Contents lists available at ScienceDirect

Acta Haematologica Polonica

journal homepage: www.elsevier.com/locate/achaem

Original research article/Praca oryginalna

Concomitant history of cancer in acute pulmonary embolism is connected with poorer outcome

Karsten Keller [1,2,*], *Martin Geyer* [1], *Johannes Beule* [3], *Meike Coldewey* [1,2], *Jörn Oliver Balzer* [4,5], *Wolfgang Dippold* [3]

[1] *Department of Medicine II, University Medical Center Mainz (Johannes Gutenberg-University Mainz) (Medical Director: University-Prof. Dr. med. T. Münzel), Mainz, Germany*

[2] *Center for Thrombosis and Hemostasis, University Medical Center Mainz (Johannes Gutenberg-University Mainz) (Medical Director: University-Prof. Dr. med. U. Walter), Mainz, Germany*

[3] *Department of Internal Medicine, St. Vincenz and Elisabeth Hospital Mainz (KKM) (Medical Director: Prof. Dr. med. W. Dippold), Mainz, Germany*

[4] *Department of Radiology and Nuclear Medicine, Catholic Clinic Mainz (KKM) (Medical Director: Prof. Dr. med. J.O. Balzer), Mainz, Germany*

[5] *Department of Diagnostic and Interventional Radiology, University Clinic, Johann Wolfgang Goethe-University Frankfurt/Main, Germany*

ARTICLE INFO

Article history:
Received: 06.04.2015
Accepted: 28.08.2015
Available online: 07.09.2015

Keywords:
- Cancer
- Risk stratification
- Pulmonary embolism
- Right ventricular dysfunction
- Right ventricular failure
- Cardiac troponin

ABSTRACT

Purpose: Cancer increases the risk of venous thromboembolism (VTE) substantially. VTE is connected with poorer outcome in cancer patients. The aim of our study was to investigate the impact of cancer on the severity and short-term outcome of pulmonary embolism (PE). **Methods:** We retrospectively analyzed the data of 182 patients with confirmed PE. PE patients were subdivided in the group with concomitant active cancer disease or history of cancer or in the group without cancer. Groups were compared with Wilcoxon–Mann–Whitney Test. Logistic regression models were calculated to investigate the association between cancer and several parameters such as age and PE severity status as well as the association between in-hospital death and the parameters age, gender, PE severity status and cancer. **Results:** While 20.3% PE patients reported an active cancer disease or a history of cancer (64.9% female), 79.7% of the PE patients did not (60.7% female). PE patients with cancer were 5 years older (76.0 (65.5/81.0) vs. 71.0 (58.5/80.5) years, $P = 0.055$) and revealed a higher PE severity status in mean (1.91 ± 0.53 vs. 1.67 ± 0.54, $P = 0.069$). Univariate logistic regression models showed an association between cancer and age (OR 1.04, CI 95% (1.01–1.08), $P = 0.017$) as well as cancer and the severity status (OR 2.38 (1.05–5.26), $P = 0.037$). In-hospital death in the early course was strongly

* *Corresponding author at*: Department of Medicine II, University Medical Center Mainz Johannes Gutenberg-University Mainz, Langenbeckstr. 1, 55131 Mainz, Germany. Tel.: +49 6131 17 2995; fax: +49 6131 17 6613.
E-mail address: Karsten.Keller@unimedizin-mainz.de (K. Keller).

Abbreviations: AHA, American Heart Association; cTnI, cardiac Troponin I; CT, computed tomography; CTEPH, chronic thromboembolic pulmonary hypertension; DVT, deep vein thrombosis; ECG, electrocardiography; ESC, European Society of Cardiology; PE, pulmonary embolism; RBBB, right bundle-branch block; RV, right ventricle; RVD, right ventricular dysfunction; RVF, right ventricular failure; SAE, serious adverse event; SD, standard deviation; sPAP, systolic pulmonary artery pressure; V/Q scan, ventilation–perfusion scan.

http://dx.doi.org/10.1016/j.achaem.2015.08.002

connected with the PE severity status (OR 36.60 (2.99–448.68), $P = 0.0049$), but not with cancer ($P = 0.65$). **Conclusions:** Concomitant history of cancer in acute PE was associated with higher PE severity status and therefore poorer outcome.

Introduction

Cancer increases the risk of venous thromboembolism (VTE = pulmonary embolism (PE) + deep vein thrombosis (DVT)) substantially [1, 2]. Patients with cancer reveal a 4- to 7-fold higher risk to develop a venous thromboembolic event in comparison to those patients without cancer [2–6]. The association between cancer and VTE is well known for a long time. As long ago as in the 19th century Armand Trousseau first described an association between cancer and venous thrombotic events [2, 6, 7].

Besides the higher risk to develop a VTE, VTE in patients with cancer is connected with poorer outcome and shorter survival [2, 3, 8–15]. VTE is – besides the cancer itself – the second leading cause of death in patients with cancer [2]. However, most of the studies do not differentiate between PE and DVT, but investigate VTE in general.

The aim of our study was to investigate the impact of cancer on the severity status of PE and on in-hospital death of the PE patients.

Methods

Study design

We performed a retrospective analysis of all patients with a confirmed diagnosis of acute PE, who were treated at the internal medicine department between May 2006 and June 2011. Medical records of 182 consecutive PE patients were reviewed for medical history (symptoms and history), examinations (transthoracic 2D-echocardiography, CT, V/Q-scan, Doppler ultrasound of the leg veins) and laboratory parameters.

In studies with retrospective analysis of diagnostic standard data no ethic statement is needed in Germany.

Enrolled subjects

Patients were eligible for our study if they were at least 18 years old, treated in the internal medicine department of the hospital and had a confirmed acute PE. The patients were identified by performing a search on the hospital information system database for the diagnostic code of PE (ICD-10-Code I26).

Confirmation of PE was defined if the patient had one of the following criteria:

1. Computed tomography (CT) pulmonary angiogram of the chest with an identified filling defect in the pulmonary artery system.
2. Positive venous ultrasound of an extremity consistent with DVT in patients with typical symptoms of PE (chest pain or dyspnea) and positive D-dimer.
3. Scintigraphic ventilation–perfusion (V/Q) scan read as high probability for PE.

All of the radiographic images were analyzed by experienced radiologists. If the diagnosis of PE was not confirmed by these criteria, then the patients were not included in this study.

Study groups

In this study, PE patients were subdivided into 2 groups:

1. **PE + cancer** group with PE patients with concomitant active cancer disease or a history of cancer. We did not differentiate types of cancer.
2. **PE − cancer** group without concomitant cancer or history of cancer.

Laboratory examinations

We focused for laboratory examinations on the levels of cardiac Troponin I (cTnI), CK, creatinine and D-dimer. A myocardial necrosis was defined as an elevation of cTnI value >0.1 ng/ml. D-dimer measurements were performed using an enzyme linked immunosorbent assay. D-dimer elevation was defined as a D-dimer value of >0.110 mg/l.

Severity status of PE

The PE severity status was defined according to the European Society of Cardiology (ESC) guidelines and AHA scientific statement [16, 17]. PE patients with a systolic blood pressure of <90 mmHg were classified as high-risk PE patients (massive PE = PE status 3 in statistical calculation) [16, 17]. Normotensive PE patients were included in the non-high-risk PE patient group [17]. Further classification of hemodynamic stable patients was made according to the RVD and the biomarker levels (especially cTnI) [17].

RVD was defined according to the AHA scientific statement [16] as a right ventricular (RV) septal–lateral diameter in 4 chamber view in a CT or echocardiography divided by a left ventricular (LV) septal–lateral diameter >0.9 [16]. Moreover, the RVD was defined as RV hypokinesis and tricuspid regurgitation in echocardiography [16]. Pulmonary artery pressure was measured as systolic pulmonary artery pressure (sPAP) in a 4-chamber view of transthoracic echocardiography.

Normotensive PE patients (non-high-risk PE patients) were classified as patients with intermediate risk due to existing RVD or positive biomarker levels as cTnI (submassive PE = PE status 2 in statistical calculation), and PE patients with low