Role of a 12-Lead Electrocardiogram in the Diagnosis of Cardiac Tamponade as Diagnosed by Transthoracic Echocardiography in Patients With Malignant Pericardial Effusion

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ABSTRACT

Background: Few studies have looked at the utility of the 12-lead electrocardiogram (ECG) in diagnosing cardiac tamponade in malignant pericardial effusion (PE). The aim of this study was to determine the sensitivity (Se), specificity (Sp), positive predictive value (PPV), and negative predictive value (NPV) of 12-lead ECG in diagnosing cardiac tamponade in PE.

Hypothesis: Abnormalities on a 12 lead ECG can be used to diagnose or exclude cardiac tamponade in patients with malignant PE.

Methods: Using echocardiography as the gold standard for diagnosis of cardiac tamponade, we determined the Se, Sp, PPV, and NPV for individual and combinations of the 3 ECG abnormalities (low-voltage complexes, electrical alternans, and sinus tachycardia).

Results: For PEs of all sizes, the Se, Sp, PPV, and NPV for detecting cardiac tamponade were: low-voltage complexes (56%, 74%, 81%, 46%), electrical alternans (23%, 98%, 95%, 39%), and sinus tachycardia (76%, 60%, 79%, 56%), respectively. Presence of all 3 and any of the 3 ECG abnormalities had a Se, Sp, PPV, and NPV of 8%, 100%, 100%, 36% and 89%, 47%, 77%, 69%, respectively, for cardiac tamponade. The odds ratios for cardiac tamponade in PE were 3.7 (95% confidence interval [CI]: 1.65-8.30) for low-voltage complexes, 12.3 (95% CI: 1.58-95.17) for electrical alternans, and 4.9 (95% CI: 2.22-10.80) for sinus tachycardia. Presence of any of 3 ECG abnormalities had an odds ratio of 7.3 (95% CI: 2.9-18.1) for cardiac tamponade.

Conclusions: In malignant PE, combination of ECG abnormalities can supplement clinical examination in the diagnosis of echocardiographic cardiac tamponade. Due to its low NPV, 12-lead ECG cannot be used as a screening tool to exclude cardiac tamponade with malignant PE.

Introduction

Cardiac tamponade occurs when a large amount of fluid accumulates in the pericardium, leading to hemodynamic compromise.^{1,2} Although the incidence of cardiac tamponade in the general population is low, its occurrence is relatively common in patients with malignant pericardial effusions (PE).³ Early diagnosis is crucial in limiting morbidity and mortality from this life-threatening condition. The utility of the 12-lead electrocardiogram (ECG) in detecting

cardiac tamponade in this unique population has not been rigorously evaluated.

The clinical sign of pulsus paradoxus (decrease in systolic blood pressure of >10 mm Hg with inspiration) is a strong indicator of cardiac tamponade. A recent systematic review noted its predictive prowess in detecting cardiac tamponade.⁴ However, pulsus paradoxus is not exclusive to the presence of cardiac tamponade. Not only can patients with other pulmonary conditions (asthma, chronic obstructive pulmonary disease exacerbation) demonstrate pulsus paradoxus,⁵ but patients with cardiac tamponade in the presence of other conditions (left ventricular hypertrophy, hypovolemia, large atrial septal defects) may not demonstrate pulsus paradoxus.⁶ Further, in the series reported by Levine et al, of the 50 consecutive patients who underwent pericardiocentesis for cardiac tamponade,

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only 36% of patients exhibited pulsus paradoxus and only 50% of the patients had a clinical suspicion of tamponade.⁷ Electrocardiogram abnormalities associated with PE and cardiac tamponade include low-voltage ECG complexes, PR-segment depression, low-voltage P waves, and sinus tachycardia.^{1,8,9} One such finding very specific to cardiac tamponade is electrical alternans.⁹

The technical gold standard for the diagnosis of cardiac tamponade would be heart catheterization to document equalization of pressures in the left and right ventricles. Intra-arterial pressure transducers before and after pericardiocentesis can demonstrate improvement in hemodynamics with drainage of a PE.⁹ A transthoracic echocardiogram (TTE) is currently the most practical and noninvasive means of confirming cardiac tamponade^{4,7,10}; however, TTE requires trained personnel to acquire images and an experienced cardiologist for interpretation. Further, TTE and/or a skilled interpreter may not always be readily available, especially in rural facilities. Point-of-care ultrasonography, now more readily available, aims to bridge this gap, but operator skill levels vary. An ECG is a more universal tool, and a majority of health care providers are proficient in ECG interpretation. Utilizing the 12-lead ECG to screen for cardiac tamponade might be a more cost-effective and expedient technique in the initial evaluation of patients with a previously diagnosed PE. Echocardiography is the gold standard for diagnosing cardiac tamponade, and the 12-lead ECG would never replace it, but it would be a good starting point for the evaluation of this patient population before a cardiologist is available. The aim of this study was to determine the diagnostic accuracy of a 12-lead ECG in diagnosing cardiac tamponade in a patient with a preexisting malignant PE.

Methods

Study Population

This was a retrospective cross-sectional study of patients with a malignant PE and was approved by the institutional review board of University of Texas MD Anderson Cancer Center (MDACC). We identified about 185 consecutive patients who were admitted to MDACC between 2003 and 2007 with a diagnosis of malignant PE. Of these, 97 had a diagnosis of cardiac tamponade and 88 did not. We excluded patients without an ECG tracing obtained within 24 hours of the TTE that was used to diagnose or exclude cardiac tamponade. This led to the exclusion of 14 patients in the cardiac tamponade group and 44 patients in the PE group. We then calculated the sensitivity (Se), specificity (Sp), positive predictive value (PPV), and negative predictive value (NPV) for the 127 patients (84 tamponade, 43 PEs). Baseline clinical and demographic data were collected from a retrospective review of the patients' electronic health records.

Electrocardiography

The index 12-lead ECGs (obtained within 24 hours of the TTEs used to determine the presence or absence of cardiac tamponade) for the study patients were reviewed independently by a cardiologist. Electrical alternans was defined as an alternating appearance of P, QRS, ST, or

T waveforms, or any combination of these, in a regular rhythm and provided the waveforms originated from a single pacemaker site.¹¹ Low-voltage QRS complex was defined as (1) QRS complexes <5 mm in all limb leads or (2) QRS complexes <10 mm in all precordial leads. Sinus tachycardia was defined as a heart rate of >100 bpm on the ECG tracing.¹¹

Echocardiography

A complete TTE with color Doppler was independently evaluated by a cardiologist using standard guidelines.^{12,13} A PE was diagnosed on a TTE as a fluid-filled space at the myocardium-pericardium interface. An effusion was defined as large if the distance between the pericardium and myocardial surface was >2 cm; as moderate if this distance was between 1 and 2 cm; and as small if the distance was ≤1 cm.^{13,14} All subjects with a primary malignancy and with subsequent development of a PE were considered as having a malignant PE. For this study, a cytological diagnosis was not required to define a malignant PE, as only patients undergoing pericardiocentesis would have met such a definition.

Cardiac Tamponade

The echocardiogram was the gold standard for the diagnosis of cardiac tamponade in this study. A diagnosis of cardiac tamponade was made if the TTE showed at least 1 of the following: (1) right atrial collapse in diastole, (2) right ventricular collapse in diastole, and (3) respiratory transmitral flow variation >25%.^{14,15}

An ultrasound or fluoroscopically guided pericardiocentesis was performed in patients with cardiac tamponade and fluid was obtained for cytology. A malignant pericardial effusion was confirmed with the identification of malignant cells in the pericardial fluid or when a pericardial biopsy was positive for metastatic malignant disease. Cytologic diagnosis was not available for patients without cardiac tamponade, as, understandably, they did not undergo a pericardiocentesis.

Statistical Analysis

The Se, Sp, PPV, and NPV of each of the different ECG abnormalities (low-voltage QRS complexes, electrical alternans, and sinus tachycardia) were evaluated. Univariate logistic regression models were constructed by entering the ECG abnormalities separately as the predictor variables and the presence of cardiac tamponade as the binary outcome variable. Odds ratios (OR) were computed with 95% confidence intervals (CI) for the association between ECG abnormalities and their combinations, and presence of cardiac tamponade. A *P* value <0.05 was considered to be statistically significant. All statistical analyses were performed using STATA version 9.3 (StataCorp, College Station, TX).

Results

A total of 127 patients with malignant PE were included in the study, of which 84 (66%) had cardiac tamponade. Table 1 depicts the demographic characteristics of the study population. The mean age of the group was 52.68 ± 13 years.

Table 1. Patient Demographics for the Pericardial Effusion and Cardiac Tamponade Groups

	Pericardial Effusion		Cardiac Tamponade	
	N	%	N	%
Age, y				
15–35	7	16.27	9	10.71
36–55	12	27.9	36	42.86
56–75	21	48.83	39	46.43
76–95	3	6.97	0	0.00
Total	43	100.00	84	100.00
Ethnicity				
Caucasian	27	62.80	62	73.81
African American	7	16.28	10	11.90
Hispanic	6	13.95	7	8.33
Other	2	4.65	5	5.95
Unknown	1	2.33	0	0.00
Total	43	100.00	84	100.00
Sex				
F	23	53.49	47	55.95
M	20	46.51	37	44.05
Total	43	100.00	84	100.00
Abbreviations: F, female; M, male.				

Table 2. Primary Malignancies Associated With Pericardial Effusion and Cardiac Tamponade in the Study Population

Type of Malignancy	Pericardial Effusion		Cardiac Tamponade	
	N	%	N	%
Lung	15	35	29	34
Breast	2	5	15	18
Hematological	16	37	21	25
GI/GU	9	21	18	21
Others	1	2	1	2
Total	43	100.00	84	100.00
Abbreviations: GI, gastrointestinal; GU, genitourinary.				

Lung carcinoma, breast carcinoma, and hematological cancers were the predominant malignancies in the study population (Table 2). Table 3 shows the prevalence of various ECG abnormalities in the PE and cardiac tamponade groups. As expected, a majority of the effusions in the cardiac tamponade group were large in size, and those in the PE-only group were small.

Table 4 shows the Se, Sp, PPV, and NPV of each ECG abnormality (low-voltage QRS complexes, electrical alternans, and sinus tachycardia) and their combinations

Table 3. Echocardiogram and ECG Characteristics of the Pericardial Effusion and Cardiac Tamponade Groups

	Pericardial Effusion		Cardiac Tamponade	
	N	%	N	%
Size of effusion				
Large	7	16.28	75	89.29
Moderate	12	27.91	9	10.71
Small	24	55.81	0	0.00
Total	43	100.00	84	100.00
Echo: RA diastolic collapse				
Present	0	0.00	65	77.38
Absent	43	100.00	17	20.24
Undetermined	0	0.00	2	2.38
Total	43	100.00	84	100.00
Echo: RV diastolic collapse				
Present	0	0.00	53	63.10
Absent	43	100.00	28	33.33
Undetermined	0	0.00	3	3.57
Total	43	100.00	84	100.00
Echo: Transmitral flow variation				
Present	0	0.00	77	91.67
Absent	43	100.00	5	5.95
Undetermined	0	0.00	2	2.38
Total	43	100.00	84	100.00
ECG: Low-voltage complexes				
Present	11	25.58	47	55.95
Absent	32	74.42	37	44.05
Total	43	100.00	84	100.00
ECG: Electrical alternans				
Present	1	2.33	19	22.62
Absent	42	97.67	65	77.38
Total	43	100.00	84	100.00
ECG: Sinus tachycardia				
Present	17	39.53	64	76.19
Absent	26	60.47	20	23.81
Total	43	100.00	84	100.00
Abbreviations: ECG, electrocardiogram; RA, right atrium; RV, right ventricle.				

Table 4. Parameters of Validity for Different ECG Abnormalities in Diagnosing Cardiac Tamponade

Size of Effusion	ECG Abnormality	Se, %	Sp, %	PPV, %	NPV, %
All sizes	Low-voltage complexes	55.95	74.44	81.03	46.37
	Electrical alternans	22.61	97.67	95.00	39.25
	Sinus tachycardia	76.19	60.46	79.01	56.52
	All abnormalities ^a	8.33	100.00	100.00	35.83
	Any abnormality ^b	89.28	46.51	76.53	68.96
Large	Low-voltage complexes	58.66	71.42	95.65	13.88
	Electrical alternans	24.00	85.71	94.73	9.52
	Sinus tachycardia	78.66	28.57	92.18	11.11
	All abnormalities ^a	8.00	100.00	100.00	9.21
	Any abnormality ^b	92.00	28.57	93.24	25.00
Moderate	Low-voltage complexes	33.33	66.66	42.85	57.14
	Electrical alternans	11.11	100.00	100.00	60.00
	Sinus tachycardia	55.55	58.33	50.00	63.63
	All abnormalities ^a	11.11	100.00	100.00	60.00
	Any abnormality ^b	66.66	33.33	42.85	57.14
Small	Low-voltage complexes	—	78.26	—	—
	Electrical alternans	—	100.00	—	—
	Sinus tachycardia	—	69.56	—	—
	All abnormalities ^a	—	100.00	—	—
	Any abnormality ^b	—	56.52	—	—

Abbreviations: ECG, electrocardiogram; NPV, negative predictive value; PPV, positive predictive value; Se, sensitivity; Sp, specificity.
^a“All abnormalities” indicates presence of all 3 ECG abnormalities.
^b“Any abnormality” indicates presence of at least 1 of the following: low-voltage complexes, electrical alternans, or sinus tachycardia.

in predicting cardiac tamponade. Among individual ECG abnormalities, low-voltage complexes and electrical alternans had higher specificities, whereas sinus tachycardia and low-voltage complexes had higher sensitivities for diagnosing a cardiac tamponade in effusions of all sizes (Table 4). In patients with a large PE, the PPV of electrical alternans was 95% for the presence of cardiac tamponade. When stratified by the size of the PE, among patients with large effusions, the sensitivity of “any ECG abnormality” for the presence of tamponade was higher than that in patients with moderate-sized PE.

Upon logistic regression analysis, for effusions of all sizes, the OR was 3.7 (95% CI: 1.65–8.30) for low-voltage complexes, 12.3 (95% CI: 1.58–95.17) for electrical alternans, and 4.9 (95% CI: 2.22–10.80) for sinus tachycardia in predicting cardiac tamponade (Table 5). The presence of any 1 of the 3 ECG abnormalities had an OR of 7.25 (95% CI: 2.9–18.1) for the presence of cardiac tamponade. In our database, there was no patient who had all 3 ECG abnormalities without

Table 5. Univariate Analyses of the Association Between ECG Abnormalities and Cardiac Tamponade

Size of Effusion	ECG Abnormality	OR (95% CI)	P Value
All sizes	Low-voltage complexes	3.7 (1.65–8.30)	0.002
	Electrical alternans	12.28 (1.58–95.17)	0.016
	Sinus tachycardia	4.89 (2.22–10.80)	0.000
	Any abnormality ^a	7.25 (2.9–18.1)	0.000
Large	Low-voltage complexes	1.9 (0.21–16.80)	0.566
	Electrical alternans	3.55 (0.65–19.48)	0.145
	Sinus tachycardia	1.48 (0.26–8.32)	0.660
	Any abnormality ^a	4.6 (0.73–28.96)	0.104
Moderate	Low-voltage complexes	1.0 (0.16–6.25)	1.000
	Electrical alternans	—	—
	Sinus tachycardia	1.75 (0.31–10.02)	0.530
	Any abnormality ^a	1.0 (0.16–6.25)	1.000
Small	Low-voltage complexes	—	—
	Electrical alternans	—	—
	Sinus tachycardia	—	—
	Any abnormality ^a	—	—

Abbreviations: CI, confidence interval; ECG, electrocardiogram; OR, odds ratio.
^a“Any abnormality” indicates presence of at least 1 of the following: low-voltage complexes, electrical alternans, or sinus tachycardia.

echo-detected cardiac tamponade, and hence we could not compute an OR for this variable. When we stratified the patients by the size of PE, the regression model lost power to predict the presence of cardiac tamponade, and none of the associations were statistically significant ($P > 0.05$).

Discussion

In our study, the presence of all 3 ECG abnormalities (low-voltage QRS complexes, electrical alternans, and sinus tachycardia) had a high Sp and PPV for the diagnosis of cardiac tamponade in patients with malignant PE. Though several studies have looked at individual ECG abnormalities to help aid the diagnosis of cardiac tamponade, to our knowledge, ours is the only study to examine a combination of ECG abnormalities in screening for cardiac tamponade in patients with malignant PE.

The prevalence of malignant effusions in the cancer population is approximately 20%.³ In our study, the malignancies commonly associated with PE are consistent with reports in the extant literature.^{3,16} Several ECG abnormalities have been associated with PE and cardiac tamponade.^{7,8,17} These include sinus tachycardia, PR-segment depression, ST-segment elevation, low QRS voltage, and electrical alternans. Though electrical alternans is not consistently present in cardiac tamponade, it is very specific for this condition.^{8,18} Electrical alternans occurs due

to a beat-to-beat variation of the myocardial electrical axis on account of a swinging motion of the heart inside a fluid-filled pericardium.¹ Sinus tachycardia is most commonly present in tamponade as a compensatory mechanism.^{1,16} Eisenberg et al studied the diagnostic value of the 12-lead ECG in PE and cardiac tamponade and found that low-voltage QRS complex and PR-segment depression were highly specific but not sensitive for diagnosing cardiac tamponade.¹⁸ However, this study looked predominantly at small PEs. Bruch et al investigated QRS-voltage changes in patients with cardiac tamponade vs patients with PE but without tamponade physiology.¹⁹ The authors concluded that low-voltage QRS was associated with cardiac tamponade, but not PE.¹⁹

Meyers et al studied 2 temporally separate ECGs for 46 patients, obtained before and after the development of a PE. They found that development of sinus tachycardia and reduction in QRS voltage were associated with the development of a PE. A weak correlation ($r = 0.3$) was noted between QRS voltage and the effusion size. Electrical alternans occurred only in 1 of the 5 patients with a large effusion but not in others. In addition, the authors also compared the ECGs of PE patients with those of age- and sex-matched control subjects. They found that sinus tachycardia and change in QRS voltage were associated with the presence of a PE. However, no ECG abnormality was sensitive for diagnosis of a PE.²⁰

In our study, 77% of patients with cardiac tamponade had sinus tachycardia and 89% had at least 1 of the 3 ECG abnormalities (low-voltage complexes, sinus tachycardia, or electrical alternans), irrespective of the effusion size. When the presence of at least 1 ECG abnormality ("any abnormality") was evaluated as a screening tool, it had a high Se and PPV in detecting cardiac tamponade. The PPVs of the different ECG abnormalities to detect cardiac tamponade are the highest in patients with large effusions, whereas they are lower in effusions of all sizes and are the lowest for patients with moderate-sized effusions (Table 4). Conversely, the NPVs are the lowest in the large-effusion group. This is consistent with a well-known phenomenon associated with screening in clinical epidemiology: As prevalence decreases, the PPV for a screening test correspondingly decreases and NPV increases. In our study population, effusions were predominantly large and prevalence of cardiac tamponade was very high, and expectedly, this lowered the NPVs for the various ECG abnormalities and their combinations.

Though development of a tamponade could be suspected based on physical examination parameters alone, in certain patient populations this may not be easy. An evaluation of central venous pressure is important, as it is mostly elevated in tamponade, except in patients who are volume depleted. The findings of this study support the use of serial and follow-up ECGs in the evaluation of patients with PE to prompt an early diagnosis and further workup for possible underlying cardiac tamponade, especially in light of the high PPVs in patients with large effusions.

Study Limitations

The hallmark of a useful screening test is its Se and NPV. Despite high Se for some ECG abnormalities, their NPVs,

one of the most useful attributes of a screening test, are unacceptably low. This is most probably due to the very high prevalence of tamponade in our study population. The most plausible explanation for this effect is the sampling method for our study population: a convenience sample of consecutive patients admitted for management of malignant PE. Most of these patients had large and probably symptomatic effusions, which would have led to a deliberate over-sampling of the tamponade group and an under-sampling of the effusion-only group. To evaluate the true NPV of the screening tool "any abnormality" in detecting cardiac tamponade in the real world, prospective studies looking at all comers with malignant pericardial effusions are needed.

The MDACC is an institution specializing in caring for patients with various forms of cancer. As a result, our study only included patients with malignant PEs, and hence the results from this analysis cannot be generalized to patients without malignant PEs. The accumulation of effusions is faster in these patients. Whether this would affect the development of ECG abnormalities in these patients is not known. Pericardial thickening and deposits are pronounced in malignancy and can affect the voltage amplitude of ECG. One of the limitations of this study is the definition used for a malignant PE. Cytologic and biochemical analyses confirming a neoplastic etiology for the effusion were only available for patients who underwent pericardiocentesis (cardiac tamponade group). So, other potential causes for a PE in the PE-only group cannot be ruled out. Another limitation of this study is the retrospective design and the small sample sizes, especially for patients with moderate and small effusions.

Conclusion

The 12-lead ECG can aid in the diagnosis of cardiac tamponade in patients with malignant PEs and can be a supplemental tool for the quick bedside diagnosis of this life-threatening condition. Though the presence of all 3 ECG abnormalities is highly suggestive of tamponade (100% specificity), the absence of all 3 ECG abnormalities cannot rule out the presence of a tamponade in patients with a previously diagnosed malignant effusion.

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