The Ability to Predict Death in Patients with Acute PE

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Article

The Ability to Predict Death in Patients with Acute PE

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Abstract: Background: Pulmonary emboli (PE) is a life threatening condition that discovered in many patients only "post mortem". Sub massive and massive PE that led to hemodynamic collapse characterized by right ventricular (RV) dysfunction, leading to a higher risk of death. **Objectives:** To assess the ability to predict in hospital death of patients with acute PE, using a non-gated computed tomography pulmonary angiography (CTPA), based on the dimensions of the right ventricle. **Methods:** A retrospective study that analyzed CTPA images of patients admitted with acute PE during the years 2012-The cohort study included 300 patients with documented acute PE, among them 255 hospitalized in medical (non-intensive care unit) wards, 45 were hospitalized in an intensive care unit (ICU). **Results:** Among the 45 patients admitted to the ICU 8% died. Larger RV diameters predicted mortality (OR=10.14, 95% CI [1.09-93.86]) as well as lower systolic and diastolic blood pressure measurements (p=0.001 and 0.01). Among the 255 patients admitted to the Internal Medicine Ward 7% died. Older age (p=0.028), sepsis and cancer (both p<0.001), high WBCs count (p<0.001), and renal failure (p<0.001) predicted death. Lower blood pressure (systolic and diastolic) (p<0.001, 0.008), older age (p<0.007), sepsis (p<0.001), cancer (p=0.006), higher WBCs count (p<0.001), and impaired renal function (p<0.001) predicted death in patients admitted with acute PE. **Conclusions:** Clinical parameters and hematological parameters could predict death of patients admitted with acute PE. RV diameter, measured by the non-ECG gated CTPA, had an additive predictive value for patients who admitted to the ICU.

1. Background

Pulmonary emboli (PE) is a life threatening condition that diagnosed in more than 80% of the patients only "post mortem" [1]. In many patients, the presenting clinical manifestation of PE is sudden death. About 10% of the patients with asymptomatic deep vein thrombosis (DVT) develop sudden death due to acute PE [2]. Early diagnosis and treatment of PE are important because of the high mortality rate if not treated urgently [3]. Patients with massive PE may present with cardiogenic shock or with multi- organ failure [4]. PE diagnosis is based mainly on clinical characteristics (Wells criteria and Geneva score) [4]. There are biomarkers that may support the diagnosis of PE and its severity like the plasma D-dimer (a fragment generated from fibrin degradation), troponin (represents myocardial damage), and brain natriuretic peptide (BNP) or NT-terminal Pro-BNP (NT-Pro-BNP), that estimate the burden on the right ventricle in patients with confirmed PE [5]. Non-ECG gated CT pulmonary angiography (CTPA) with multi-detector scanning technique is the "gold standard" to diagnose PE with high sensitivity and high specificity [6].

ECG gated CTPA imaging is the procedure of choice for RV diameter measurements. RV diameter in patients with acute PE may predict in-hospital death, 30-day mortality and 3-month mortality [7–10]. Patients admitted with a suspicion of acute PE undergo a non-ECG gated CTPA in order to confirm or exclude the diagnosis of PE. However, in that method, measurement of the RV diameter is not accurate enough.

Our aim was to examine the ability to predict in-hospital death of patients with acute PE based on the RV diameter measured by the non-ECG gated CTPA.

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2. Methods:

Study Design

A retrospective study that analyzed non-ECG gated CTPA of patients with PE (documented and proved by non-ECG gated CT pulmonary angiography) in the years 2012-2017 in Baruch Padeh Medical Center. 300 patients were found, among them 255 were admitted to the internal medicine wards, and 45 patients were admitted to the ICU.

Demographic and clinical data included age, sex, length of stay in the hospital, active cancer, infections, type 2 diabetes mellitus, heart failure, and autoimmune disease.

Laboratory data included white blood cells (WBCs), D-DIMER, troponin, brain natriuretic peptide (BNP), C - reactive protein (CRP), alkaline phosphatase, bilirubin, BUN and creatinine.

Measurements of the diameters of the RV, LV and the RV/LV ratios recorded according to the method described by Gonzalez and Jimenez [11]. We measured RV diameter in the largest diameter observed, using the non-ECG gated CTPA images of patients that diagnosed with PE.

3. Results

Two hundred eighty patients survived and 20 patients died. Differences between the two groups were tested using Pearson's Chi-squared test for categorical variables, or one-way ANOVA for continuous variables. Descriptive statistics measures were performed with frequencies for categorical variables (e.g. sex) and averages with standard deviations for continuous variables (e.g. age). Univariate analyses compared between patients who survived and patients who died using Pearson's Chi-squared test for categorical variables, or one-way ANOVA for continuous variables.

P-value lower than 5% was considered significant.

Table 1 demonstrated that patients who died were older (78.00±12.04 vs. 66.46±18.64 years old, p=0.007), had sepsis (60% vs. 20.4%, p<0.001), active cancer (45% vs. 19.3%, p=0.006), with higher white blood cells counts (19.20±12.24 vs. 10.52±4.21, p<0.001), and impaired renal function (creatinine of 1.29±1.08 vs. 0.88±0.42 mg/dL, p<0.001).

Parameters that predicted death in patients admitted to the intensive care unit (8%) included: larger RV diameters (measured by the non-ECG gated CTPA0 (5.47±0.67 cm vs. 4.55±0.80 cm, p=0.03), lower systolic blood pressures (84.5±37.92 vs. 134.10±24.68 mmHg, p<0.001), lower diastolic blood pressure (54.75±23.40 vs. 75.37±14.02 mmHg, p=0.01), and higher WBC counts (16.20±11.41 vs. 11.17±4.09 x10^3/L, p=0.06)(Table 2).

Old age (p=0.028), sepsis (p<0.001), cancer (p<0.001), high WBC count (p<0.001), and impaired renal function (p<0.001) predicted death (7%) among patients with acute PE that were admitted to the Internal Medicine Ward (Table 3).

Table 1. All patients (N = 300); clinical & laboratory parameters on admission.

	Survival (N=280)	Death (N=20)	P-value
Intensive care	41 (14.6%)	4 (20.0%)	0.517
Thrombolysis	16 (5.7%)	3 (15.0%)	0.100
SBP (mm HG)	128.08±22.34	114.65±27.02	0.011
DBP (mm HG)	74.81±13.24	66.60±14.51	0.008
RV diameter (cm)	4.19±0.70	4.04±1.05	0.379
LV diameter (cm)	3.34±0.79	3.15±1.09	0.325
RV/LV Ratio	1.30±0.40	1.38±0.70	0.410
Pulmonary artery (cm)	2.97±0.41	2.85±0.52	0.200
Age (years)	66.46±18.64	78.00±12.04	0.007
Female	163 (58.2%)	14 (70.0%)	0.301
Diabetes mellitus	76 (27.1%)	6 (30.0%)	0.782

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Heart failure	77 (27.5%)	8 (40.0%)	0.231
Renal failure	24 (8.6%)	3 (15.0%)	0.332
Autoimmune disease	22 (7.9%)	2 (10.0%)	0.733
Infection	57 (20.4%)	12 (60.0%)	0.001
Cancer	54 (19.3%)	9 (45.0%)	0.006
D-dimer (pg/mL)	3.84 ± 2.94	5.77 ± 3.91	0.203
Troponin (ng/L)	51.74 ± 282.68	2.42 ± 3.50	0.547
BNP (pg/mL)	295.18± 372.29	138.33± 142.63	0.471
CRP (mg/L)	56.43 ± 38.45	71.63 ± 37.07	0.318
WBC (x10^3/L)	10.52 ± 4.21	19.20 ± 12.24	0.001
BUN (mg/dL)	21.12 ± 12.79	43.79 ± 34.98	0.001
Creatinine (mg/dL)	0.88 ± 0.42	1.29 ± 1.08	0.001
Bilirubin (mg/dL)	1.25 ± 7.69	0.98 ± 0.60	0.885
Alkaline Phosphatase (U/L)	107.88 ± 91.14	146.33 ± 63.38	0.080
Hospitalization days	10.07 ± 9.54	8.35 ± 6.49	0.427

Values represent means ± standard deviations for continuous variables and counts (proportions) for categorical variables. P-value comparing the two groups using ANOVA for continuous variables and the Chi-square test for categorical variables.

Table 2. ICU patients (N = 45); clinical parameters on admission.

	Survival (N=41)	**Death (N=4)**	**P-value**
Immediate	29 (10.4%)	2 (10.0%)	0.393
Days in intensive care	5.10±5.49	2.00±2.00	0.273
Days to intensive care	3.92 ± 3.78	2.00 ± 1.41	0.504
Thrombolysis	6 (14.6%)	2 (50.0%)	0.077
SBP (mm HG)	134.10±24.68	84.50±37.92	0.001
DBP (mm HG)	75.37±14.02	54.75±23.40	0.011
RV diameter (cm)	4.55±0.80	5.47±0.67	0.030
LV diameter (cm)	3.22±0.87	3.12±1.82	0.845
RV/LV Ratio	1.54±0.55	2.10±1.05	0.081
Pulmonary artery (cm)	3.00 ± 0.35	3.25 ± 0.80	0.238
Age (years)	62.54 ± 18.68	79.75 ± 10.50	0.078
Female	22 (53.7%)	2 (50.0%)	0.889
Diabetes mellitus	8 (19.5%)	0 (0.0%)	0.330
Heart failure	9 (22.0%)	1 (25.0%)	0.889
Renal failure	2 (4.9%)	0 (0.0%)	0.651
Autoimmune disease	2 (4.9%)	0 (0.0%)	0.651
Infection	6 (14.6%)	0 (0.0%)	0.411
Cancer	6 (14.6%)	0 (0.0%)	0.411
D-dimer (pg/mL)	4.91±3.03	NA	
Troponin (ng/L)	60.30±224.23	0.08±0.06	0.649
BNP (pg/mL)	279.52±321.80	NA	
CRP (mg/L)	21.70±24.09	NA	
WBC (x10^3/L)	11.17±4.09	16.20±11.41	0.060
BUN (mg/dL)	18.37±8.15	23.00±11.79	0.359
Creatinine (mg/dL)	0.88±0.31	1.17±0.21	0.132
Bilirubin (mg/dL)	0.82±0.36	1.13± .31	0.150
Alkaline Phosphatase (U/L)	87.37±30.67	118.33±29.28	0.098
Hospitalization days	15.78±14.41	4.50±4.04	0.130

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Table 3. Patients admitted to the internal medicine ward (non ICU) (N = 255).

	Survival (N=239)	Death (N=16)	P-value
Thrombolysis	10 (4.2%)	1 (6.2%)	0.694
SBP (mmHG)	127.05 ± 21.80	122.19 ± 18.29	0.385
DBP (mmHG)	74.72 ± 13.13	69.56 ± 10.50	0.125
RV diameter (cm)	4.13 ± 0.66	3.69 ± 0.80	0.011
LV diameter (cm)	3.36 ± 0.78	3.16 ± 0.92	0.330
RV/LV Ratio	1.26 ± 0.36	1.21 ± 0.47	0.545
Pulmonary artery (cm)	2.96 ± 0.42	2.74 ± 0.40	0.044
Age (years)	67.14 ± 18.59	77.56 ± 12.68	0.028
Female	141 (59.0%)	12 (75.0%)	0.206
Diabetes mellitus	68 (28.5%)	6 (37.5%)	0.440
Heart failure	68 (28.5%)	7 (43.8%)	0.194
Renal failure	22 (9.2%)	3 (18.8%)	0.214
Autoimmune disease	20 (8.4%)	2 (12.5%)	0.569
Infection	51 (21.3%)	12 (75.0%)	< 0.001
Cancer	48 (20.1%)	9 (56.2%)	< 0.001
D-dimer (pg/mL)	3.61 ± 2.89	5.77 ± 3.91	0.150
Troponin (ng/L)	49.94 ± 294.04	3.19 ± 3.75	0.635
BNP (pg/mL)	297.52 ± 381.36	138.33 ± 142.63	0.476
CRP (mg/L)	57.82 ± 38.36	71.63 ± 37.07	0.364
WBC (x10^3/L)	10.41 ± 4.23)	19.96 ± 12.68)	< 0.001
BUN (mg/dL)	21.60 ± 13.38	47.69 ± 36.70	< 0.001
Creatinine (mg/dL)	0.88 ± 0.43	1.32 ± 1.18	< 0.001
BUN/creatinine ratio	26.36 ± 17.52	38.85 ± 18.91	0.006
Bilirubin (mg/dL)	1.33 ± 8.39	0.95 ± 0.65	0.863
Alkaline Phosphatase (U/L)	111.74 ± 98.02	151.93 ± 67.48	0.120
Hospitalization days	9.10 ± 8.08	9.31 ± 6.72	0.917

Values represent means ± standard deviations for continuous variables and counts (proportions) for categorical variables. P-value comparing the two groups using ANOVA for continuous variables and the Chi-square test for categorical variables.

4. Discussion

Our study showed that there are two groups of patients with acute PE. Those who present in the emergency department with signs and symptoms of hemodynamic compromise, and those who are admitted without signs of shock or other clinical and laboratory signs of hemodynamic instability and multi-organ failure.

Our study showed that RV diameter measured by non-ECG gated CTPA could predict death among patients admitted with acute PE to ICU. Our study has demonstrated that using non-ECG gated CTPA is feasible, and can be part of the criteria to define patients at risk admitted to the ICU with acute PE.

The ability to predict mortality in patients admitted with acute PE to the ICU is in line with previous studies that had demonstrated that acute RV dilatation and dysfunction lead to acute hemodynamic de-compensation of patients with PE [10]. Since death in patients, presenting with shock occurs within the first hours of presentation, a rapid therapeutic action and monitoring is required [17]. In acute RV pressure overload, RV systolic pressure increases and function begins to

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decline. The clinical presentation is decreased cardiac output, decreased blood pressure and multi-organ failure [1].

Our study showed that the ability to predict death among patients with acute PE (but without hemodynamic compromise) is based on clinical and laboratory simple affordable data like blood pressure, old age, sepsis on admission, cancer, and impaired renal function (even mild renal failure).

In sub massive PE (25% of the patients) we find right ventricular dilatation and dysfunction with normal systemic arterial pressures. These patients are prone to deteriorate with a high risk of death [11]. PE may cause right ventricular overload with RV dilatation and dysfunction. RV dysfunction may lead to RV failure, severe hemodynamic compromise and death [12–16].

Non-ECG gated CTPA is the gold standard method to diagnose PE [17]. Studies have shown an increased RV/LV diameter ratio (measured in the standard axial or reformatted four-chamber views) as a predictor of mortality in patients with PE [18]. In the current study, we used a non-ECG gated CTPA protocol to measure RV and LV as a diagnostic tool [19,20].

We also found that clinical parameters and simple laboratory tests are valuable for risk estimation and have a prognostic value. Age, white blood cells count, sepsis, cancer, renal function, and blood pressure are still key factors that can predict the clinical outcome in patients with acute PE.

4.1. Study Limitations

This study has several limitations:

The sample size for this study was relatively small (N=300), which limits the statistical power to achieve significant results. Specifically, the sample size of the intensive-care patients is limited (N=45), and therefore less significant results were found in the models conducted on this sample.

4.2. Summary

Among patients admitted to the ICU (based on clinical parameters) RV diameter (non-ECG gated CTPA) predicted death. Among patients that did not have clinical parameters of cardiogenic shock or multi-organ failure and admitted to the department of internal medicine, RV diameter did not predict death. In this group older patient, those who had higher leukocyte counts, impaired renal function, active cancer, or sepsis were at a higher risk to die within the hospital stay.

Author Contributions: Alexander Chijik MD – collected the data from the files and measured the RV dimensions. Michael Jerdev MD – collected the data and measured the RV dimensions. Wadie Abu Dahoud MSc – performed the statistical analysis. Yaron Sela PhD – performed the statistical analysis and helped to write the first draft Arnon Blum MD – conceived the trial, organized the whole plan, wrote the Ethics protocol and the protocol of the study, and wrote the first and the final drafts of the MN.

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