The interpretation of the electrocardiogram in patients with pulmonary hypertension: the need for clinical correlation

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Key words:
Electrocardiogram; Hypertrophy; Pulmonary hypertension.

Background. **The detection and treatment of pulmonary hypertension have become increasingly important for the clinician. While the electrocardiogram is often used as a screening tool in patients suspected of having pulmonary hypertension, the sensitivity for detecting right ventricular hypertrophy in the era of computerized electrocardiogram analysis is highly suspect. The aim of the study was to determine the importance of clinical information in providing an accurately edited electrocardiographic system.**

Methods. **The interpretation of the electrocardiograms of 64 consecutive symptomatic patients (12 males, 52 females, mean age 43 ± 13 years) with isolated pulmonary hypertension provided by the computer program and the cardiologist following editing during routine daily reading sessions were reviewed. The reader (blinded cardiologist) was unaware of the clinical diagnosis. Subsequently, a cardiologist given clinical information regarding age and symptoms, edited the computer interpretation.**

Results. **The unblinded cardiologist diagnosed right axis deviation > 90°, right ventricular hypertrophy, right ventricular strain, and right atrial enlargement in 76.6, 78.1, 71.9 and 20.3% of patients, respectively. In 6 (9.4%) patients, the electrocardiogram was normal. The blinded cardiologist and computer program diagnosed right ventricular hypertrophy in 43.8 and 39.1% respectively and most often characterized right ventricular strain as non-specific or inferior or as antero-lateral ischemia.**

Conclusions. **The electrocardiogram has a high degree of sensitivity for the detection of abnormalities in symptomatic patients with isolated pulmonary hypertension. Correlation with the clinical parameters is essential to optimize the usefulness of the electrocardiogram. Consideration should be given to tailoring computerized electrocardiogram interpretative software to clinical information.**

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Introduction

The detection and treatment of pulmonary hypertension have become increasingly important for the clinician. Pulmonary vascular occlusive disease is a frequent cause of deterioration and death in rheumatic disease, pulmonary embolization, and the late stages of cirrhosis[1,2]. Further, reports that commonly used anorectic drugs (dexfenfluramine and fenfluramine with phentermine) are associated with a 20-50-fold increase in the risk of primary pulmonary hypertension and have increased the need for clinicians to suspect and detect this condition[3,4].

A screening chest X-ray, an electrocardiogram (ECG) along with an echo-Doppler exam are usually the initial diagnostic algorithms[1]. A high index of suspicion, experience in the cardiovascular exam, and a reliable interpretation of the ECG can identify most patients with pulmonary hypertension. For example, in mixed connective tissue disease, clinical and laboratory findings including right ventricular hypertrophy (RVH) on the ECG have a 92% sensitivity and a 100% specificity for the detection of pulmonary hypertension, and in primary pulmonary hypertension there is ECG evidence of RVH in over 80% of cases[5-9].

While the ECG is one of the most frequently utilized and least expensive diagnostic tools in medicine, its sensitivity for the detection of RVH and thus pulmonary hypertension, particularly in the era of computerized ECG analysis, is highly suspect[10-12]. In a study comparing eight cardiologists blinded to clinical information, with nine different computer ECG programs in 55 validated cases of RVH, the computer analyses were less likely to detect RVH than the cardiologists (31.8 vs 46.6%, $p < 0.01$), and neither had an adequate sensitivity[13]. The incremental accuracy that could be provided by simple clinical information has not been assessed.

The objective of this study was to determine the importance of clinical information in providing an accurately edited ECG system to experienced cardiologists responsible for editing ECG, with and without clinical knowledge of the patient.

Methods

Study population. Patients with pulmonary hypertension due to pulmonary vascular occlusive disease were evaluated in the Pulmonary Hypertension Clinic at the University of Michigan. Each underwent a thorough history, physical exam, ECG, echocardiogram, pulmonary function testing, and right heart catheterization. Symptoms (type and duration), effort tolerance, and New York Heart Association (NYHA) functional class were recorded during the initial visit. Pulmonary hypertension was defined as a mean pulmonary artery pressure > 25 mmHg. Patients were excluded if they presented with evidence of chronic lung disease, left ventricular hypertrophy, mitral or aortic valve disease, congenital heart disease, coronary artery disease or cardiomyopathy.

Electrocardiography. Standard (American Heart Association) 12-lead ECGs were obtained with the patient in the supine position and using a Marquette computerized ECG unit (Marquette Electronics, Milwaukee, WI, USA, Muse Network Series system, MAC VU with the 12SL software version) which provided an unedited interpretation. The ECG and computer interpretations were reviewed by one of twelve experienced faculty cardiologists during routine daily reading sessions. The reader (blinded cardiologist) was unaware of the clinical diagnosis or study. Subsequently, a cardiologist (unblinded) provided the age and clinical diagnosis (e.g. pulmonary embolization, possible primary pulmonary hypertension, CREST) and edited the computer interpretation utilizing standard ECG nomenclature and definitions[14,15].

Statistical analysis. All ECG interpretative data were computed and analyzed by an independent observer. Where applicable, variables were described using the mean ± SD. The agreement between the unblinded cardiologist, blinded cardiologist, and computer ECG analysis was described using the kappa statistics. The relationship between the ECG criteria suggestive of pulmonary hypertension and the NYHA class was examined using Fisher's exact tests. SPSS version 8.0 (SPSS 2003 Inc., Chicago, IL, USA) was used for all analyses.

Results

Sixty-four consecutive patients (12 males, 52 females, mean age 43 ± 13 years) with isolated pulmonary hypertension constituted the study group; 79.7% were in NYHA class III or IV. The clinical diagnosis, functional class, hemodynamic, and demographic data are listed in table I[16,17]. The majority of patients had idiopathic or triggered forms of pulmonary hypertension.

Electrocardiographic findings. The blinded and unblinded cardiologist and computer program analysis agreed regarding the rate and rhythm in each case. Sinus rhythm was present in 96.9% of patients; one patient had an ectopic atrial rhythm and one had a junctional rhythm. The heart rate averaged 84.1 ± 15.5 b/min. Sinus bradycardia was present in 5, sinus tachycardia in 6, and first degree atrioventricular block in 7 patients; 2 patients had a complete right bundle branch block.

The results of the unblinded cardiologist's interpretation (Table II) are summarized as follows: electrical clockwise rotation (ratio of R to S voltages-R/S ≤ 1 beyond V_3) was present in 43 (67.2%) and counterclockwise (R/S ≥ 1 prior to V_3) in 5 (7.8%). Right axis deviation (RAD) > 90°, RVH, right ventricular strain (RVS), and right atrial enlargement (RAE) were present in 76.6, 78.1, 71.9 and 20.3% of the patients, respectively. The combination of RAD, RVH and RVS was present in 39 (60.9%) patients of whom 8 (12.5%) also had RAE. Other patterns included RAD in 7 (10.9%), RVH and RVS in 4 (6.2%), and RAE with RVH and RVS in 3 (4.7%). In 6 (9.4%) patients the ECG was normal.

Table I. Demographics, functional class, clinical diagnosis and hemodynamic data of the study group.

Age (years)	43 ± 13 (range 17-78)
Sex (M/F)	12 (19%)/52 (81%)
NYHA class	
II	13 (20.3%)
III	45 (70.3%)
IV	6 (9.4%)
Diagnostic classification[16,17]	
Primary pulmonary hypertension	8 (12.5%)
related to:	
Obesity	14 (21.9%)
Systemic hypertension	11 (17.2%)
Connective tissue disease	8 (12.5%)
Thyroid disorders	6 (9.4%)
Portal hypertension	4 (6.2%)
Oral contraceptives	4 (6.2%)
Anorectic drugs	4 (6.2%)
Cocaine	3 (4.7%)
HIV infection	2 (3.2%)
Hemodynamic data	
RA (mmHg)	12 ± 6 (3-29)
mPA (mmHg)	58 ± 12 (32-94)
CO (l/min)	4.2 ± 1.7 (1.7-9.3)
PCWP (mmHg)	12 ± 3.7 (5-22)
PVR (Wood units)	11.8 ± 6 (1.2-25)

CO = cardiac output; mPA = mean pulmonary artery pressure; NYHA = New York Heart Association; PCWP = pulmonary capillary wedge pressure; PVR = pulmonary vascular resistance; RA = right atrial pressure.

Table II. Major diagnostic interpretations.

Diagnostic interpretations	Computer	Blinded cardiologist	Unblinded cardiologist
Right atrial enlargement	6 (9.4%)	6 (9.4%)	13 (20.3%)
Right ventricular hypertrophy	25 (39.1%)	28 (43.8%)	50 (78.1%)
ST-T abnormalities			
Right ventricular strain	8 (12.5%)	10 (15.6%)	46 (71.9%)
Non-specific	16 (25.0%)	20 (31.3%)	2 (3.1%)
Left ventricular ischemia	35 (54.7%)	31 (48.4%)	12 (18.8%)
Anterior	11 (17.2%)	13 (20.3%)	10 (15.6%)
Lateral	5 (7.8%)	4 (6.2%)	
Inferior	16 (25.0%)	16 (25.0%)	5 (7.8%)
Antero-lateral	13 (20.3%)	11 (17.2%)	
Infero-lateral	2 (3.1%)	3 (4.7%)	
Myocardial infarction	14 (21.8%)	12 (18.7%)	
Septal	7 (10.9%)	6 (9.4%)	
Infero-posterior	4 (6.2%)	4 (6.2%)	
Inferior	2 (3.1%)	2 (3.1%)	
Anterior	1 (1.6%)		

The interpretations by the computer program, blinded cardiologist and unblinded cardiologist are compared in table II. The blinded cardiologist and computer program diagnosed RVH in 43.8 and 39.1% of patients respectively, which is substantially < 78.1% as determined by the unblinded reader. RAE was evident in 20.3% of patients, but diagnosed by the computer and blinded cardiologist in only 9.4%. RVS was present in 71.9% of patients, and was most often characterized by the blinded cardiologist and the computer program as non-specific or inferior or antero-lateral ischemia.

The agreement between the three diagnostic interpretations was analyzed using the kappa statistits, where a value of 1 indicates perfect agreement, and 0 indicates that the agreement is no better than that attributable to chance alone. The blinded cardiologist and unedited computer interpretation had a strong agreement for each of the variables. There was no more agreement than that attributable to chance alone between the unblinded cardiologist and the computer program or blinded cardiologist for RAE, RVH, RVS, left ventricular ischemia or the presence of a myocardial infarction (Table III).

The blinded cardiologist and computer program were most likely not to suggest RVH when left ventricular ischemia or myocardial infarction were being considered. Left ventricular ischemia was diagnosed by the computer program in 54.7% of patients, by the blinded cardiologist in 48.4%, and by the unblinded cardiologist in 18.8%. The computer program concluded that a myocardial infarction was present in 21.9% of patients and the blinded cardiologist in 18.8%, but no myocardial infarction was diagnosed by the unblinded reader. The most common errors by the computer and blinded cardiologist were the diagnosis of an antero-septal infarction based on the presence of a qR in V_1 (10.9%), and of an infero-posterior myocardial infarction because of the presence of a "pathologic" Q wave in II, III and aVF associated with a prominent R in V_1 (6.2%) (Table II).

Discussion

The ECG may be helpful in confirming a clinical impression of pulmonary hypertension without a high degree of false positives, but is highly dependent upon the availability of clinical information. In our study, 78.1% of men and women with a mean pulmonary artery pressure > 25 mmHg had ECG evidence of RVH (composite) and only 9.4% were normal. Furthermore, the ECG was sensitive for the detection of RVH and

Table III. Agreement between ECG diagnostic interpretations: kappa statistics.

	Computer vs unblinded cardiologist	Blinded vs unblinded cardiologist	Computer vs blinded cardiologist
Right atrial enlargement	0.457	0.457	1.00
Right ventricular hypertrophy	0.193	0.241	0.904
Right ventricular strain	0.106	0.135	0.871
Left ventricular ischemia	0.026	0.076	0.875
Myocardial infarction	*	*	0.807

* kappa statistics could not be computed; the unblinded reader did not diagnose myocardial infarction.

pulmonary hypertension independent of the severity of symptoms. There was no significant difference in the frequency of ECG evidence of RVH, RVS, RAD, or RAE in patients appertaining to NYHA class II, III, and IV (Table IV). All NYHA class IV patients had RVH and 83.3% had RVS. Nine of 13 patients (69.2%) with mild dyspnea on exertion had ECG evidence of RVH and 76.9% had RAD > 90°.

There is widespread concern that clinical information may bias the result of diagnostic tests that rely upon visual qualitative methods[18-23]. Besides, there is evidence that the clinical history does not improve the diagnostic accuracy of the ECG for acute myocardial infarction[19]. However, it has been shown that the predictive accuracy and interobserver agreement in the interpretation of chest radiographs improve markedly with clinical information[18,23]. For this reason, radiologists generally insist upon accurate clinical information and reason for request, a process often ignored in electrocardiography. In contrast, diagnostic codes and reason for request can be entered for billing purposes, and not to assist the cardiologist responsible for editing.

Electrocardiographic findings. The frequency of ECG criteria consistent with RVH in our series (78.1%), as detected by the cardiologist aware of the clinical data, is comparable to that reported by other authors for primary pulmonary hypertension (> 80%)[6-9]. The sensitivity for the detection of RVH in our series was high when the clinical findings were known. The ECG changes attributable to both pressure and volume overload of the right ventricle may be confused with other clinical entities, which emphasizes the need for clinical information. The RAD (frontal plane axis > 90°) characteristic of RVH may be found in young healthy individuals and in case of left posterior fascicular block and lateral wall infarction[14,15]. Isolated RAD with an otherwise normal ECG is not common in pulmonary hypertension, occurring in only 10.9% of our study population, and would have a low sensitivity for RVH. Significant septal Q waves (qR in V_1) were found in 10.9% of cases and were attributed to a myocardial infarction by the computer program and blinded cardiologist. However the qR pattern is characteristic of RVH with clockwise rotation, and even in the absence of clinical information, RVH should be suggested. Inferior and infero-posterior infarctions may be falsely identified because of "abnormal" Q waves in the inferior leads and prominent R waves in the right precordial leads. The association of the latter findings with RAD and asymmetric downsloping ST segments and T wave inversion in the inferior and anterior leads should strongly suggest RVH and strain rather than coronary artery disease. In the absence of clinical information RVH should, at the very least, be included in the differential diagnosis. The majority of ECGs with ST segment changes typical of RVS (71.9%) were considered non-specific or due to ischemia by the computer program and blinded cardiologist.

The most common misinterpretation by the blinded reader was the conclusion of ECG findings consistent with coronary artery disease. This is not surprising considering the frequency of coronary artery disease in the population undergoing ECG testing. Abnormal QRS and T wave patterns in the right precordial and inferior leads due to RVH have been known to mimic myocardial infarction or ischemia since the early observations by Myers[24] and Sodi-Pallares et al.[25] nearly 50 years ago.

Study limitations. We cannot exclude concomitant coronary artery disease in our patients. However, the likelihood of coronary artery disease in this predominantly young female population is very low. Furthermore, echocardiography did not confirm segmental wall motion abnormalities or thinning consistent with myocardial ischemia or infarction in any patient.

In conclusion, the ECG has a high degree of sensitivity for the detection of RVH in symptomatic patients with pulmonary hypertension. Correlation with the clinical parameters is essential to optimize the usefulness of the ECG. Without clinical information, the computer program and blinded cardiologist more often suggested evidence of myocardial infarction and ischemia, which undoubtedly trigger an inappropriate diagnostic algorithm in many patients.

Table IV. ECG diagnosis (unblinded cardiologist) by the New York Heart Association (NYHA) functional class.

EGG diagnosis	Total	NYHA functional class			p (ANOVA)
		II	III	IV	
RVH	50/64 (78.1%)	9/13 (69.2%)	35/45 (77.8%)	6/6 (100%)	NS
RVS	46/64 (71.9%)	9/13 (69.2%)	32/45 (71.1%)	5/6 (83.3%)	NS
RAD	49/64 (76.6%)	10/13 (76.9%)	35/45 (77.8%)	4/6 (66.7%)	NS
RAE	13/64 (20.3%)	4/13 (30.8%)	8/45 (17.8%)	1/6 (16.7%)	NS
None	6/64 (9.4%)	1/13 (7.7%)	5/45 (11.1%)	0/6 (0%)	NS

RAD = right axis deviation > 90°; RAE = right atrial enlargement; RVH = right ventricular hypertrophy; RVS = right ventricular strain.

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