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Epidemiology of Pulmonary Embolism in Apulia from analysis of current data

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ABSTRACT: ***Epidemiology of Pulmonary Embolism in Apulia from analysis of current data. A.M. Moretti, S. Tafuri, D. Parisi, C. Germinario.***

***Background and aims*. Pulmonary embolism (PE) is a relatively common cardiovascular emergency: present evidence suggests that PE is the third most acute cardiovascular disease after cardiac ischemic syndromes and stroke. The aim of this study is to evaluate hospital admissions for PE in the Apulia Region of Italy in the period 2001-2007 through an analysis of the Apulia Region hospital patient discharge database.**

***Methods*. Patients were selected on the basis of admissions between 01/01/2001 and 31/12/2007 with ICD-9-CM code of 415.11 (Iatrogenic pulmonary embolism and infarction) or 415.19 (Other pulmonary embolism and infarction) as principal or secondary diagnosis.**

***Results*. The number of patients selected from the database was 4,303. The raw annual admission data shows an increasing trend from 13.9x100,000 residents in 2001 to 18.9x100,000 residents in 2007. The average patient age was 68.7 years and 59% were females and 41%. There were 470 deaths in hospital (10.9% of patients).**

***Conclusions*. PE is associated with much health care and a substantial economic burden, yet many PE and general venous thromboembolism (VTE) events are preventable. It remains the responsibility of individual hospitals to identify specific areas in which they can improve their VTE prophylaxis rates to obtain positive results from the reporting initiatives and incentive programs.**

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Key words: Pulmonary embolism, Epidemiology, Health information systems, Patient safety.

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Introduction

Pulmonary embolism (PE) is a relatively common cardiovascular emergency: present evidence suggests that PE is the third most acute cardiovascular disease after cardiac ischemic syndromes and stroke [1].

Although PE and deep vein thrombosis (DVT) are two clinical presentations of venous thromboembolism (VTE) and, in most cases, PE is a consequence of DVT, PE has features that are distinct from DVT [2]. The risk of death related to the initial acute episode of recurrent PE is greater in patients diagnosed with PE than in those diagnosed with DVT [3]. According to prospective cohort studies, the acute case fatality rate for PE ranges from 7 to 11% [4].

PE can occur in patients without any identifiable patient-related predisposing factors. In fact, in the International Cooperative Pulmonary Embolism Registry the proportion of patients with idiopathic or unproved PE was about 20%, but it is usual to identify one or more of the predisposing factors which include age, history of previous VTE, active cancer, neurological disease with extremity paresis, medical disorders causing prolonged bed rest, such as heart or acute respiratory failure, and congenital or acquired thrombophilia, hormone replacement therapy and oral contraceptive therapy [5].

In the United States, the prevalence of PE among hospitalised patients, according to data collected between 1979 and 1999 was 0.4%, while 40-53 per 100,000 persons were diagnosed with PE per year [6].

The corresponding figures for Europe are not available, but various surveys have been performed among both hospitalised and non-hospitalised populations. A survey carried out in France in a defined population of 342,000 inhabitants shows the incidence of PE at 60 per 100,000 per year; many of whom had been hospitalized within the previous three months [7].

In Italy, analysis of current hospital admission data gives an estimated new PE incidence rate of 30-33 per 100,000 inhabitants per year [8]. However the diagnosis of PE is difficult and can be missed because of its non specific clinical presentation. Several studies seem to indicate that the real incidence rate is higher than that shown by the data, especially those carried out on deceased patients which have shown that PE is still under-diagnosed in hospitalised patients [9, 10]. An ad-hoc study performed within the Tuscany region of Italy

showed a PE incidence rate of around 100 per 100,000 inhabitants per year [1].

The aim of this study is to evaluate hospital admissions for PE in the Apulia Region of Italy in the period 2001-2007.

Methods

The analysis of hospital admission and in-hospital death was carried out using the Apulia Region hospital patient discharge database for the years 2001-2007, selecting those patients with an ICD-9-CM code of 415.11 (Iatrogenic pulmonary embolism and infarction) or 415.19 (Other pulmonary embolism and infarction) as principal diagnosis or one of the five secondary diagnoses.

Comorbidities of patients with a principal diagnosis of PE were ascertained from the codes recorded in the secondary diagnoses. When PE was a secondary diagnosis, the principal diagnosis was also identified.

Lethality-hospital was calculated as a proportion of deaths of total patients admitted with a diagnosis of pulmonary embolism.

For calculation purposes, the number of residents in Apulia was taken as the population resident at 01/01/2004 (data from the Italian National Statistics Office - ISTAT).

A linear regression model was used to analyse trends and the differences in trends were calculated utilisng the *Chi* square test for trend, with a value of $p<0.05$ considered significant. The analysis was carried out with the statistical software Epi-Info 6.00 (public domain software - CDC Atlanta, Georgia; WHO Geneva, Switzerland).

Results

The hospitals in the Apulia region have 18,844 beds, of which 18,522 are for acute cases. Every year, 870.000 patients were hospitalised in Apulia.

The number of patients with a diagnosis of PE selected from the database was 4,303. The raw annual hospital admission data shows an increasing trend from 13.9 per 100,000 residents in 2001 to 18.9 per 100,000 residents in 2007; this increasing trend was at the limit of statistical significance ($r^2= 0.6$; $p=0.05$; table 1).

For males (41%), the hospitalisation rate per 100,000 increased from 11.2 in 2001 to 15.7 in 2007, while for females (59%) the rate per 100,000 increased from 16.5 to 21.8 in the same period. No significant differences in hospital admission were observed between the sexes (chi-square for linear trend: 0.04; $p=0.83$).

More than half of the patients were over 71 years of age (table 2). The average patient age for the period relating to the study was 68.7 years, with

Table 1. - Number of admissions and raw hospitalisation rates for pulmonary embolism per 100,000 residents. Apulia 2001-2007

Year	Admissions	Raw hospitalization rate per 100.000
2001	563	13.9
2002	559	13.8
2003	621	15.4
2004	549	13.6
2005	622	15.4
2006	626	15.5
2007	763	18.9

Table 2. - Number of admissions and raw hospitalization rates for pulmonary embolism per 100,000 residents by age range and sex. Apulia 2001-2007

Age range	M		F		Total	
	N°	Rate x100.000 residents	N°	Rate x100.000 residents	N°	Rate x100.000 residents
[0-10]	3	1.3	0	–	3	0.7
[11-20]	25	9.8	14	5.8	39	7.9
[21-40]	125	20.5	148	24.1	273	22.3
[41-60]	315	63.7	367	69.8	682	66.8
[61-70]	415	221.7	479	224.5	894	223.2
[71-80]	585	449.5	861	492.4	1446	474.1
[>80]	298	624.8	668	771.8	966	719.6

a progressive and linear increase from 66.5 in 2001 to 70.7 in 2007; (r^2=0.86; p<0.01) (not shown).

Pulmonary embolism was the principal diagnosis in 66.9% (n°=2881) of cases and a secondary diagnosis in 33.1% (n°=1419) of cases (in 3 cases it was both primary and secondary diagnosis and therefore discarded). There were 299 (7%) records with a principal diagnosis of PE with no secondary diagnosis.

The most frequent secondary diagnoses in patients with a primary diagnosis of PE were: diseases of the circulatory system particularly arterial hypertension, cardiac dysrhythmias and phlebitis; diseases of the respiratory system particularly chronic obstructive pulmonary disease; and endocrine disorders (table 3).

In patients with a secondary diagnosis of PE, the most frequent primary diagnoses were: diseases of the circulatory system particularly ischemic heart disease, cardiac dysrhythmias and thrombosis; diseases of the respiratory system particularly chronic obstructive pulmonary disease; neoplasms; injuries particularly fractures (table 4).

Most admissions for pulmonary embolism were in General Medicine (n=1202, 27.9%), Cardiology (n=956, 22,2%), Pneumology (n=492, 11.4%) and Coronary Intensive Care Units (n=479, 11.1%; table 5).

There were 470 in-hospital deaths (10.9% of patients) during the period under study, with an average age of 73.5 years; 195 (41.5%) were males and 275 (58.5%) females. There is a rising trend in the number of in-hospital deaths per year (figure 1).

Most in-hospital deaths occurred in patients admitted to General Medicine (21.9%, n=103), Intensive Care (21.1%, n=99) and Coronary Intensive Care Units (15.1%, n=71) (table 6). Lethality was highest in Intensive Care, Neurology, Cardiac Surgical ward and Pediatric Nephrology. In the period studied, the last 2 wards had 5 and 1 patients with a PE diagnosis (table 6).

Table 3. - Secondary diagnoses of patients with a primary diagnosis of pulmonary embolism. Apulia 2001-2007

Diagnosis	**N°**
Infectious and parasitic diseases	82
Neoplasms	285
Endocrine, nutritional and metabolic diseases, and immunity disorders	691
Disorders of thyroid gland	*90*
Diseases of the blood and blood-forming organs	155
Mental disorders	57
Diseases of the nervous system and sense organs	106
Diseases of the circulatory system	3245
Arterial hypertension	*908*
Cardiac dysrhythmias	*490*
Phlebitis and thrombophlebitis	*465*
Ischemic heart disease	*264*
Embolism and thrombosis	*217*
Heart failure	*162*
Diseases of arteries, arterioles, and capillaries	*123*
Diseases of pulmonary circulation	*111*
Diseases of the respiratory system	906
Chronic obstructive pulmonary disease	*447*
Diseases of the digestive system	220
Diseases of the genitourinary system	259
Complications of pregnancy, childbirth, and the puerperium	6
Diseases of the skin and subcutaneous tissue	31
Diseases of the musculoskeletal system and connective tissue	103
Congenital anomalies	14
Symptoms, signs, and ill-defined conditions	202
Injury and poisoning	154
Fracture	*113*
Factors influencing health status and contact with health services	235

Discussion

With a lack of standardised tools to evaluate pulmonary embolism, hospitalisation records can be useful for epidemiologic analysis. The records are systematically compiled by medical personnel and are subject to quality controls at various levels (hospital trust, regional, ministerial), however they are also dependent on the quality of the diagnosis and its coding. Clinical signs and symptoms allow the physician to formulate only a pre-test probability of a patient having pulmonary embolism (the clinical probability), they are insufficient in themselves to either diagnose or rule out the condition [11]. Laboratory testing and imaging are thus required in all patients with suspected pulmonary embolism [12] but there are a large number of diagnostic tests and strategies available, with varying diagnostic value. Ventilation perfusion lung scan, spiral computed tomography and ultrasonography of leg veins have shown positive likelihood ratios for confirmation of PE [13], but hospital patient discharge records do not show which diagnostic tests have been carried out and consequently we cannot be sure of a correspondence between the diagnosis and the diagnostic algorithms recommended by the guidelines [14].

Hospital admission rates in Apulia seem to be lower than those found in surveys carried out in the USA [6] and in France [7]. The present study shows an increasing trend in hospitalisation for this pathology. This, together with a strategic regional policy of reducing hospital admissions, is indicative of a real increase in its incidence.

Table 4. - Primary diagnosis of patients with a secondary diagnosis of pulmonary embolism. Apulia 2001-2007

Diagnosis	**N°**
Infectious and parasitic diseases	14
Neoplasms	187
Endocrine, nutritional and metabolic diseases, and immunity disorders	15
Diseases of the blood and blood-forming organs	17
Mental disorders	5
Diseases of the nervous system and sense organs	27
Diseases of the circulatory system	373
Ischemic Heart Disease	*50*
Cardiac dysrhythmias	*52*
Thrombosis	*19*
Diseases of the respiratory system	260
Diseases of the digestive system	86
Diseases of the genitourinary system	44
Complications of pregnancy, childbirth, and the puerperium	8
Diseases of the skin and subcutaneous tissue	3
Diseases of the musculoskeletal system and connective tissue	69
Congenital anomalies	3
Symptoms, signs, and ill-defined conditions	113
Injury and poisoning	172
Fracture	*144*
Factors influencing health status and contact with health service	23

Table 5. - Discharge ward for patients admitted with pulmonary embolism. Apulia 2001-2007

Discharge ward	**N°**	**%**
General Medicine	1202	27.9
Cardiology	956	22.2
Pneumology	492	11.4
Coronary Intensive Care	479	11.1
Geriatrics	218	5.1
Orthopedics trauma ward	173	4.0
Intensive Care	132	3.1
General surgery	129	3
Long stay	101	2.3
Physical medicine and rehabilitation	65	1.5
Neurology	60	1.4
Vascular surgery	41	0.9
Infectious disease	40	0.9
Urology	32	0.7
Nephrology	30	0.7
Neurosurgery	25	0.6
Hematology	23	0.5
Obstetrics and gynecology	20	0.5
Oncology	20	0.5
Chest surgery	17	0.4
Endocrinology	10	0.2
Gastroenterology	8	0.2
Radiotherapy	7	0.2
Ear nose and throat	5	0.1
Cardiac Surgical ward	4	0.1
Dentistry	3	0.1
Psychiatry	3	0.1
Pediatrics	2	0.05
Oncologic radiotherapy	2	0.05
Plastic surgery	1	0.02
Ophthalmology	1	0.02
Dermatology	1	0.02
Pediatric nephrology	1	0.02

The low admission rate demonstrated in the Apulia Region could be related to the lack of awareness of the disease, which can be the cause of the low number of admissions and the level of misdiagnosis. It is very important to consider the diagnosis if there is any suspicion of pulmonary embolism. Prompt diagnosis and treatment can dramatically reduce the morbidity and mortality of the disease. Unfortunately, the diagnosis is often missed, because pulmonary embolism frequently causes only vague and non-specific symptoms. Failure to identify pulmonary embolism due to lack of diagnosis remains the last major problem confronting successful detection of pulmonary embolism. If the healthcare providers, patient, and family are not aware of the risk factors and common clinical presentations of pulmonary embolism, the diagnosis will be overlooked. More widespread education of practitioners and the pub-

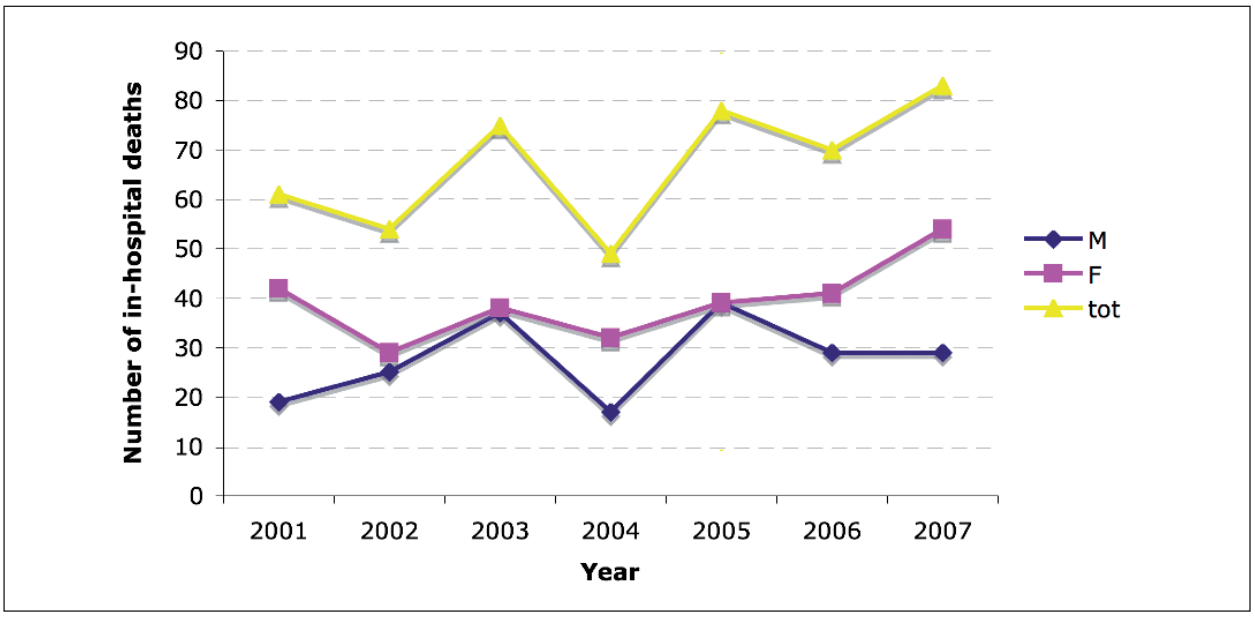

Fig. 1. - Number of in-hospital deaths for patients admitted with pulmonary embolism by sex and year of death. Apulia 2001-2007.

lic about the potentially vague presentation of pulmonary embolism will raise awareness, improve vigilance, and result in fewer missed cases of this potentially fatal illness [15]. Hospital directors should improve the adoption of clinical protocols, especially in emergency care, to ensure correct assessment and management of the patient with suspect PE.

Patients who develop PE have frequent comorbidities. In a third of the cases evaluated, PE was a secondary diagnosis, however the discharge records do not allow us to ascertain whether the pathology was present at admission or if it arose later, also due to exposure of risk factors linked to hospitalisation. Additionally, an important proportion (7%) of the records had no reported comorbidity, which can indicate the limitations of the recording system. These limitations and the high lethality of the pathology demonstrate the need to reinforce the risk assessment and management of the hospitalised patient and to adopt suitable primary and secondary prophylaxis protocols. Currently, three such protocols have been validated in a sufficient number of patients to be of clear utility: the Canadian, or Wells, score [16], the revised Genova score [17], and the PISA-PED score [18]. All these rules have potential pitfalls, and none is currently considered clearly better than the others. This situation has brought a certain lack of confidence in the application of this rigorous approach, likely limiting its use in clinical practice. Furthermore, the continuous attempts to modify, improve and simplify these scores make it difficult to complete and compare the prospective validation studies that are much needed for a widespread diffusion of this approach [19].

PE is associated with a substantial healthcare and economic burden, yet many PE and VTE in general events are preventable. Despite the availability of evidence-based guidelines detailing effective thromboprophylaxis strategies, the underuse and inappropriate prescribing of VTE prophylaxis is common. It remains the responsibility of individual hospitals to identify specific areas in which they can improve their VTE prophylaxis rates to obtain positive results from the reporting initiatives and incentive programs. If performance measures are to be met, all hospital departments will need to implement effective VTE prevention policies, including early risk assessment, appropriate prophylaxis prescribing, monitoring, and follow-up. Multifaceted, integrated initiatives involving risk assessment tools, decision support, electronic alert systems, and hospital-wide education, with a mechanism for audit and feedback, may help ensure that all healthcare professionals comply with VTE-prevention policies and initiatives [20].

In fact, the *Commission on Accreditation of Healthcare Organizations* considers the frequency of thromboembolic episodes in hospitalised patients an important safety indicator [21, 22].

The wide range of hospital wards where patients in the study have been treated, with eighty percent in four different wards (General medicine, Cardiology, Pneumology, Coronary Intensive Care Units) and the other twenty percent found in a grand variety of medical and surgical wards, allows us to see that the approach towards the pathology is not homogeneous, which could possibly cause a reduction in the levels of the appropriateness of treatment and patient safety, especially in as much as there is no defined protocol at hospital or regional level.

The Apulia Region hospital patient discharge database does not allow access either to the assessment procedures or to the prophylaxis protocols adopted, so no evaluation can be made of their appropriateness. Such an evaluation would require examination of the patients case notes which would be impracticable for epidemiological purposes.

Table 6. - Number of in-hospital deaths and lethality in patients admitted for pulmonary embolism by discharge ward. Apulia 2001-2007

Ward	N°	% of total deaths	Lethality (%)
General Medicine	103	21.9	8.6
Intensive Care	99	21.1	75
Coronary Intensive Care	71	15.1	14.8
Pneumology	29	6.2	5.9
Geriatrics	25	5.3	11.5
Cardiology	23	4.9	2.4
General surgery	23	4.9	17.8
Orthopedics trauma ward	22	4.7	12.7
Neurology	19	4	31.7
Long stay	15	3.2	14.9
Infectious disease	7	1.5	17.5
Neurosurgery	7	1.5	28
Nephrology	5	1.1	16.7
Cardiac Surgical ward	4	0.9	100
Physical medicine and rehabilitation	4	0.9	6.2
Hematology	3	0.6	13
Oncology	3	0.6	15
Urology	3	0.6	9.4
Vascular surgery	1	0.2	2.4
Dermatology	1	0.2	100
Endocrinology	1	0.2	10
Pediatric nephrology	1	0.2	100
Obstetrics and gynecology	1	0.2	5

There is the need, within the regional health service, to adopt the monitoring of thromboembolic episodes to record risk factors, the risk class, the diagnostic procedures carried out and the treatment plans and so these can be integrated with the existing information channels.

Such monitoring and recording would give support to healthcare staff and allow the hospital management to evaluate the appropriateness and safety of the treatments. When adjusted for risk class and comorbidity, events such as "thromboembolic complications" and "in-hospital death due to thromboembolic complications", within the different clinical settings, could be properly evaluated against the quality of care given to determine which is best in class and which needs corrective intervention. Without this information, simple indicators such as frequency of events and lethality are limited in scope, not being able to take into consideration the case-mix within the hospital structure, so limiting the usefulness of the information here reported.

Clearly, the discharge database cannot give any information of incidence or death from pulmonary embolism which arise after hospital discharge of a patient. Such information can be obtained only through the adoption and upkeep of suitable information systems such as patient-files at primary care level and their data integration with the activities within secondary care.

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