ELECTROCARDIOGRAPHIC CHANGES IN ACUTE PULMONARY EMBOLISM WITH RIGHT HEART STRAIN AND IT'S ASSOCIATION WITH ADVERSE CLINICAL EVENTS

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ABSTRACT

Objective: To determine the frequency of electrocardiographic changes in right heart strain RHS due to acute pulmonary embolism PE and its effect on mortality.
Study Design: Prospective cross-sectional study.
Place and Duration of Study: AFIC/NIHD Rawalpindi, from Dec 2015 to Jan 2018.
Material and Methods: 70 patients with acute pulmonary embolism were enrolled in this study. The primary outcome was right heart strain (RHS) on echocardiogram. The secondary outcome was mortality.
Results: Mean age was 50.16 ± 18.754 and male were 51 (72.9%). Thirty eight (54.28%) had right heart strain RHS on echocardiography. Mortality was 14 (20%). Provocating factors were identified in 34 (48.6%). Major contributing factors were high altitude in 11 (15.7%) and postoperative and malignancy cases in 7 (10%) each. ECG changes with significant association with RHS included: Tachycadia in 13 (34%) (*p*-value 0.013), S wave in lead I in 12 (31.57%) (*p*-value 0.039), T wave inversion TWI in lead VI and lead V2 in 10 (26.31%) and TWI in lead VI to V3 in 8 (21.05%) (*p*-value 0.03). ECG changes with significant association with mortality included- Tachycardia ≥100 bpmin 7 (50%) (*p*-value 0.012), SIQ3T3 in 5 (35.71%) (*p*-value 0.022), S wave in lead I in 8 (57.14%) (*p*-value 0.001), TWI in leads V1 through V2 in 5 (35.71%) (*p*-value 0.054) and TWI in leads V1 through V3 in 5 (35.71%) (*p*-value 0.013).
Conclusions: ECG can identify patients with RHS in acute PE and this in turn helps in identifying patients vulnerable to adverse clinical events.

Keywords: Pulmonary embolism, Right heart strain, Thrombolysis.

INTRODUCTION

Acute pulmonary embolism (PE) is a serious complication of venous thromboembolism (VTE) with an annual incidence of 100 ± 200 per 100,000 persons[1]. Depending upon the thrombotic burden it can have In-hospital mortality as high as 59%[2]. Four year adverse event rate of 50%[3] and a 5 year mortality rate of up to 32%[4] speaks of the high long term morbidity and mortality despite treatment[5].

PE can be classified as massive, sub-massive, or non-massive based on the hemodynamic.

Status and right ventricular (RV) function of the patient. Massive PE is characterized by systemic hypotension or cardiogenic shock, submassive PE is characterized by RV dysfunction without hypotension, and non-massive PE has neither systemic hypotension nor RV dysfunction[6].

In-hospital mortality varies with severity as high as 25-50% with massive PE, 3-15% with sub-massive and 5% or less with non-massive PE[7] Sub-massive PE can have mortality approaching massive PE with attendant difficult risk assessment[8].

While there is a consensus that in patients with massive PE should receive either systemic thrombolysis, catheter directed interventions, or surgery[6]. The management of patients with sub-massive PE remains controversial, the risk-benefit

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ratio of thrombolytic or invasive therapies versus bleeding is unclear[8].

Patients with PE are risk stratified so as to estimate the probability of circulatory shock and 30-day all-cause mortality[6]. Patients with low risk PE might be considered for immediate treatment at home[9,10]. Fibrinolytic therapy is recommended for patients with PE and RV failure as they may have hemodynamic collapse[6]. Risk stratification includes clinical scoring systems, biomarkers (troponins I and T, brain natriuretic peptides), RV strain on echocardiography[11-13] and RV dilatation on computed tomography (CT) scanning[14,15].

Right heart strain (RHS) is suggested by certain ECG findings and this helps in prioriting care in high risk patients[16-19]. Several ECG components (particularly heart rate, inverted T waves in leads V2 and V3, and ST elevation in aVR) have ORs higher than echocardiographic/ CT scanning/biomarker findings of RV strain[6,20]. Echocardiography is not available during the whole day in many hospitals[21] which makes ECG a useful risk stratifying tool.

The purpose of this study is to ascertain the frequency of electrocardiographic changes with RHS and its association withmortality, so as to recommend ECG as a risk marker of RHS and identifying patients in need of thrombolytic therapy in centers where echocardiographic facility is unavailable.

MATERIAL AND METHODS

This is a prospective cross-sectional study carried out at AFIC/NIHD Rawalpindi from December 2015 to January 2018. Institutional ethical review board approval was obtained. Verbal consent was obtained from patients. Data collection tool was developed to measure demographics, response to treatment and outcome. Doppler ultrasound of lower limbs was carried out for DVT. Diagnosis of Pulmonary Embolism was based on CTPA showing filling defect.

12-lead electrocardiogram was obtained on arrival at ER and was used as the primary predictor. The ECG was assessed for heart rate (HR), rhythm, S wave in lead I,SIQIIITIII pattern, Q wave /T wave inversion in lead III, incomplete or complete right bundle branch block (RBBB), ST-segment elevations/depressions, and T-wave inversions (TWI).

Primary outcome was right heart strain on echocardiography. Echocardiography was carried out within 24 hours. RHS was based on RV dilatation, hypokinesis, Mc Connel Sign, Peak pulmonary artery pressure and Trans annular peak systolic excursion TAPSE. TAPSE was determined by the longitudinal motion of annulus at peak systole with the M-mode cursor at the lateral tricuspid annulus.

Secondary outcome was death as the only adverse clinical event, assessed during the period of hospitalization.

Statistical analysis was carried out on IBM SPSS version 23. Categorical data was presented as percentages and frequency whereas descriptive statistics were expressed as mean and standard deviation for quantitative analyses. Chi square test was applied to analyze the data. A *p*-value of ≤0.05 was considered statistically significant.

RESULTS

Between December 2015 and January 2018, 70 patients with pulmonary embolism were enrolled. Table-I shows basic characteriatics of the enrolled patients. Mean age was 50.16 ± 18.75. Male were 51 (72.9%). An Emergency deptt ECG was available for review in all 70 (100%) patients. CTPA confirmed acute PE in 70 (100%). Doppler study was carried out in all patients and revealed DVT in 29 (42%). Echocardiography was carried out in all patients and revealed Right heart strain RHS in 38 (54.28%). Mortality was 14 (20%). Provocating factors were identified in 34 (48.6%). Major contributing factors were high altitude in 11 (15.7%) and postoperative and malignancy cases in 7 (10%) each.

ECG changes with significant association with RHS included; Tachycadia in 13 (34%) (*p*-value 0.013), Swave in lead I in 12 (31.57%)

(*p*-value 0.039), T wave inversion TWI in lead VI and lead V2 in 10 (26.31%) and TWI in lead VI to V3 in 8 (21.05%) (*p*-value 0.03).

ECG changes with significant association with mortality included-Tachycardia ≥100 bpmin 7 (50%) (*p*-value 0.012), SIQ3T3 in 5 (35.71%) (*p*-value 0.022), S wave in lead I in 8 (57.14%) (*p*-value 0.001), TWI in leads V1 through V2 in 5 (35.71%) (*p*-value 0.054) and TWI in leads V1 through V3 in 5 (35.71%) (*p*-value 0.013).

Table-I: Baseline characteristics of enrolled patients no (70).

Characteristic	**n (%) or ± SD**
Mean age (years)	50.16 ± 18.754
Male	51(72.9%)
Symptom	
Dyspnoe	62 (88.57%)
Haemoptysis	10 (14.28%)
Chest discomfort	20 (28.57%)
Syncope	2 (2.8%)
Comorbidity	
Hypertension	7 (10%)
Diabetes mellitus	1 (1.4%)
Chronic kidney disease	17 (24.63%)
Smoker	1 (1.4%)
Hypothroidism	1 (1.4%)
Cerebrovascular accident	2 (2.9%)
Past history pulmonary embolism	3 (4.3%)
Past history ischaemic heart disease	3 (4.3%)

Table-II: Provocating factors.

Characteristic	**No (%)**
Provoked	34 (48.6%)
High altitude	11 (15.7%)
Fracture	7 (10%)
Postoperative	7 (10%)
Bedridden	5 (7.1%)
Long travel	1 (1.4%)
Steroid intake	1 (1.4%)

DISCUSSION

In a patient with symptoms suggestive of pulmonary embolism ECG is usually the first investigation to be carried out. Its role is primarily to exclude other conditions like acute myocardial infarction. However with certain findings it provides clue to the possibility of pulmonary embolism. Recently its role has been enhanced as a tool for detection of right heart strain. This is particularly important from the fact that echocardiography is not available in all the centers.

The right ventricular (RV) strain and severe pulmonary hypertension after PE is corroborated by certain ECG findings[21]. Daniel et al in 2001 developed a scoring system that predicted increased pulmonary arterial pressure[16]. It was based on scores as in parenthesis: sinus tachycardia (2); incomplete right bundle branch block (2); complete right bundle branch block (3); T-wave inversion, graded by magnitude (V1 [0 to 2], V2 [1 to 3], V3 [1 to 3], V1 through V4 all inverted 2 mm [4]); S1Q3T3 complex components (S wave in lead I [0], Q wave in lead III [1], inverted T wave in lead III [1], and the entire

S1Q3T3 complex [2]). The maximum score was 21 points. At a cutoff point of ≥ 10 points, it was 97.7% specific and 23.5% sensitive for the detection of PE with severe pulmonary hypertension, and 52% of patients had fatal PE[16]. A systematic review and meta-analysis of 3,007 patients by Shopp et al found six ECG findings (heart rate, S1Q3T3, cRBBB, inverted T waves in V1–V4, ST elevation in aVR, and atrial fibrillation) which predict hemodynamic collapse and death within 30 days after acute PE[22]. In another study by Hariharan et al in 2015, 3 ECG characteristics were independently associated with RHS. This was the basis of a ten point score as in parenthesis: TWI in leads V1 through V3 (5 points), S wave in lead I (2 points), and sinus tachycardia (3 points). 85% of acute PE patients could be effectively stratified using this score. A TwiST ECG score ≤2 points excludes RHS with 85% sensitivity, and a score of ≥5 points has 93% specificity for RHS in acute PE. A Twist score (≤2 points) makes RHS unlikely, which further limits further tests[23]. TWI in leads V1 through V3) has the strongest association with RHS[21].

In our study ECG changes with significant association with RHS included as shown in table-II; Tachycadia in 13 (34%) (*p*-value 0.013), S-wave in lead I in 12 (31.57%) (*p*-value 0.039), T wave inversion TWI in lead VI and lead V2 in 10 (26.31%) and TWI in lead VI to V3 in 8 (21.05%) (*p*-value 0.03). Mortality was significantly associated with ECG changes that included-Tachycardia ≥100 bpmin in 7 (50%) (*p*-value 0.012), SIQ3T3 in 5 (35.71%) (*p*-value 0.022), S wave in lead I in 8 (57.14%) (*p*-value0.001), TWI in leads V1 through V2 in 5 (35.71%) (*p*-value 0.054) and TWI in leads V1 through V3 in 5 (35.71%) (*p*-value 0.013) as shown in table-III. Our findings are corroborated by a systematic review and meta-analysis by Qaddoura et al, in which ECG signs that were good predictors of a negative outcome for in-hospital mortality

Table-II: ECG changes in Pulmonary embolism with and without RHS.

Characteristic	RHS present 38 (54.28%)	RHS absent 32 (45.72%)	*p*-value
Sinus tachycardia	13 (34%)	3 (9.3%)	0.013
S wave lead 1	12 (31.57%)	3 (9.3%)	0.039
Q wave lead III	7 (18.42%)	4 (12.5%)	NS
T wave lead III	11 (28.94%)	7 (21.87%)	NS
S1QIIITIII pattern	7 (18.42%)	3 (9.3%)	NS
TWIV1-V2	10 (26.31%)	2 (6.25%)	0.031
TWI V1-V3	8 (21.05%)	1(3.12%)	0.033
Partial RBBB	4 (10.52%)	1 (3.12%)	NS
Complete RBBB	4 (10.52%)	1 (3.12%)	NS
Non sinus rhythm	3 (8.5%)	0 (0%)	NS

ECG, Electrocardiogram; RHS, Right heart strain; TWI,T wave inversion;RBBB, Right bundle branch block.

Table-III: ECG changes in acute PE and association with mortality.

ECG Characteristics	Death14 (%)	Alive 56 (%)	*p*-value
Tachycardia ≥100 bpm	7 (50%)	9 (16.07%)	0.012
SIQ3T3	5 (35.71%)	5 (8.92%)	0.022
S wave in lead I	8 (57.14%)	7 (12.5%)	0.001
TWI in leads V1 through V2	5 (35.71%)	7 (12.5%)	0.054
TWI in leads V1 through V3	5 (35.71%)	4 (7.14%)	0.013
Complete RBBB	2 (14.2%)	3 (5.35%)	0.260
Incomplete RBBB	2 (14.2%)	3 (5.35%)	0.260

ECG: Electrocardiogram, PE: Pulmonary embolism

included S1Q3T3 (OR: 3.38, 95% CI: 2.46-4.66, p<0.001), complete right bundle branch block (OR: 3.90, 95% CI: 2.46-6.20, p<0.001), T-wave inversion (OR: 1.62, 95% CI: 1.19-2.21, p=0.002), right axis deviation (OR: 3.24, 95% CI: 1.86-5.64, p<0.001), and atrial fibrillation (OR: 1.96, 95% CI: 1.45-2.67, p<0.001)[18].

Our study has provided simple ECG findings that suggest RHS and help in risk stratifying significant number of patient with pulmonary embolism who are at risk of adverse clinical event. This is important for centers without echocardiography facility.

CONCLUSION

ECG is a simple easily available investigation which not only rules out other conditions like acute myocardial infarction but also helps in risk stratifying patients with PE, which makes it a useful investigative tool in centers without echocardiography facility. This can help in decision making in intermediate risk patients for consideration of thrombolytic therapy as well as for decision making for home treatment.

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CONFLICT OF INTEREST

This study has no conflict of interest to be declare by any author. The authors certify that they have no affiliation with or involvement in any organization or entity with any financial interest in the subject matter or materials discussed in the manuscript.

REFERENCES

1. Ho WK, Hankey GJ, Eikelboom JW. The incidence of venous thromboembolism: A prospective, community-based study in Perth, Western Australia. Med J Aust 2008; 189(3): 144-7.
2. Vieillard-Baron A, Page B, Augarde R, Prin S, Qanadli S, Beauchet A, et al. Acute cor pulmonale in massive pulmonary embolism: Incidence, echocardiographic pattern, clinical implications and recovery rate. Intensive Care Med 2001; 27(9): 1481-6.
3. Klok FA, Zondag W, van Kralingen KW, van Dijk AP, Tamsma JT, Heyning FH, et al. Patient outcomes after acute pulmonary embolism. A pooled survival analysis of different adverse events. Am J Respir Crit Care Med 2010; 181(5): 501-6.
4. Ng AC, Chung T, Yong AS, Wong HS, Chow V, Celermajer DS, et al. Long-term cardiovascular and noncardiovascular mortality of 1023 patients with confirmed acute pulmonary embolism. Circ Cardiovasc Qual Outcomes 2011; 4(1): 122-8.
5. Den Exter PL, van der Hulle T, Lankeit M, Huisman MV, Klok FA. Long-term clinical course of acute pulmonary embolism. Blood Rev 2013; 27(4): 185-92.
6. Konstantinides SV, Torbicki A, Agnelli G, Danchin N, Fitzmaurice D, Galie N, et al. ESC Guidelines on the diagnosis and management of acute pulmonary embolism: The task force for the diagnosis and management of acute pulmonary embolism of the European Society of Cardiology (ESC) Endorsed by the European Respiratory Society (ERS). Eur Heart J 2014; 35: 3033–69.
7. Torbicki A, Perrier A, Konstantinides S, Agnelli G, Galiè N, Pruszczyk P, et al. Guidelines on the diagnosis and management of acute pulmonary embolism: The Task Force for the Diagnosis and management of acute pulmonary embolism of the European Society of Cardiology (ESC). Eur Heart J 2008; 29(18): 2276-315.
8. Meyer G, Vicaut E, Danays T, Agnelli G, Becattini C, Westendorf JB et al. Fibrinolysis for patients with intermediate-risk pulmonary embolism. N Engl J Med 2014; 370(15): 1402-11.
9. Beam DM, Kahler ZP, Kline JA. Immediate discharge and home treatment of low risk venous thromboembolism diagnosed in two U.S. emergency departments with rivaroxaban: A one year preplanned analysis. Acad Emerg Med 2015; 22: 788-95.
10. Vinson DR, Drenten CE, Huang J, Morley JE, Anderson ML, Reed ME, et al. Impact of relative contraindications to home management in emergency department patients with low-risk pulmonary embolism. Ann Am Thorac Soc 2015; 12: 666-73.
11. Khemasuwan D, Yingchoncharoen T, Tunsupon P, Kenya-Kusunose K, Moghekar A, Klein A, et al. Right ventricular echocardiographic parameters are associated with mortality after acute pulmonary embolism. J Am Soc Echocardiogr 2015; 28(3): 355-62.
12. Weekes AJ, Thacker G, Troha D, Johnson AK, Chanler-Berat J, Norton HJ, et al. Diagnostic accuracy of right ventricular dysfunction markers in normotensive emergency department patients with acute pulmonary embolism. Ann Emerg Med 2016; 3: 277-91.
13. Pruszczyk P, Goliszek S, Lichodziejewska B, Kostrubiec M, Ciurzyński M, Kurnicka K et al. Prognostic value of echocardiography in normotensive patients with acute pulmonary embolism. JACC Cardiovasc Imaging 2014; 7(6): 553-60.
14. George E, Kumamaru KK, Ghosh N. Computed tomography and echocardiography in patients with acute pulmonary embolism: Part 2: prognostic value. J Thorac Imaging 2014; 29(1): W7-12.
15. Becattini C, Agnelli G, Germini F, Vedovati MC. Computed tomography to assess risk of death in acute pulmonary embolism: A meta-analysis. Eur Respir J 2014; 43(6): 1678-90.
16. Daniel KR, Courtney DM, Kline JA. Assessment of cardiac stress from massive pulmonary embolism with 12-lead ECG. Chest 2001; 120(2): 474-81.
17. Piran S, Le GG, Wells PS, Gandara E, Righini M, Rodger MA, et al. Outpatient treatment of symptomatic pulmonary embolism: A systematic review and meta-analysis. Thromb Res 2013; 132(5): 515-9.
18. Qaddoura A, Digby GC, Kabali C, Kukla P, Zhan ZQ, Baranchuk AM. The value of electrocardiography in prognosticating clinical deterioration and mortality in acute

pulmonary embolism: A systematic review and meta-analysis. Clin Cardiol 2017; 40(10): 814-24.
19. Digby GC, Kukla P, Zhan ZQ, Pastore CA, Piotrowicz R, Schapachnik E, et al. The value of electrocardiographic abnormalities in the prognosis of pulmonary embolism: A consensus paper. Ann Noninvasive Electrocardiol 2015; 20(3): 207-23.
20. Kukla P, McIntyre WF, Fijorek K, Mirek-Bryniarska E, Bryniarski L, Krupa E, et al. Electrocardiographic abnormalities in patients with acute pulmonary embolism complicated by cardiogenic shock. Am J Emerg Med 2014; 32(6): 507-10.
21. Jones AE, Kline JA. Availability of technology to evaluate for pulmonary embolism in academic emergency departments in the United States. J Thromb Haemost 2003; 1: 2240-42.
22. Shopp JD, Stewart LK, Emmett TW , Kline JA. Findings From 12-lead Electro - cardiography That Predict Circulatory Shock From Pulmonary Embolism: Systematic Review and Meta-analysis. Acad Emerg Med 2015; 22(10): 1127-37.
23. Hariharan P, Dudzinski DM, Okechukwu I, Takayesu JK, Chang Y, Kabrhel C. Association between electrocardiographic findings, right heart strain, and short-term adverse clinical events in patients with acute pulmonary embolism. Clin Cardiol 2015; 38(4): 236-42.