Pulmonary embolism: multicenter registry in tertiary hospitals

Embolia pulmonar: registro multicêntrico da prática clínica em hospitais terciários

André Volschan[1], Denílson Campos de Albuquerque[2], Bernardo Rangel Tura[3], Marcos de Freitas Knibel[4], Paulo César Pereira da Silva e Souza[5], Maria Luiza Toscano[6] e Investigadores do EMEP – Estudo Multicêntrico de Embolia Pulmonar

1. Master, Physician at the Emergency Unit of Hospital ProCardíaco, Rio de Janeiro (RJ), Brazil.
2. PhD, Adjunct Professor of Cardiology, Universidade do Estado do Rio de Janeiro UERJ - Rio de Janeiro (RJ), Brazil.
3. PhD, Physician at the Instituto Nacional de Cardiologia - Rio de Janeiro (RJ), Brazil.
4. Master, Physician at the Intensive Care Center, Hospital São Lucas,
5. Physician at the Intensive Care Center, Hospital de Clínicas de Niterói, Niterói (RJ), Brazil.
6. Physician at the Hospital Municipal Miguel Couto - Rio de Janeiro (RJ), Brazil.

Received from Emergency Unit of Hospital ProCardíaco, Rio de Janeiro (RJ), Brazil.

Submitted on July 29, 2009
Accepted September 23, 2009

Author for Correspondence
André Volschan
Rua General Polidoro, 192 - Botafogo
CEP: 22471-270 - Rio de Janeiro (RJ), Brazil.
Phone: (21) 2528-1505
E-mail: volschan@uol.com.br

ABSTRACT

Introduction: The clinical profile as well as the therapeutic and diagnostic strategies for patients with pulmonary embolism, describes clinical practice in the approach of the disease. Such information, scarce in national studies, enables a better understanding of pulmonary embolism.

Methods: A multicenter trial included 727 patients with pulmonary embolism who were admitted in emergency or intensive care unit. Diagnostic criteria for inclusion were: 1. Visibility of thrombus in the pulmonary artery at pulmonary arteriography, helical computer tomography, magnetic resonance or echocardiogram. 2. High probability at pulmonary scintigraphy. 3. Venous duplex-scan with thrombus and clinical manifestations of pulmonary embolism. Clinical and complementary exams were analyzed.

Results: Mean age was 68 years, 42% were male. Most prevalent risk factors were: age>40 years, bed rest and neoplasm. More frequent signs and symptoms were: dyspnea, tachypnea, sinus tachycardia, and chest pain. Changes were observed at electrocardiogram in 30%, at chest X-ray in 45%, at venous duplex-scan in 67%, at transthoracic echocardiogram in 37%. . D-dimer, troponin I and CKMB were positive in, respectively, 93, 9 and 8%. Most frequently used methods to confirm diagnosis were helical computer tomography and non-fractioned heparin was the treatment most used. In-hospital mortality was 19.5%.

Conclusions: It was observed that age>40 years, prolonged rest and neoplasms were the most prevalent risk factors and dyspnea and tachypnea were the more frequent clinical manifestations. Helical computer tomography was the most often used method to confirm diagnosis and non-fractioned heparin was the main form of treatment.

Keywords: Pulmonary embolism/diagnosis; Pulmonary embolism/drug therapy; Heparin/therapeutic use; Tomography, X-ray computed/methods

INTRODUCTION

Pulmonary embolism (PE) is a challenge to clinical practice. Presence of risk factors for venous thromboembolism associated with signs and symptoms of PE is the initial condition to raise clinical suspicion. The nonspecificity of clinical manifestations and limited availability of complementary methods, the main obstacles to diagnosis, distort epidemiological assessments, generating approximate and unreliable results. Complementary tests are essential for diagnosis of patients with clinical suspicion and to evaluate prognosis of those with an already diagnosed EP.

The standard treatment with unfractionated heparin has as alternative low molecular weight heparin (LMWH) and thrombolytic therapy, the first being restricted to stable patients and the second given to patients with hemodynamic instability.[1] Although the therapeutic option following general rules, it may present variations for certain subgroups of patients.

The scarcity of records representing clinical practice was a stimulus for this study. There are few Brazilian publications on the subject and those with the largest casuistry are relating to necropsy studies or those carried out by medical chart review.[2,3]

The observational study that aims to assess the clinical profiles of the diagnosis and treatment strategies is the one that best portrays the reality of clinical practice. With this type of evaluation results will not be subject to interferences generated in controlled studies, with close surveillance of the patients included.

Based upon this premise, a record was designed to analyze the clinical profile and the diagnostic s and treatment approach for patients with pulmonary embolism.

METHODS

Multicenter prospective cohort study conducted in 20 research centers from tertiary hospitals in Brazil (Chart 1), from January 1998 to May 2003 (EMEP-Multicenter Study of Pulmonary Embolism).

Clinical suspicion was defined by the physician assessing the patient, based upon risk factors, signs and symptoms of PE. In addition to the clinical suspicion documentation on EP by one or more of the following complementary methods was necessary:

Angiography with visualization of the thrombus in pulmonary artery.

Helical computed angiotomography with visualization of the thrombus in the pulmonary artery.

Magnetic resonance angiography with visualization of the thrombus in the pulmonary artery.

Echocardiogram with visualization of the thrombus in the pulmonary artery.

Pulmonary ventilation / perfusion with high probability of pulmonary embolism.

Duplex-scan with visualization of the thrombus and reduced compressibility in the deep venous system.

In-hospital mortality was defined as that occurring in the same hospitalization that motivated admission by EP, regardless of the cause of death.

For analysis the following variables: were considered age, gender, history of venous thromboembolism, fracture of pelvis or lower limbs in the last 90 days, abdominal or pelvic surgery in the last 30 days, malignancy, bed rest > 72 hours, chronic obstructive pulmonary disease

Chart 1- Research centers

Investigating center	City	State
Hospital Procardíaco*	Rio de Janeiro	Rio de Janeiro
Hospital Samaritano	Rio de Janeiro	Rio de Janeiro
Hospital RioMar	Rio de Janeiro	Rio de Janeiro
Clínica São Vicente	Rio de Janeiro	Rio de Janeiro
Casa de Saúde São José (CU)	Rio de Janeiro	Rio de Janeiro
Casa de Saúde São José (ICU)	Rio de Janeiro	Rio de Janeiro
Hospital São Lucas (CU)	Rio de Janeiro	Rio de Janeiro
Hospital São Lucas (ICU)	Rio de Janeiro	Rio de Janeiro
Hospital Cardiotrauma	Rio de Janeiro	Rio de Janeiro
Hospital Prontocor	Rio de Janeiro	Rio de Janeiro
Hospital do Câncer	Rio de Janeiro	Rio de Janeiro
Hospital Barra D'Or	Rio de Janeiro	Rio de Janeiro
Hospital Copa D'Or	Rio de Janeiro	Rio de Janeiro
Hospital São Vicente de Paulo	Rio de Janeiro	Rio de Janeiro
Hospital de Clínicas de Niterói	Niterói	Rio de Janeiro
Hospital Mario Lioni	Duque de Caxias	Rio de Janeiro
Hospital Português	Salvador	Bahia
Hospital Prontocor	Belo Horizonte	Minas Gerais
Hospital São Lucas	Porto Alegre	Rio Grande do Sul
Santa Casa da Misericórdia	Santos	São Paulo

*Coordinating center CU – Coronary unit; ICU - Intensive care unit

, smoking, cardiac failure, stroke, chest pain, tachycardia (heart rate> 100 bpm), syncope, dyspnea, tachypnea (respiratory rate > 20 bpm), fever (axillary temperature> 37°C), coughing, cyanosis and hemoptysis and/or hemopics.

In the multicenter registry, data on the electrocardiogram, chest X-ray, d-dimer, troponin I, the creatinine kinase MB, the duplex of the lower limbs and echocardiography were collected and analyzed about frequencies of completion and percentage of positivity. Were considered as changes in the standard electrocardiogram S1Q3T3 (presence of S wave in V1 derivation and presence of Q wave and inverted T wave in lead D3), known as McGuinn - White standard, T-wave inversion in leads V1 to V4, right bundle branch block or QRS axis deviation to the right, changes related to right ventricular overload.[4]

At chest X-ray, presence of pleural effusion, infiltrates or pulmonary atelectasia were the changes observed.[5] In relation to troponin I and the d-dimer, the cut- off point was accepted for positivity of each surveyed center and in this case, three different methods (ELISA, or latex or immunoturbidimetry were used depending on the availability at each center. Visualization of the thrombus or reduction of venous compressibility was the factor that defined the change in venous duplex scan,[6] and the presence of dilation or right ventricular dysfunction correlated with echocardiography.[7]

Use of unfractionated heparin, intravenous unfractionated subcutaneous heparin, low molecular weight subcutaneous heparin, , thrombolytic agents (rt-PA or streptokinase), coumarin, vena cava filter and surgical embolectomy. The mortality rate was analyzed in the first 24 hours of diagnosis and during hospital stay.

Data was statistically analyzed using: tables containing frequency distributions, percentages, averages, medians, standard deviations, minimum and maximum values. Continuous variables were reported as mean ± standard deviation.

The study was approved by the Ethics Research Committee of the Pro-Cardiac Hospital, according to Resolution 196/96 and 251/97 of the National Health Council. The original database (EMEP Study - Multicenter Study of Pulmonary Embolism) was partially funded by the Sanofi - Aventis Laboratory.

RESULTS

We evaluated 727 patients with a mean age of 68.9 ± 15.8 years, and 421 (57.9%) were female.

More prevalent risk factors were age over 40 years (93.4%) and bed rest> 72 h (38.5%), in 24.3% of patients. there was presence of neoplasm. Prevalence of risk factors was documented in all patients included, as described in table 1.

Table 1 – Prevalence of risk factors

Risk factor	N	%
Age > 40 years	679	93.4
Bed rest > 72h	280	38.5
Neoplasm	177	24.3
Previous history of DVP / PE	119	16.4
Smoking	115	15.8
CCF	112	15.4
Abdominal or pelvic surgery	70	10.7
Hip/lower limb fracture < 90 dias	52	7.2
Stroke	46	6.3
Chronic cor pulmonale	44	6.1
Estrogen use	33	7.8*
Pregnancy and postpartum	3	0.7*

CCF - Congestive cardiac failure; DVT/PE Deep venous thrombosis or pulmonary thrombolisis; * percentage relating to female gender patients.

Dyspnea (78.4%) and tachypnea (65.3%) - were the most frequent clinical respiratory manifestations while 44% of patients had tachycardia and 42.6%. Chest pain Indicators of hemodynamic instability - such as hypotension and syncope were observed respectively in 19.9% and 6.2% of the sample, as shown in table 2.

Table 2 – Prevalence of signs and symptoms

Signs and symptoms	N	%
Dyspnea	570	78.4
Tachipnea	475	65.3
Sinus tachicardia	320	44.0
Chest pain	310	42.6
Cough	155	21.3
Arterial hypotension	145	19.9
Cianosis	132	18.1
Fever	80	11.0
Syncope	45	6.2
Hemoptysis/hemoptotics	44	6.1

Complementary tests were used according to availability of each research center and table 3 shows each method's frequency of use. The electrocardiogram showed specific changes in 222 (30.5%) patients and of them 27 (12.1%) had axis deviation to the right,

78 (35.1%) standard S1Q3T3, 78 (35.1%) wave "T" inversion in leads V1 to V4 and 108 (48.6%) right bundle branch block. Chest X-ray showed specific changes in 333 (45.8%) of which, 128 (38.4%) had pleural effusion, 69 (20.7%) atelectasis, 31 (9.3%) area of hypoperfusion and 201 (60.3%) pulmonary infiltrates. Determination of d-dimer was positive in 93.2%, CK-MB in 8.39% and troponine in 9.63% of the samples. The venous duplex scan with specific changes, visualization of thrombus or reduction of venous compressibility, was found in 426 (67.5%) and echocardiogram showed right ventricular dysfunction in 182 (36.5%) and TEE in 78, 1% of the exams. Methods considered to confirm diagnosis are listed in table 4.

Table 3 – Frequency of complementary exams

Complementary exams	N	%
Chest X-ray	704	96.8
Electrocardiogram	687	94.5
Transthoracic echocardiogram	643	88.4
Venous duplex-scan	631	86.8
Creatinephosophokinase	455	62.5
Troponin I	417	57.4
D-dimer	398	54.7
Helical tomography	400	55.0
Ventilation/perfusion scintigraphy	171	23.5
Lung angiography	84	11.6
Transesophageal echocardiogram	82	11.3
Magnetic resonance	18	2.5

Table 4- Determinant criteria for inclusion

Complementary exams	%
Helical computed tomography	47.2
Lung scintigraphy	14.0
Vernous duplex-scan	14.0
Echocardiogram	12.7
Lung angiography	9.1
Magnetic resonance	1.7

Of the 727 patients analyzed, 99.2% underwent some form of treatment. Untreated died between confirmation of diagnosis and onset of therapy. Heparins (unfractionated heparin and low molecular weight) were the most often used form of treatment, with 7 patients treated with placement of a vena cava filter. In these patients the procedure was established because of their previous use of coumarin. One patient treated only with coumarin, which was already using the drug, the assisting physician did not elect to place the vena cava filter. Table 5 shows frequency of each type of treatment use. Mortality rate within 24 hours of admission and during hospital stay was respectively 3.4% and 19.5%.

Table 5 – Type of treatment used

Treatment	%
Nonfractionated heparin IV	50.2
Low m olecular weight heparin	29.2
Thrombolytic	11.7
Vena cava filter	3.3
Nonfractionated heparin SC	2.6
Cumarin	1.0
Embolectomy	0.1
Others	0.5
Not treated	0.8

IV- intravenous; SC - sub-cutaneous

DISCUSSION

Findings of this study demonstrate the clinical practice in the approach to PE in which risk factors, clinical manifestations, diagnosis and therapy were assessed. The study was limited to document data, without any interference in medical conducts employees, thus depicting the care given to patients with EP. The technological availability of research centers in the study was the basis for laboratory tests, vital for investigation of EP. Inclusion criteria, which required anatomic or functional substantiation of pulmonary embolism, although limiting the number of patients, warranted more accurate diagnosis.

Patients included were admitted to coronary emergency rooms, or coronary intensive care in tertiary centers which may have led to select the more severe cases. The mean age observed in our study was 68.9 years therefore higher than those observed in the ICOPER[8] (62.3 years), MAPPET[9] (63.5 years) and JASPER (60 years)[10] studies. Most studies show a tendency towards even distribution by gender. In our study we observed a higher prevalence of the n female gender (57.9%), which was also reported in ICOPER (55%)[8] and JASPER (60.5%),[10] but not in the MAPPET study (41%).[9]

Risk factors more frequently observed in literature were assessed. There are predisposing conditions not covered in the study, nevertheless just as important, such as thrombophilia.[11] Analysis of risk factors identified age over 40 years (93.4%) and bed rest for more than 72 hours (38.5%) as the most prevalent, corroborating epidemiological data in literature.[12]

The emergence of endothelial degenerative changes - associated with presence of diseases that predispose to thrombus formation, more frequent in patients over 40 years of age - explains the high prevalence of this risk factor in the EP. With the increasing life expectancy of the population, age should become an increasingly prevalent risk factor.

The importance of the muscle pump action of to maintain adequate venous returncan be assessed by the high prevalence of restraint to prolonged bed rest in patients with EP.

The tumor able to promote activation of the coagulation system[13] was detected in almost one quarter of cases, corroborating data of the studies PIOPED (18.3%),[14] ICOPER (22.5%)[8] and JaSPER (23%),[10] as shown in table 6. This high prevalence promotes discussion on the need of routine investigation of cancer in patients with EP, as well as strategies of a comprehensive primary prevention of thrombosis.

The endothelial changes caused by a first episode of deep vein thrombosis (DVT) predispose to disease recurrence. Previous occurrence of DVT or PE had been reported in 14% of our cases, 25% in ICOPER[8] and 29% in MAPPET.[9] These observations indicate possible benefit of continued use of elastic stockings for such patients.

A hip or lower limb fracture was documented in 9% of the sample, similar to JaSPER (9%)[10] and MAPPET (11%).[9] Such similarities are not repeated in the history of abdominal or pelvic surgery, with prevalence of 8% in our sample and 36% and 27% respectively, in the other two reports. This difference can be explained by the characteristics of hospitals involved in each of the studies.

Congestive heart failure (CHF) and chronic pulmonale was present respectively in 15.4% and 6.1% of our patients and in 11% and 12% in the ICOPER study.[8] The situation in favor of thrombosis involving vein stasis, activation of procoagulant substances[15] and present endothelial changes suggest the possible underestimation of PE diagnosis in this population based surveys.

Prevalence of 0.7% of expectant mothers is somewhat lower than those observed in ICOPER[8] (2.5%) and MAPPET (1.4%),[9] while the use of estrogen was higher in ICOPER (12.3%)[8] than in the women examined in this study (7.8%). Difference in use of estrogen suggests greater use of hormone replacement therapy in the United States and Europe, where the ICOPER[8] was carried out.

The small number of patients with a history of stroke (6.3%) was also reported in MAPPET[9] (2%). The low prevalence of history of stroke, a subgroup often with multiple risk factors, may have been influenced by the chronic use of aspirin by these patients by promoting prevention of DVT.

Smoking was reported by 15.8% of patients and quitting should be encouraged as it is one of the few risk factors considered avoidable.

In the analysis of signs and symptoms, respiratory symptoms and chest pain, were as prevalent as in other studies.[16.17] In the JaSPER[10] dyspnea was present in 66% and chest pain in 49%, the most frequent symptoms reported.

Dyspnea is one of the diagnostic challenges in emergency rooms. LV decompensation, the EP and inflamma-

Table 6- Comparison between prevalences of risk factors

Risk factors	ICOPER (%)	MAPPET (%)	JaSPER (%)	EMEP (%)
Bed rest	28	NA	23	38.5
Neoplasma	23	12	23	24.3
CHF	11	32	NA	15.4
History DVT/PE	25	29	NA	16.4
Smoking	18	NA	NA	15.8
Hip/lower limb fracture	NA	11	9	7.2
Abdominal/pelvic surgery	NA	27	36	10.7
Chronic cor pulmonale	12	11	NA	6.1
Stroke	NA	2	NA	6.3
Estrogen use/hormone replacement	12.3	NA	NA	7.8*
Pregnancy/post-partum	2.5	1.4	NA	0.7*

CHF- Congestive heart failure; DVT/PE - Deep venous thrombosis /pumonary thrombolisis; * percentage related to female gender patients; NA - not available; ICOPER - International Cooperative Pulmonary Embolism Registry; MAPPET - Management Strategy and Prognosis of Pulmonary Embolism Registry; JaSPER - Japanese Society of Pulmonary Embolism Research; EMEP - Estudo Multicêntrico de Embolia Pulmonar.

tory lung diseases isolated or in sets are the first differential diagnoses. The sudden onset of dyspnea is the feature that alerts the physician on diagnosis of PE, although the symptoms may appear gradually or aggravating chronic cardiopulmonary conditions. In 727 patients evaluated, dyspnea was present in 78.4%, similar to the result of Stein et al.[16] that demonstrated presence of dyspnea in 78% and Hoellerich et al. 74%.[17]

Pleuiritic chest pain is more correlated with the EP, but e angina pain may occur in patients with ischemia of the right ventricle (RV). Pleuritic chest pain was reported in 85% of patients in the Bell et al.,[18] study and 66% in the PIOPED study.[14] In this study a prevalence of 42.6% of chest pain was found, similar to the findings of ICOPER[8] (49%) and JaSPER[10] (46%).

Clinical signs of hemodynamic instability were present in one fifth of patients evaluated with hypotension observed in 19.9%, regardless of volume replacement. In the main studies, prevalence of forms of presentation diverge greatly as shown in table 7. In ICOPER[8], only 5% had arterial hypotension, while MAPPET[9] and JaSPER[10] showed higher prevalence that our observations. Notwithstanding these differences there is agreement that this is a greater severity subgroup, for which thrombolytics or embolectomy may be indicated.[1]

Cough was present in approximately 22% of our patients, with lesser prevalence than in the two studies of Stein et al. that documented it in 37% and 55% of patients.[16,19] Hemoptysis was observed in 6.1%, while in 7% of patients in ICOPER.[8] The low occurrence of hemoptysis suggests a lower number of cases of pulmonary infarction in the sample.

Fever was observed in 11%, similar to the 14% reported in all the sub-studied by PIOPED,[14] demonstrating the importance of differential diagnosis of PE in inflammatory lung diseases.[20]

Overall, prevalence of signs and symptoms of PE is similar in most studies as exemplified in table 7.

The electrocardiogram, chest x-ray, transthoracic echocardiogram and venous duplex scan of lower limbs were carried out n more than 90% of patients studied. Laboratory evaluation of d-dimer, creatinine kinase, troponin I, blood gases, in more than half of the cases, allowed analysis of large volumes of data. Compared to the ICOPER,[8] study, less scintigraphy and angiography were made as seen in, table 8, a condition explained by the widespread use of helical computed tomography for diagnosis in our sample.

Table 8 – Percentage of exams performed

Exam	ICOPER (%)	MAPPET (%)	EMEP (%)
Chest X-ray	95	NA	96.5
Electrocardiogram	90	98	98.5
Cintilografia	84*	56	21.2
Echocardiogram	47	74	95.5
D-dímer (Latex)	21	NA	48.5
D-dimer (ELISA)	18	NA	21.2
Lung angiography	19	17.5	11.3

*only perfusion scintigraphy. NA- not available; ICOPER - International Cooperative Pulmonary Embolism Registry; MAPPET- Management Strategy and Prognosis of Pulmonary Embolism Registry; EMEP - Estudo Multicêntrico de Embolia Pulmonar.

The electrocardiogram was positive in one third of patients and only four types of changes were considered, representing RV overload. Stein[21] showed electrocardiographic abnormalities in 94% of cases of massive PE and 77% of submassive however the patterns of right ventricular hypertrophy were present in only 26%.

Table 7 – Comparison between prevalence of clinical manifestations

Clinical manifestation	ICOPER (%)	Stein (%)	MAPPET (%)	JaSPER (%)	EMEP (%)
Dyspnea	82	73	96	66	78.4
Tachypnea	60	70	NA	NA	65.3
Tachicardia	40	30	71	NA	44.0
Chest pain	49	66	NA	46	42.6
Cough	20	37	NA	11	21.3
Arterial hypotension	5	NA	34	36	19.9
Cyanosis	NA	1	NA	NA	18.1
Fever	9	7	NA	13	11.0
Síncope	14	NA	35	20	6.2
Hemoptysis/hemoptotic	7	13	NA	6	6.1

ICOPER - International Cooperative Pulmonary Embolism Registry; Stein[18]; MAPPET - Management Strategy and Prognosis of Pulmonary Embolism Registry; JaSPER - Japanese Society of Pulmonary Embolism Research; EMEP - Estudo Multicêntrico de Embolia Pulmonar.

While radiographic changes were observed in 47.2%, the ICOPER analyzed chest X-rays of 2322 patients and found abnormal in 78%, although it assessed more variables. The ICOPER showed that pleural effusion was present in 23%, atelectasis in 18% and areas of pulmonary infiltrates in 17%.[22] Our findings identified pleural effusion in 17%, 10% in atelectasis and pulmonary infiltrates in 27%. Given the possibility of interobserver variability and subjective analysis of changes, we consider this difference between the observations acceptable.

The realization of d-dimer in suspected PE, has greater application for exclusion of diagnosis due to its high negative predictive value, as shown by Gingsberg et al. in 1998.[23] In our analysis, the technique of latex was positive in 87.7% and the ELISA in 93%, confirming the higher sensitivity of the latter and corroborating the data of Kline et al.[24] Probably association of low clinical probability of the negative d-dimer enables exclusion of PE diagnosis with large safety margin.[25]

The elevation of markers of myocardial necrosis in 19.7% of samples taken was lower than expected in a group in which 37.8% had RV dysfunction. When separately analyzed, creatininekinase was high n 16.9%, while troponin I in 11.2%. These data contrast with the work of Meyer et al., who identified 39% of patients with PE, troponin I value above the normal range.[26]

Studies using objective criteria for diagnosis of RV dysfunction on transthoracic two-dimensional differ on the methodology employed. Goldhaber et al. diagnosed the RV dysfunction by assessing the end-diastolic area measured by planimetry[27] while the study of Hamel et al. used the relationship between end-diastolic volume of right and left ventricles> 0.6.[28] In our study, the subjective analysis of RV dysfunction through tow-dimensional echocardiogram may have caused bias in the results. While we recognize this methodological limitation, we believe that the information regarding the RV is in most cases, results of this subjective analysis. Therefore, we believe we are portraying the actual practice, as proposed in this work. The percentage of patients with RV dysfunction on echocardiography was 37.8%, similar to results found in ICOPER[25] and lower than those of Ribeiro et al.[29] Choice of the method was directly influenced by the availability and the clinical practice of each investigator's center. Considered a standard, the pulmonary arteriography substantiated diagnosis in 11.3% while scintigraphy in 21.2% and helical tomography (CT) in 44.5% of the patients. Patient inclusion by the venous duplex scan criterion with thrombus and the presence of signs or symptoms of PE may generate questions about t absence of evidence of disease in the lung. The incorporation of this criterion was defined by the embolic potential of DVT and the high probability of PE, when associated with clinical manifestations.

Although available in most centers participating in the study, the AGP is still little used. If in the past, technical limitations and risk of complications of pulmonary arteriography are not often requested, the main reason is, today, the possibility of diagnosis through less complex exams.

A scintigraphic study of ventilation and perfusion was the diagnostic method for co-21.2%, and similarly to the AGP, the low utilization can be explained by the expand use of spiral CT.

Spiral CT has a sensitivity between 66 and 93% and specificity of 89 to 97%,[30] furthermore, enable the evaluation of differential diagnosis of PE, such as acute diseases of the aorta, pulmonary inflammations and pneumothorax. These characteristics have made the spiral CT exam I mandatory in latest diagnostic algorithms.

MRI remains underused, mainly due to lower availability of the-helical CT. The diagnostic accuracy similar to CT and the use of contrast without risk of nephrotoxicity or anaphylaxis should encourage greater use of MRI for diagnosis of PE in the near future.

The HNF is the most widely used treatment in our patients (55.1%). The proven efficacy of UFH and low risk of bleeding make this therapeutic strategy most often employed for EP.

LMWH has proved as effective as UFH in the treatment of EP, as well as its advantages, such as subcutaneous administration and no need for laboratory control.[31] These characteristics are increasing in use of this therapeutic strategy in the EP, and this study, LMWH was used in 23.7% of patients. LMWH should be only be used for clinically stable patients without RV dysfunction and treated in hospital setting.

Thrombolytic treatment was used in 15.2% of patients in this study. The finding that 20.8% had hypotension suggests that we may be underdoing the thrombolytic agent in our patients. In the JaSPER[10] the thrombolytic was administered to 50% of patients in the sample, in which 36% had cardiogenic shock. Goldhaber,[32] in an editorial, reviews results of the main publications and reinforces the need for more evidence to stresses thrombolytic therapy for clinically stable patients and RV dysfunction, such as submassive PE.

The type, dose and route of administration of throm-

bolytic therapy approved by the FDA for treatment of PE may vary, depending on clinical presentation. The only study comparing heparin with thrombolytic therapy, which showed a reduction in mortality, used dose of streptokinase 1.500.000U,[33] different from the scheme approved by the FDA.

The intravenous route is the most used for the administration of thrombolytic therapy in patients with EP. The patients undergoing pulmonary arteriography as the diagnostic method may use thrombolytic agents directly into the pulmonary artery. This strategy requires a lower dose of the drug and may be indicated for hemodynamically unstable patients with high risk of bleeding.

Probably, just as today we stratify patients for use of heparin or thrombolytic therapy in the future we may define doses and administration routes depending on the patient and on the presentation of disease.

Treatment of PE should not only be defined by clinical instability or dysfunction of the RV, but also by variables such as age, presence of proximal DVT and previous cardio respiratory condition. A possible subtilization of thrombolytics in this study is suggested when comparing percentage of patients with hypotension or syncope (25.8%) with use of thrombolytic therapy (15.2%).

In-hospital mortality of 22.7% is higher than the ICOPER study[8] formerly reported 17.5% of deaths in three months, and in the group with clinical instability, the mortality rate was 58.3%. Kasper et al. showed a steady increase in mortality according to worsening of the hemodynamic status.[9]

The assessed sample was of patients admitted to emergency rooms and intensive care and advanced age which may reflect a selection bias, regarding severity of the population studied. Among the deaths observed, 54.3% occurred in the first seven days of stay. This suggests that almost half of the patients had complications of the EP's, which led to longer hospital stays, these complications may have contributed to death.

Finally, this study was limited to descriptive information, and the intention to establish a correlation between the variables studied was never intended. With the continuation of the project certainly these reviews will be carried out.

This study has some limitations. The research centers that participated in the study have the structure for diagnosis and treatment above the average of the Brazilian hospitals. Therefore, this study demonstrates the clinical practice of qualified centers. Data from additional tests were included according to diagnosis of the researcher; a center for independent validation of them was not available. The patients were admitted in emergency and intensive care units, which may have led to selection of a population of greater severity.

CONCLUSIONS

Presence of multiple risk factors was common in patients with PE, where age over 40 years and bed rest were the most prevailing, while dyspnea and tachypnea were the most common clinical manifestations observed. Among the complementary methods, classical research strategies in percentages in some cases, higher than the average described in literature. The most widely used diagnostic criteria for inclusion by researchers was helical CT angiography also reproducing a tendency of diagnostic studies and heparin the most often prescribed treatment following the guidelines of therapeutic consensus. Perhaps, in-hospital mortality of 19.5%, slightly higher than in most studies published, is due to characteristics of the greater severe in the population admitted to intensive care units.

ACKNOWLEDGMENTS

We appreciate the participation of researchers from the EMEP (Multicentric Study of Pulmonary Embolism)) for collecting study data

Evandro Tinoco Mesquita (Pro-Cardiac Hospital, Rio de Janeiro, RJ), John Mansur son and Joseph Kezen Camillo Jorge (Samaritan Hospital, Rio de Janeiro, RJ), Gustavo Nobre (Hospital Rio Mar, Rio de Janeiro, RJ), Mark Baptista, Arthur Nelson, Mark and Marcelo Knibel Lugarinho (Hospital São Lucas, Rio de Janeiro, RJ); Glaucia Maria and Ricardo Eiras (Prontocor Hospital, Rio de Janeiro, RJ), Gustavo Gouvea, Alexander Drummond, Eduardo Eiras Emanuel and Salgueiro (Casa de Saúde São José, Rio de Janeiro, RJ); Monica Callafiori (Hospital CardioTrauma, Rio de Janeiro, RJ), Paulo César Pereira da Silva e Souza and Marcelo Magalhães (Hospital de Clinicas de Niteroi, Niterói, RJ), Ana Paula Lacerda (Hospital Barra D'Or, Rio de Janeiro, RJ), Fernando Pacheco (Hospital Copa D'Or, Rio de Janeiro, RJ), Marcelo Vieira Gomes and Luis Felipe Camille (Clínica São Vicente , Rio de Janeiro, Brazil), Guilherme Aguiar (Hospital São Vicente de Paulo, Rio de Janeiro, RJ), Maria Luiza Caetano, Roberto Toscano (National Cancer Institute, Rio de Janeiro, Brazil),

Jose Pericles Esteves and Carolina Barbosa (Portuguese Hospital, Salvador, BA), Francisco Silveira (Prontocor Hospital, Belo Horizonte, MG), Alex Macedo (Hospital Santa Casa, Santos, SP), Luis Carlos Bodanese (Hospital Sao Lucas, Porto Alegre, RS).

RESUMO

Introdução: O perfil clínico e as estratégias diagnósticas e terapêuticas nos pacientes com embolia pulmonar demonstram a prática clínica na abordagem da doença. Essas informações, escassas nos estudos nacionais, possibilitam melhor conhecimento da embolia pulmonar.

Métodos: Estudo multicêntrico de 727 pacientes admitidos em unidades de emergência ou terapia intensiva, com o diagnóstico de embolia pulmonar confirmado por um ou mais dos seguintes exames: arteriografia pulmonar angiotomografia computadorizada helicoidal angioressonância magnética, ecodopplercardiograma, cintilografia pulmonar ou duplex-scan venoso. Dados demográficos, comorbidades, manifestações clínicas e métodos complementares foram analisados.

Resultados: A média de idade foi 68 anos, sendo 42% homens. Os fatores de risco mais prevalentes foram: idade > 40 anos, repouso no leito e neoplasia. A dispnéia, taquipnéia, taquicardia, dor torácica, foram as manifestações clínicas mais frequentes. O eletrocardiograma apresentou alterações em 30%, a radiografia de tórax em 45%, o duplex-scan venoso em 69% e o ecodopplercardiograma em 37%. O D-dímero a troponina e a CKMB foram positivos em respectivamente 93, 9 e 8%. Os métodos mais utilizados para o diagnóstico foram: tomografia computadorizada: 47%, duplex-scan venoso: 14% e cintilografia pulmonar: 14%. As formas mais freqüentes de tratamento foram: heparina não fracionada 50%, heparina de baixo peso molecular 30% e trombolítico 12%. A mortalidade intra-hospitalar foi de 19,5%.

Conclusões: Observou-se que a idade > 40 anos, imobilização prolongada e neoplasia foram os fatores de risco de maior prevalência e a dispnéia a apresentação clínica mais freqüente. A angiotomografia computadorizada helicoidal foi o método mais utilizado para o diagnóstico e a heparina não fracionada a principal forma de tratamento.

Descritores: Embolia pulmonar/diagnóstico; Embolia pulmonar/quimioterapia; Heparina/uso terapêutico; Tomografia computadorizada por raios-x/métodos

REFERENCES

1. Torbicki A, Perrier A, Konstantinides S, Agnelli G, Galiè N, Pruszczyk P , Bengel F, Brady AJ, Ferreira D, Janssens U, Klepetko W, Mayer E, Remy-Jardin M, Bassand JP, Vahanian A, Camm J, De Caterina R, Dean V, Dickstein K, Filippatos G, Funck-Brentano C, Hellemans I, Kristensen SD, McGregor K, Sechtem U, Silber S, Tendera M, Widimsky P, Zamorano JL, Zamorano JL, Andreotti F, Ascherman M, Athanassopoulos G, De Sutter J, Fitzmaurice D, Forster T, Heras M, Jondeau G, Kjeldsen K, Knuuti J, Lang I, Lenzen M, Lopez-Sendon J, Nihoyannopoulos P, Perez Isla L, Schwehr U, Torraca L, Vachiery JL; Task Force for the Diagnosis and Management of Acute Pulmonary Embolism of the European Society of Cardiology. 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.
2. Menna-Barreto S, Cerski MR, Gazzana MB, Stefani SD, Rossi R. Tromboembolia pulmonar em necropsias no Hospital de Clínicas de Porto Alegre, 1985-1995. J Pneumol. 1997;23(3):131-6.
3. Mesquita CT, Morandi Júnior JLB, Perrone FT, Oliveira CS, Barreira LJ, Nascimento SSCA, et al. Diagnóstico clínico versus confirmação patológica de embolia pulmonar fatal em pacientes hospitalizados. Arq Bras Cardiol. 1999;73(3): 251-8.
4. Abecasis J, Monge J, Alberca D, Grenho MF, Arroja I, Aleixo AM. Electrocardiographic presentation of massive and submassive pulmonary embolism. Rev Port Cardiol. 2008;27(5):591-610.
5. Greenspan RH, Ravim CE, Polansky SM, and McLoud T. Accuracy of chest radiography in diagnosis of pulmonary embolism. Invest Radiol. 1982; 17(6): 539-43.
6. Lensing AW, Prandoni P, Brandjes D, Huisman PM, Vigo M, Tomasella G, et al. Detection of deep-vein thrombosis by real-time B-mode ultrasonography. N Engl J Med. 1989;320(6):342-5.
7. Torbicki A, Pruszczyk P. The role of echocardiography in suspected and established PE. Semin Vasc Med. 2001;1(2):165-74.
8. Goldhaber SZ, Visani L, De Rosa M. Acute pulmonary embolism: clinical outcome s in the International Cooperative Pulmonary Embolism Registry (ICOPER). Lancet. 1999;353(9162):1386-9.
9. Kasper W, Konstatinides S, Geibel A, Olschewski M, Heinrich F, Grosser KD, et al. Management strategies and determinants of outcome in acute major pulmonary embolism: results of a multicenter registry. J Am Coll Cardiol. 1997;30(5):1165-71.
10. Nakamura M, Fujioka H, Yamada N, Sakuma M, Okada O, Naganishi N, et al. Clinical characteristcs of acute pulmonary thromboembolism in Japan: results of a multicenter registry in the Japonese Society of Pulmonary Embolism Research. Clin Cardiol. 2001;24(2):132-8.
11. Kruse L, Mitchell AM, Camargo CA Jr, Hernandez J,

Kline JA. Frequency of thrombophilia-related genetic variations in patients with idiopathic pulmonary embolism in an urban emergency department. Clin Chem. 2006;52(6):1026-32.

12. Anderson FA Jr, Wheller HB, Goldberg RJ, Hosmer DW, Patwardhan NA, Jovanovic B, et al. A population-based perspective of the hospital incidence and case-fatality rates of deep vein thrombosis and pulmonary embolism. The Worcester DVT Study. Arch Intern Med. 1991;151(5): 933-8.
13. Luzzatto G, Schafer Al. The prethrombotic state in cancer. Semin Oncol. 1990;17(2):147-59. Review.
14. Value of the ventilation/perfusion scan in acute pulmonary embolism. Results of the prospective investigation of pulmonary embolism diagnosis (PIOPED). The PIOPED Investigators. JAMA. 1990;263(20):2753-9.
15. Yamamoto K, Ikeda U, Furuhashi K, Irikawa M,Nakayama T, Shimada K. The coagulation system is activated in idiopathic cardiomyopathy. J Am Coll Cardiol. 1995;25(7):1634-40.
16. Stein PD, Willis PW 3rd, DeMets DL. History and physical examination in acute pulmonary embolism in patients without preexisting cardiac or pulmonary disease. Am J Cardiol. 1981;47(2):218-23.
17. Hoellerich VL, Wigton RS. Diagnosing pulmonary embolism using clinical findings. Arch Intern Med. 1986;146(9):1699-704.
18. Bell WR, Simon TL, DeMets DL. The clinical features of submassive and massive pulmonary emboli. Am J Med. 1977; 62(3):355-60.
19. Stein PD, Terrin ML, Hales CA, Palevsky HI, Saltzman HA, Thompson BT, Weg JG. Clinical, laboratory, roentgenographic, and electrocardiographic findings in patients with acute pulmonary embolism and no pre-existing cardiac or pulmonary disease. Chest. 1991;100(3):598-603.
20. Stein PD, Afzal A, Henry JW, Villareal CG. Fever in acute pulmonary embolism. Chest. 2000;117(1): 39-42.
21. Stein PD, Dalen JE, McIntyre KM, Sasahara AA, Wenger NK, Willis PW 3rd. The electrocardiogram in acute pulmonary embolism. Prog Cardiovasc Dis. 1975;17(4):247-57.
22. Elliott CG, Goldhaber SZ, Visani L, DeRosa M. Chest radiographs in the acute pulmonary embolism. Results from the International Cooperative Pulmonary Embolism Registry. Chest. 2000;118(1): 33-8.
23. Ginsberg JS, Wells PS, Kearon C, Anderson D, Crowther M, Weitz JI, et al. Sensitivity and specificity of a rapid whole-blood assay for D-dimer in the diagnosis of pulmonary embolism. Ann Intern Med. 1998;129(12):1006-11.
24. Kline JA, Johns KL, Colucciello SA, Israel EG. New diagnostic test for pulmonary embolism. Ann Emerg Med. 2000;35(2):168-80.
25. Carrier M, Righini M, Djurabi RK, Huisman MV, Perrier A, Wells PS, et al. VIDAS D-dimer in combination with clinical pre-test probability to rule out pulmonary embolism. A systematic review of management outcome studies. Thromb Haemost. 2009;101(5):886-92.
26. Meyer T, Binder L, Hruska N, Luthe H, Buchwald AB. Cardiac troponin I elevation in acute pulmonary embolism is associated with right ventricular dysfunction. J Am Coll Cardiol. 2000;36(5):1632-6.
27. Goldhaber SZ, Haire WD, Feldstein ML, Miller M, Toltzis R, Smith JL, et al.. Alteplase versus heparin in acute pulmonary embolism: randomised trial assessing right-ventricular function and pulmonary perfusion. Lancet. 1993;341(8844): 507-11.
28. Hamel E, Pacouret G, Vincentelli D, Forissier JF, Peycher P, Pottier JM, Charbonnier B. Thrombolysis or heparin therapy in massive pulmonary embolism with right ventricular dilatation: results from a 128-patient monocenter registry. Chest. 2001;120(1):120-5.
29. Ribeiro A, Lindmarker P, Juhlin-Dannfelt A, Johnsson H, Jorfeldt L. Echocardiography Doppler in pulmonary embolism: right ventricular dysfunction as a predictor of mortality rate. Am Heart J. 1997;134(3):479-87.
30. Hogg K, Brown G, Dunning J, Wright J, Carley S, Foex B, Mackway-Jones K. Diagnosis of pulmonary embolism with CT pulmonary angiography: a systematic review. Emerg Med J. 2006;23(3):172-8.
31. Simonneau G, Sors H, Charbonnier B, Page Y, Laaban JP, Azarian R, et al. A comparison of low-molecular-weight heparin with unfractionated heparin for acute pulmonary embolism. The THESEE Study Group. Tinzaparine ou Heparine Standard: Evaluations dans l'Embolie Pulmonaire. N Engl J Med. 1997;337(10):663-9.
32. Goldhaber SZ. Thrombolysis in pulmonary embolism: a large-scale clinical trial is overdue. Circulation. 2001;104(24):2876-8.
33. Jerjes-Sanchez C, Ramirez-Rivera A, de Lourdes García M, Arriaga-Nava R, Valencia S, Rosado-Buzzo A, et al. Streptokinase and heparin versus heparin alone in massive pulmonary embolism: A randomized controlled trial. J Thromb Thrombolysis. 1995;2(3):227-9.