fraction of the sample was 57.9±9.8%. The average global resting Regional Wall Motion Score Index (RWMSI) was 1.04±0.07 and mean resting RWMSI_{LAD} was 1.07±0.13. In the sample, peak GLS and RLS_{LAD} at rest were -17.8±2.9 and -18.0±2.7 respectively. Majority 70% (n=22) had critical proximal LAD stenosis which was defined as ≥90% luminal stenosis. Out of the sample, 50% (n=15) had single vessel disease involving LAD. Addition to that 16.6% (n=5) and 20% (n=6) had double and triple vessel disease respectively. All who had critical LAD stenosis underwent PCI. At the end of the 30th day and 90th day following PCI, none of them had cardiac death, re-infarction or residual angina.

Conclusion: In Wellens' syndrome, elevation of cardiac Troponin, echocardiographic parameters such as GLS or RWMSI might not enable the prediction of significant LAD stenosis. Therefore, the high degree of clinical vigilance is important to identify this condition in a timely manner.

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INTRODUCTION

Wellens' syndrome was first described in the early 1980s by de Zwaan Wellens and colleagues, who identified a subset of patients with angina who had specific precordial T-wave changes in Electrocardiograph (ECG) and subsequently developed a large anterior wall Myocardial Infarction (MI) ¹. It

is actually referring to a subtype of unstable angina with negative or minimally elevated markers of myocardial necrosis, biphasic or inverted T-waves in the precordial leads V₂ and V₃ in ECGs (*Figure 01a*) and having a critical stenosis of the Left Anterior Descending (LAD) coronary artery (*Figure 01b*).

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Figure 01a ECG showing typical T inversion in anterior leads in Wellens' syndrome

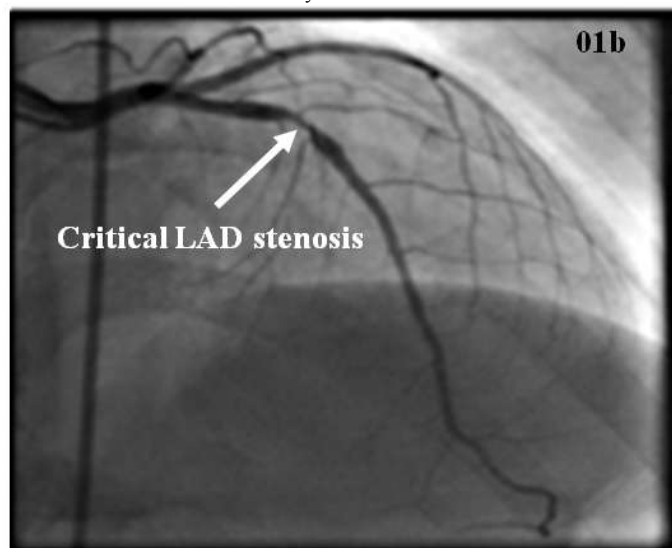


Figure 01b Coronary angiography demonstrating critical LAD stenosis in a Wellens patient

One of the interesting phenomena is that the patients may be pain free by the time the ECG is taken and may have normal or minimally elevated cardiac enzymes. However, they are at extremely high risk for extensive anterior wall MI within the next few days to weeks².

After the original description of the syndrome in 1980 and a series of case reports, emergency physicians have become increasingly aware of this high-risk subset of patients but the etiology of the Wellens' T-waves remains undetermined.

Though the diagnosis of Wellens' syndrome is clinical with supportive ECG changes, the interest is still focused on the identification of any other subtle differences in cardiac imaging modalities such as advanced 2D echocardiography. If such a non invasive parameter is having a predictive value to diagnose this condition that index also helpful to improve the diagnostic accuracy of Wellens' syndrome.

As a result of critical LAD stenosis, these patients usually require invasive therapy, do poorly with medical management and may suffer MI or cardiac arrest if inappropriately subject to stress tests³. Therefore, the timely diagnosis of this condition is utmost important.

In the present study, we hypothesized that the presence of ischemic myocardium in Wellens' syndrome may be associated with characteristic Regional Wall Motion Abnormalities (RWMA) in 2D echocardiography and abnormal results of Global or Regional Longitudinal Strain (GLS/RLS) other than the typical ECG findings. Apart from that the Percutaneous Coronary Interventions (PCI) would have a better sustainable result as one of the main therapeutic strategy to treat these patients as well. Therefore, the study was mainly aimed to

describe the clinical, echocardiographic and coronary angiographic characteristics of patients with Wellens' syndrome and to follow up the patients who underwent PCI.

METHODOLOGY

Study design and setting

The study was conducted at cardiology unit, teaching (General) hospital Kandy, Sri Lanka in 2017. It was design as a descriptive cross-sectional study on patients with clinical diagnosis of Wellens' syndrome obtaining a convenient sample. Apart from the serial ECG monitoring, cardiac troponin I was assessed in all patients after 6 hours of chest pain. A comprehensive 2D echocardiogram was carried out in all within 24 hours of admission and prior to any coronary intervention for the valuation of RWMA and GLS.

All the 2D echocardiograms were performed by two operators only to minimize the inter individual bias in echocardiography. Demographic and other clinical data was collected through interviewer administered questionnaire.

Subsequent Management of the patients

Dual antiplatelet therapy and subcutaneous enoxparin treatment was initiated as for the management of unstable angina or /Non ST elevated MI according to standard guidelines. After the initial assessment, all the patients were subjected for coronary angiogram within 24 hours of admission. Patients who had PCI amenable lesions were treated with angioplasty and stenting. Rests of the patients were managed with either medical management or Coronary Artery Bypass Grafting (CABG). All the patients were reviewed in 30th day and 90th day for Major Adverse Cardiac Events (MACE). MACEs were defined as cardiac death, re-infarction or having residual angina following the treatments.

Inclusion criteria

Patients with following ECG and clinical criteria were recruited for the study. Those included, deeply-inverted or biphasic T waves in V₂₋₃ (may extend to V₁₋₆), having isoelectric or minimally-elevated ST segment (< 1mm), absence of precordial Q waves and preserved precordial R wave progression². All of them had a history of recent angina and patients who had classical ECG pattern even in the pain-free period also considered, if they had classical angina within seven days.

Exclusion criteria

Patients who had any previous history of MIs, having pathological Q-waves in their ECG, ongoing arrhythmias, left bundle branch block or more than having mild valvular heart disease were excluded from the study.

Electrocardiographic assessment

12 lead ECG was obtained in a standard rate of 25 mm/sec speed, and a gain of 10 mV. ECG analysis was carried out by experience two cardiologists and all ECG tracings were electronically recorded. Typical ECG pattern in Wellens' syndrome was defined as deeply-inverted or biphasic T waves in V₂₋₃ (may extend to V₁₋₆), isoelectric or minimally-elevated

ST segment (< 1mm,) without having precordial Q waves and preserved precordial R wave progression².

Echocardiographic assessment

Standard echocardiographic examination was performed within 12 hours of admission using Philips 7C cardiovascular ultrasound system. Image loops of three consecutive heart cycles with frame rates of 50–80 frames/s were recorded and stored digitally for later offline analysis by Q lab software. Left ventricular ejection fraction was calculated using biplane Advanced 2 Dimensional Quantification (A2DQ) method. Two-dimensional speckle tracking analysis was performed using commercially available software by the investigator blinded to clinical and other data (Figure 02).

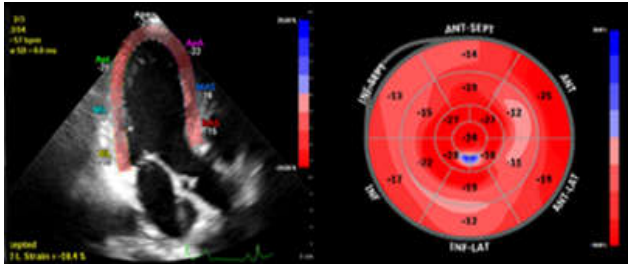


Figure 2 Echocardiographic evaluation by two dimensional speckle tracking analysis.

segmental peak systolic strain values³ and the study was performed separately by two individual investigators.

Assessment of regional wall motion abnormality

Wall motion of each Left Ventricular (LV) segment was assessed visually on the basis of its motion and systolic thickening in the 17-segment model. Each segment was graded using a conventional four-point scale (1, normokinesis; 2, hypokinesis; 3, akinesis; 4; dyskinesis). The wall motion score index (WMSI) was calculated as the mean value of all segments in each subject⁹. Regional WMSI in LAD territory (WMSI_{LAD}) was calculated as the mean wall-motion score of six segments closely mimicking the anatomic perfusion area of LAD (basal anterior wall, mid anterior wall, apical anterior wall, basal anteroseptum, mid anteroseptum and apical anteroseptum)¹⁰.

Angiographic Assessment

Coronary angiography was performed by Seimons Axiom Sensis XP - Digital Cardio Imaging system. Coronary angiograms were assessed by an experienced 2 individual cardiologists. Each major coronary artery was inspected for significant lesions in two orthogonal planes. Stenosis in LAD more than 90% was considered as critical LAD stenosis.

Statistical analysis

Continuous variables were presented as mean with standard deviation (SD) and categorical variables as percentages. The Statistical Package for Social Sciences version 17 (SPSS) was used for all calculations.

Ethical clearance

Ethical clearance was obtained from the ethical review committee of teaching hospital Kandy, Sri Lanka. Informed written consent was obtained from all patients while in the hospital stay.

RESULTS

There were 30 patients (Mean age of 56.6±9.3 years) with 60% (n=18) of males. There were 80%, (n=24) of patients with negative cardiac Troponin I. The baseline characteristics are illustrated in Table 01. Normal Cutoff for GLS in Phillips was considered as -17.5.¹⁴

Table 1 Baseline characteristics of the study sample

Variable	Results n (%)
Age (mean ± SD)	56.6±9.3 years
Gender	
Male	60.0% (n=18)
Female	40.0% (n=12)
Co-morbidities	
Diabetes	36.7% (n=11)
Hypertension	53.3% (n=16)
Dyslipidemia	33.3% (n=10)
Smoking	33.3% (n=10)

SD= Standard Deviation

Echocardiographic characteristics

Mean ejection fraction (A2DQ) of the sample was 57.9±9.8%. The average global resting RWMSI was 1.04±0.07 and mean resting RWMSI_{LAD} was 1.07±0.13. In the sample, peak GLS and RLS_{LAD} at rest were -17.8±2.9 and -18.0±2.7 respectively (Table 02).

Table 2 Echocardiographic characteristics of the study sample

Variable (mean ± SD)	Results
Mean ejection fraction	57.9±9.8%
Average global resting RWMSI	1.04±0.07
Mean resting RWMSI _{LAD}	1.07±0.13
Peak GLS	-17.8±2.9
RLS _{LAD} at rest	-18.0±2.7

SD= Standard Deviation, RWMSI=Regional Wall Motion Score Index, RWMSI_{LAD}= Regional Wall Motion Score Index in Left Anterior Descending Artery territory, GLS= Global longitudinal strain, RLS_{LAD}= Regional Longitudinal Strain of the Left anterior Descending Artery territory

Angiographic characteristics

Majority [70% (n=22)] of them had critical proximal LAD stenosis, which was defined as ≥90% luminal stenosis. Out of the sample, 50.00% (n=15) had single vessel disease involving LAD. Addition to that 16.60% (n=5) and 20.00% (n=6) had double and triple vessel disease respectively (Figure 03). All who had critical LAD stenosis underwent PCI. At the end of the 30th day and 90th day following PCI, none of them had cardiac death, re-infarction or residual angina as MACE.

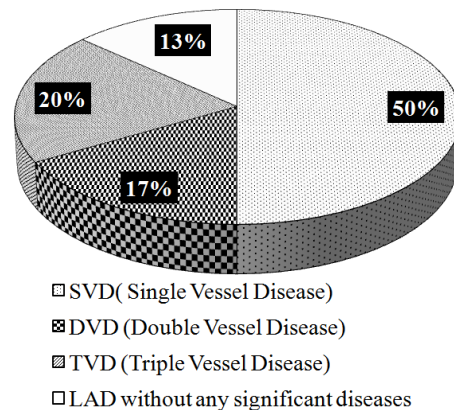


Figure 3 Vascular territorial involvement of the study sample

DISCUSSION

Wellens' syndrome is one a peculiar clinical condition, which is characterized by T-wave inversion in ECGs in a patient with intermittent angina. The interesting point is that these transient electrical changes observed in a surface ECGs more often seen during the pain-free period⁴. Though the syndrome is recognized in long time ago, the primary pathophysiology and the mechanism of these T wave changes remains unanswered.

The classical ECG characteristics of Wellens' syndrome are well described and there are two patterns, which are recognized according to the configuration of T wave inversion. The Type A pattern includes biphasic T waves which account for one fourth of cases and the type B consisted only symmetrically inverted T waves, which is more common and accounting for three fourth of the cases⁵. Here in our study, there were 40% (n=12) and 60% (n=18) belongs to Type A and B respectively. Generally, it has been recognized that the Wellens' syndrome is reported to happen in 14% to 18% of patients presenting with unstable angina⁶. Some authors consider this as a pre-infarction stage of proximal LAD plaque disease and the ECG changes are accounted for reperfusion of the already ischemic myocardium with intermittent spasms of proximal LAD artery⁷. Therefore, the identification of the typical Wellens' ECG pattern carries significant diagnostic and prognostic value since the early detection of this pre-infarction stage can be treated by early coronary revascularizations.

One of the other important point to highlight is that the stress testing is absolutely contraindicated in these patients^{9,10} as the additional myocardial stress on this specific type of unstable angina may readily increase the potential to induce an extensive MI following the completion of stress protocol.

Interestingly, some studies present that regional longitudinal strain at rest can be used to screen significant stenosis of the LAD in patients with suspected non ST elevated acute coronary syndromes¹¹. Though the conventional visual assessment of the movements of myocardial segments and wall thickening is the routine way to recognize RWMA, subclinical myocardial dysfunction due to ischemia may not always cause gross RWMA as in Wellens' type of unstable angina. Therefore, the RLS/GLS may have a superior implication of detection these subtle changes of RWMA^{12,13}. Though we hypothesises the same phenomenon in Wellence' patients, our study showed that there are no specific features in strain pattern compared to normal cutoffs.

Based on the ECG criteria, it is anticipated that the positive predictive value of Wellens' ECG sign is approximately 86%⁸. However, the conventional and advanced echocardiography still lags behind this and the ECG may be the strong indicator of an impending extensive anterior MI and this fact is further reinforced by in these patients our study findings. Since the classical ECG findings are found mostly during pain-free intervals of patients presenting with intermittent angina, this can be easily overlooked.

The most important aspect in Wellens' syndrome is the recognition of this ECG sign in a timely fashion as these patients should undergo early coronary imaging followed by appropriate interventions. One of the important points to remember is that these patients may firstly respond well to

medical management but eventually do poorly with conservative therapy and require some form of revascularization strategies in the later time. Thus, it is vital for the physicians to identify these ECG features of Wellens' syndrome for early referral to a cardiologists to arrange appropriate interventional therapy, which may reduce the mortality and morbidity form impending MI⁴. It has been found that the acute MI, LV dysfunction, and sudden cardiac death can ensue if appropriate catheter based coronary interventions are not accomplished in a timely fashion¹⁰ in these patients

CONCLUSION

In Wellens' syndrome, elevation of cardiac Troponin, echocardiographic parameters such as GLS or RWMSI might not enable the prediction of significant LAD stenosis. Therefore, there should be a high degree of clinical suspicion for the timely diagnosis of this critical condition and to implement an appropriate early reperfusion strategy for them.

Limitations

We would like to highlight some limitations in our study. Firstly, the size of the sample was relatively small. Therefore, the findings of this preliminary study should be re-validated with further large scale prospective studies with long term follow up. Secondly, if the strain patterns were compared with a control sample i.e. Wellens' ECGs with normal LAD, the conclusions can be made much stronger. Finally, we have assessed only the longitudinal strain parameters without concentrating the circumferential or radial strain. However, many researchers have shown that the longitudinal strain is more sensitive than circumferential strain for reflecting myocardial ischemia¹⁵.

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Conflict of interest

None

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