Caracterización clínico-epidemiológica del tromboembolismo pulmonar en autopsias del Instituto de Medicina Legal de Medellín 2010-2020

Clinical-epidemiological characterization of Pulmonary Thromboembolism in autopsies of the Legal Medicine Institute of Medellin 2010-2020.

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Abstract

Introduction: Pulmonary thromboembolism (PTE) is a medical complication that has caused high morbidity and mortality for a long time despite having highly effective diagnostic and therapeutic methods for treating it.

Objective: To describe the clinical-epidemiological and anatomopathological characteristics of PTE diagnoses in corpses admitted for sudden death to the National Institute of Legal Medicine and Forensic Sciences of Medellín 2010-2020.

Methods: This is a descriptive study of a retrospective cohort, formed by cases admitted to the Institute of Legal Medicine for sudden death with cause of death to be established, which were diagnosed with PTE. Analyses were performed with frequencies and summary measures in SPSS 27.0.

Results: Out of 46097 medico-legal necropsies performed in the period studied, 164 cases (0.36 %) corresponded to PTE. The average age was 57.0±19.3 years and 51.2% women. 57.9% was natural deaths, 37.2% had trauma and 36.0% presented another circulatory event. In most of the cases, the death occurred at their residence (47.0%) and public roads (25.6%). In terms of thrombosis, 45.1% were of the pulmonary artery and 34.8% of

intraparenchymal pulmonary arteries and 52.4% of the deceased had deep vein thrombosis of the lower limbs.

Conclusion: PTE is an important cause of death in in-hospital and out-of-hospital patients, despite existing diagnostic, pharmacological and non-pharmacological methods for its prevention. The performance of a greater number of clinical autopsies will reveal the true impact of this complication in our environment and improve the quality of patient care.

Keywords: Pulmonary thromboembolism, autopsy, sudden death, embolism.

Introduction

Pulmonary thromboembolism (PTE) is a common and potentially lethal form of venous thromboembolism (VTE). Most patients die from this condition, usually within the first hour of the event, with a lethality close to 10%. The mortality rate of diagnosed and treated PTE varies from 3 to 8%, but increases to about 30% in untreated PTE. In the United States it affects annually between 500,000 to 600,000 people and it is a primary or secondary cause of death in 150,000 to 200,000 of these individuals (1).

The condition is often suspected in patients who present with unexplained dyspnea, tachypnea, or chest pain, and an indistinguishable clinical picture in multiple pathologies. (1,2). Its study is usually performed when clinical findings or a history of high-risk predisposing conditions such as obesity, immobilization, trauma, recent surgeries, pregnancy, malignancy, smoking, oral contraceptives or hormone replacement therapies, and a history of pulmonary embolism or a hypercoagulability disorder are present. However, 30% of patients with pulmonary embolism do not have detectable triggers, although it is useful to indicate that the average age of patients with this event ranges from 56 to 66 years (1,3,4,5,6). In addition, the literature has indicated that for trauma-related cases the greatest increase in its incidence occurs about one or two weeks after the injury, but in other cases there is no relationship with time and its presentation can be insidious and sudden (7).

«This is a descriptive cohort study carried out through the analysis of sudden death cases with cause of death to be established that were admitted at the Institute.»

«Within the initial assessment a pre-test (Wells scale) is performed, this combines the patient's history with present signs and symptoms ...»

Despite the detection and intervention of multiple risk factors, including the intensive use of prophylaxis for deep vein thrombosis with heparins, pneumatic compression devices or pressure gradient measures, PTE continues to be one of the most feared and difficult to diagnose complications in patients receiving medical attention in a health institution. (8), this is a consequence of their broad differential diagnoses and weak sensitivity and specificity of their diagnostic tests (2,9). Within the initial assessment a pre-test (Wells scale) is performed, this combines the patient's history with present signs and symptoms, then diagnostic tests are used that may show non-specific alterations of the disease, but that are often used to rule out other diseases with similar symptoms, among which are arterial blood gases, electrocardiogram, and plain chest x-ray. It is also used in its diagnosis the D-dimer, this is a test of great sensitivity in patients suffering from VTE, but not very specific. The reference test is pulmonary arteriography (2,9,10).

Due to the decrease in the practice of clinical autopsies (probably due to the confidence of doctors in diagnostic images and laboratory tests, despite its limitations of specificity), this disease is not recognized as the cause of death in most fatal outcomes generated by it, therefore in many cases the cause of death is thoroughly unknown (11). Even an exhaustive search in the databases PubMed, Science Direct, Google Scholar, ProQuest and Embase, using the keywords "Pulmonary thrombo-embolism, Epidemiology, clinical-pathological correlation, autopsy" only allowed the finding of 32 articles and few of them were directly related to the topic of this research.

In this regard, Micallef considers that the decrease in the practice of clinical autopsies does not allow studies that provide precise statistics on the mortality rate for PTE due to the clinical diagnosis is still unspecific (11). On the other hand, Nagamalesh's group made a diagnosis of PTE by computerized tomography in 31 hospitalized patients and provided recommendations on its management (1); while Hansma's group carried out a study of thrombi found in 238 autopsies, analyzing their macroscopic and microscopic characteristics in the categories of antemortem, postmortem and agonal thrombus, which help to clarify the cause of death (12). Finally, Carrillo's group clarified the diagnostic sequence of PTE, analyzing the main

diagnostic, clinical, analytical, and imaging tools, with special emphasis on the principles that rule the evidence-based medicine (2).

The above exemplifies the small number of investigations that have been carried out recently on the subject, for this reason this study was conducted with the aim of describing the main clinical, epidemiological, and pathological characteristics of PTE in legal-medical autopsies at the National Institute of Legal Medicine and Forensic Sciences of Medellín between 2010 and 2020. This research is important given the low number of clinical necropsies currently being developed because of the confidence of many physicians in diagnostic imaging and laboratory tests despite their low diagnostic accuracy and the persistence of clinical-pathological discrepancies for diagnosis, among other aspects that require increasing research in this field (11.13).

Methods

Type of study: Descriptive of a retrospective cohort.

Study population: A total of 46097 necropsies were performed by the legal medicine institute of Medellin during 2010-2020, of which 164 were diagnosed with post-mortem PTE. Since all subjects were included, the concepts of sampling and sampling do not apply. All necropsy reports were reviewed. Of the initial cases, 15 cases were excluded in which the necropsies did not meet the requirements for the diagnosis of PTE, that is no clear descriptions or findings were required that led to the diagnosis, it did not include the exploration of the pulmonary arteries, it did not make an identification of the thrombus and omitted to look for its origin that is usually found in the lower limbs. All cases with a history of hospitalization, prior treatment to fatal outcome, basic thromboembolic disease and previous surgeries were included due to these conditions are important for the presentation of the disease and the subsequent analysis of the results of the present work.

Data collection: The source of information was secondary, it consisted of the database of the National Institute of Legal Medicine and Forensic Sciences, Medellín headquarters, where the information generated by the medico-legal necropsies carried out are recorded, System Identification Registry Disappeared and Corpses (SIRDEC by its acronym in Spanish), in this

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platform the forensic doctors pour all the information related to variables such as identification data of the deceased, form and cause of death, summaries of medical history and necropsy findings. The Institute carries out quality control of these expert reports through a peer review to have approval for their subsequent printing and sending to the judicial authorities.

Bias control: Selection bias was controlled including all subjects who met the eligibility criteria, the control of information biases was performed by forensic medicine professionals with strategies such as the audit of necropsies by reviewing 100% of the reports. For the control of biases in the extraction of data from the secondary source, double typing and logical verification were performed.

Analysis plan: age (single continuous variable) was described with mean, standard deviation, interquartile range, and range; the other variables were categorical and were described with absolute (n) and relative (%). The database and analyses were performed in SPSS 27.0.

Ethical aspects: The Declaration of Helsinki principles, Resolution 8430 of 1993 of the Ministry of Health of Colombia, the guidelines of legal medicine were applied to ensure that the use of the information was only for investigative purposes and that the analyses are based on data that do not contain information that can lead to the identification of each case, since a legal medicine professional delivers a blinded file (without case identification data).

Results

The average age of the study population was 57.0±19.3 years, with 50% of the central data between 42-72 years and range between 10 and 92. In the municipalities of the metropolitan area 9 were from Bello, 3 from Itagüí and n = 3 from Envigado, the other municipalities included Amagá (n = 2), El Retiro (n = 2), Rionegro (n = 2), Apartadó (n = 2), San Pedro de los Milagros (n = 1), Ciudad Bolívar (n = 1) and San Roque (n = 1). In other socio-demographic characteristics, it was highlighted that the majority were women, married, with a high school education and engaged in occupations classified by the ILO as elementary, such as mason, recycler, or others (Table 1).

Table 1. Sociodemographic characterization of the study population

Socio-demographic variables		n	%
Necropsy Municipality	Medellín	138	84,1
	Others in the metropolitan area	15	9,2
	Others from Antioquia	11	6,7
Sex	Female	84	51,2
	Male	80	48,8
Marital status	Married – Domestic partner	78	47,6
	Single	52	31,7
	Widower	23	14,0
	Divorce	11	6,7
Level of education	None	19	11,5
	Elementary	65	39,6
	High school	66	40,2
	Higher	14	8,5
Occupation	Elementary occupations	51	31,1
	Housewife	38	23,2
	Independent	17	10,4
	Retired	21	12,8
	Unemployed	20	12,2
	Student	6	3,7
	Professional	11	6,7

In the study subjects, 57.9% registered death from natural causes and the remaining percentage from violent causes, in these causes the presence of trauma and events of the circulatory system was more frequent, and the main places where the event occurred were in their homes, public roads and hospital centers (Table 2).

Table 2. Distribution of cases according to form, cause, and place of death

Death cases characterization		N	%
Type of death	Natural	95	57,9
	Violent - Accidental	34	20,7
	Traffic accident	22	13,4
	Homicide	8	4,9
	Violent (without typology)	4	2,4
	Suicide	1	0,6
Cause of death	General trauma	61	37,2
	Other circulatory system events	59	36,0
	Cancer	3	1,8
	Other	12	7,3
	Unspecified	29	17,7
Events scene	House	77	47,0
	Public row	42	25,6
	Hospital	16	9,7
	Farm	3	1,8
	Passenger terminals	2	1,2
	Bars	1	0,6
	Children and nursing homes	1	0,6
	Lodgings	1	0,6
	Hospices	1	0,6
	Mines	1	0,6
	Other – unspecified	19	11,6

In relation with the traumas, the highest proportion of subjects did not register trauma, and the most frequent traumas were multiple and lower limbs; 25% of subjects with previous hospitalization, 15.9% with medical treatments and less than 10% with surgical history were presented. There was a 45.1% of pulmonary arterial thrombosis (riding thrombus) and in 34.8% thrombi were recorded in segmental pulmonary arteries. 52.4% of the deceased had deep vein thrombosis of the lower limbs and 4.3% of the iliac veins (Table 3).

Table 3. Clinical characteristics of the study population

Clinical characteristics		n	%
Topographic diagnosis	No trauma	87	53,0
	Polytrauma	21	12,8
	Lower limbs	29	17,7
	Chest	15	9,1
	Head	7	4,3
	Pelvis	5	3,0
Hospitalization and treatments	Hospitalization	41	25,0
	Treatments	26	15,9
Recent surgical history	Saphenectomy	4	2,4
	Hip surgery	3	1,8
	Abdominoplastic	3	1,8
	Liposuction	2	1,2
	Mammoplasty	1	0,6
	Bariatric	1	0,6
	Laparoscopic	1	0,6
Thrombosis Characterization	Segmental pulmonary artery thrombosis	57	34,8
	Pulmonary arterial thrombosis	74	45,1
	Deep vein thrombosis	86	52,4
	Right or left artery pulmonary thrombi	32	19,5
	Iliac veins thrombi	7	4,3

Discussion

During the period from January 2008 to December 2020, 46097 medico-legal necropsies were performed at the National Legal Medicine Institute and Forensic Sciences in the city of Medellín, of which only 164 cases (0.36%) corresponded to PTE as the cause of death, which is divergent from previous studies in this field. In a 24 years retrospective study (1972-1995) with 16466 necropsies the frequency of PTE was 4.7%; (14); Alikham et al. in their retrospective study between 1991-2000 reported a frequency of 3.9% in 6833 units (15); Sweet et al. reported that between 2002-2012 of a total of 982 cases, 11% were diagnosed as PTE (16); the Mobilia group between 1999-2009 of 10288 studied 1.25% corresponded to PTE (17).

The results of the previously stated studies are much higher than those found in the present study, however it is important to note that, except for

the Mobilia study at the Legal Medicine Institute of Milan, Italy, the other studies were carried out with information collected from hospitals where clinical autopsies were performed, which explains the high number of presented cases. Therefore, the large number of violent deaths treated in our institution compared to the deaths under study due to sudden death, make the figure seem lower, but in fact it is not because in proportion it is related to the finding of Mobilia et al. In this order of ideas, the fact that in the current study it has been found that 57.9% of the deaths taken to autopsy were sudden deaths whose way of death was natural and 36% with underlying heart disease, allows to explain that PTE, as a cause of death outside of trauma, is relevant in its presentation, which is consistent with what has been pointed out in different studies in clinical autopsies (14-16, 18,19,20).

On the other hand, 13.4% of the deaths found in the present study were related to traffic accidents, while many of the studies consulted grouped trauma as a single concept (17,18), which allows us to observe a common variable in Medellín-Colombia and to be taken into account due to the complications of polytrauma and the presentation of PTE in any of the hospitalization stages..

The average age of the deceased for this study was 57.0 years of age and with a similar proportion of men and women, variables that did not present relevant differences with the studies found (14,15,16,17,18,19) except for the study of Kakkar et al. where their analyzed group had an average age of 47 years (20). None of the previous studies (14,15,16,17, 19, 20) took into account the scenario of the facts for their analysis only in one study was allowed to indicate as intra or extra hospital cases (18), the above was due to the fact that the vast majority of studies were carried out with hospitalized patients, but in the present study because they were sudden deaths with a diagnosis to be established, the figures where housing (47.0%) was the place where more deaths occurred, followed by public roads (25.6%) and hospital centers (9.7%), suggest the relationship between sudden death by PTE and its lethality, besides puts on alert in cases where there was hos-

pitalization to avoid its appearance as a trigger for death, because in many cases patients were discharged without contemplating the diagnosis as a complication.

The surgical history found in the present study, related with the previous studies, are important due to while the surgeries performed for orthopedic or other similar types of trauma are predominant in the cases (14, 15, 17, 18, 21), in Medellín the most referred (although in a low proportion) were related to cosmetic surgeries, which have increased in the last decade in the city and puts in alert to take into account the previous coagulation states of patients and the performance of related examinations such as PT, TPT, D-dimer for example.

Related to patients who required hospitalization (25.0%) in this study, 15.9% received treatment for the prevention of thrombus formation and even with that they die by PTE, which agrees with the studies reviewed (16, 22,23,24,25), this also allows us to suspect that the presence of PTE, even in patients with antithrombolytic therapy, remains a constant or event of high prevalence for which efforts to perform timely management should be increased; at the same time that measures must be increased to reduce its presence, since the existing ones have not been sufficient.

The finding of deep vein thrombosis in the lower limbs was 52.4% very similar to the finding of other authors (25,26); in relation to riding thrombi (located between the right and left pulmonary arteries) the finding was presented in 52.4%, very close to the findings of Golin et al. 68 % (14), and lower than Nakkar et al. 10.69 % (20), and according to the revision made by Ro et al. (25). Therefore, its suspicion and timeliness in diagnosis is of high importance within the management of groups at risk of presenting the complication.

The present study allowed to observe the presentation of PTE through sudden deaths that reached a legal medical necropsy in order to establish a diagnosis of cause of death and therefore it results into a limitation, since it would be important to contrast it with the clinical autopsies carried out in the different hospital centers, a fact that has currently decreased substantially, but that would be of great importance for this type of studies.

«The performance of a greater number of clinical autopsies will reveal the true impact on our environment of this complication and improve the quality of patient care.»

Despite the diagnostic methods present in the arsenal of clinical practice and thromboprophylactic application in hospitalized patients, thromboembolism remains a disease of great lethality and its suspicion must be considered among the risk groups, and it is of high importance to perform autopsies to avoid the final cause of death from being diluted in other pathophysiological disorders and the spectrum of this complex condition be invisible.

Conclusion: PTE is an important cause of death in in-hospital and out-of-hospital patients despite existing diagnostic, pharmacological and non-pharmacological methods for its prevention. The performance of a greater number of clinical autopsies will reveal the true impact on our environment of this complication and improve the quality of patient care.

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