REGISTRY OF PATIENTS HOSPITALIZED WITH PULMONARY EMBOLISM

Thesis
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List of Abbreviations

anti-Xa .....Anti-factor Xa activity

aPTT .....Activated partial thromboplastin time

BNP .....Brain natriuretic peptide

CI .....Confidence interval

CT .....Computed tomography

CTEPH .....Chronic thromboembolic pulmonary hypertension

CTPH .....Chronic thromboembolic pulmonary hypertension CTPH

CUS .....Compression venous ultrasonography

DVT.....Deep venous thrombosis

ECG .....Electrocardiogram

HIT .....Heparin-induced thrombocytopenia

ICOPER .....International Cooperative Pulmonary Embolism Registry

INR .....International normalized ratio

IVC.....Inferior vena cava

LMWH .....Low molecular weight heparin

LV .....Left ventricle

MDCT .....Multi-detector computed tomography

MI .....Myocardial infarction

NPV .....Negative predictive value

NT-proBNP N-terminal proBNP

OR .....Odds ratio

PaO_2 .....Arterial oxygen pressure

PE .....Pulmonary embolism

PIOPED .....Prospective Investigation On Pulmonary Embolism Diagnosis study

PPV.....Positive predictive value

RV .....Right ventricle

RVSP .....Right ventricular systolic pressure RVSP

UFH.....Unfractionated heparin

V/Q scan .....Ventilation–perfusion scintigraphy

VKA .....Vitamin K antagonist

VT .....Venous thrombosis

VTE.....Venous thromboembolism

Introduction

Pulmonary embolism (PE) is known to be a major cause of death in patients with venous thrombo-embolism. Yet in cohort studies, randomized clinical trials, and general reviews on this topic, the incidence of fatal PE varied from ١% to ٧%. This variability, mainly related to the type of patients studied, highlights that venous thromboembolism is a heterogeneous disease with various presentations and prognoses. *(Wells et al ٢٠٠٥)*

The key to appropriate therapy is therefore risk stratification to identify patients at high risk of death who should receive specific therapeutic management. This step is all the more important in that the use of generally recommended treatments, such as administration of fibrinolytic drugs or placement of vena cava filters in high-risk patients may be complicated by severe adverse events. However, to date, the clinical variables indicating a high risk of fatal PE in patients with venous thromboembolism remain largely unknown. *(Goldhaber et al., ٢٠٠٤)*

Acute pulmonary embolism is a major cause of complications and death associated with surgery, injury, and medical illnesses, and it may occur after long-distance air travel. Venous thromboembolism is responsible for up to ١٥% of all in-hospital deaths, and it also accounts for ٢٠ to ٣٠% of deaths associated with pregnancy and delivery in the United States and Europe. Overall, the annual incidence of pulmonary embolism has been reported to range between ٢٣ and ٦٩ cases per ١٠٠,٠٠٠ population. *(Silverstein et al., ١٩٩٨)*

Case fatality rates vary widely depending on the severity of the disease *(Kasper et al., ١٩٩٧)*; at an average case fatality rate within ٢ weeks of diagnosis of approximately ١١%, the Surgeon General estimates that venous thromboembolism accounts for at least ١٠٠,٠٠٠ deaths each year. *(Goldhaber et al., ٢٠٠٤)*

Pulmonary embolism is a commonly encountered disorder, usually precipitated by deep venous thrombosis, and is associated with significant morbidity and mortality. It accounts for ١٠% of all deaths in hospital, and is a major contributing factor in a further ١٠%. *(Linblad et al., ١٩٩١)* It can result in

pulmonary hypertension and right ventricular dysfunction, and its mortality rate of approximately ١٤%, *(Wessler et al., ١٩٨٦)* has changed little over the last ٣٠ years. *(Linblad et al., ١٩٩١)*

Recognized venous thromboembolism (pulmonary embolism and deep venous thrombosis) is responsible for more than ٢٥٠,٠٠٠ hospitalizations and approximately ٥٠,٠٠٠ deaths per year in the United States.

Because it is difficult to diagnose, the true incidence of pulmonary embolism is unknown, but it is estimated that approximately ٦٥٠,٠٠٠ cases occur annually*. (Wolfe et al., ١٩٩٨)*

Despite this high incidence, the diagnosis of pulmonary embolism continues to be difficult primarily because of the notorious vagaries of symptoms and signs in its presentation. *(Manolis et al., ١٩٩٠)*

Most patients who succumb to pulmonary embolism do so within the first few hours of the event. In patients who survive, recurrent embolism and death can be prevented with prompt diagnosis and therapy. Unfortunately, the diagnosis is often missed because

patients with pulmonary embolism present with nonspecific signs and symptoms. If left untreated, approximately one third of patients who survive an initial pulmonary embolism die from a subsequent embolic episode. *(Burge et al., ٢٠٠٨)*

The most important conceptual advance regarding pulmonary embolism over the last several decades has been the realization that pulmonary embolism is not a disease; rather, pulmonary embolism is a complication of venous thromboembolism, most commonly deep venous thrombosis (DVT). Virtually every physician who is involved in patient care (eg, internist, family physician, orthopedic surgeon, gynecologic surgeon, urologic surgeon, pulmonary subspecialist, cardiologist) encounters patients who are at risk for venous thromboembolism, and therefore at risk for pulmonary embolism. *(Kuklina et al. ٢٠٠٩)*

Aim of Work

Aim of this registry is to follow-up and assess a broad sample of patients hospitalized with confirmed or high clinical probability of pulmonary embolism regarding risk factors, clinical presentation, diagnosis, management and outcome.

Historical Perspective

In ١٨٤٦, Rudolf Virchow, then ٣٥ years old, described the triad of stasis, vessel wall injury, and hypercoagulability and its association with the development of venous thrombosis. **(Figure ١)** This association is perhaps one of the most enduring themes in medicine. Every scenario recognized to date that can be considered a risk factor for this disease is derived from this triad. The presence of risk factors may lead to suspicion of the presence of deep venous thrombosis (DVT) or pulmonary embolism, collectively referred to as venous thromboembolism (VTE), as well as being critical in determining appropriate prophylaxis among patients at risk.

In ١٨٨٠, Beniamino Luzzatto described at least ١٦٠ cases of PE in a manuscript entitled “Embolism of the Pulmonary Artery”, in which he emphasized the predilection for the lower lobes and the predisposing role of stasis and preexisting cardiopulmonary disease.