Contemporary Management and Clinical Course of Acute Pulmonary Embolism: The COPE Study

Cecilia Becattini[1]   Giancarlo Agnelli[1]   Aldo P. Maggioni[2]   Francesco Dentali[3]   Andrea Fabbri[4]
Iolanda Enea[5]   Fulvio Pomero[6]   Maria Pia Ruggieri[7]   Andrea di Lenarda[8]   Ludovica Anna Cimini[1]
Giuseppe Pepe[9]   Susanna Cozzio[10]   Donata Lucci[2]   Michele M. Gulizia[2,11] on behalf of COPE
Investigators*

Background

- Acute pulmonary embolism (PE) is a common and potentially fatal disease associated with substantial burden to the health systems.

- Mortality in patients with acute PE varies based on patients' features and severity of disease at presentation.

- In this scenario, international scientific societies endorsed evidence-based strategies for the management of patients with acute PE.

- Currently available data on the initial management and early course of the PE in clinical practice rely on studies conducted more than 10 years ago or including both patients with PE and patients with deep vein thrombosis.

AIM of the study

- To assess contemporary management strategies in terms of diagnosis, risk stratification, disposition, treatment and the short-term clinical course in patients with acute confirmed PE.

Methods

- The COntemporary management of PE (COPE) is a prospective, multicenter study of adult patients with acute, symptomatic, objectively diagnosed PE.

- Patients aged 18 years old or older with symptomatic objectively confirmed PE were included in the study after release of informed consent.

- Patients were evaluated at the time of diagnosis, at discharge, and at 30 days from the index PE.

- Patients were stratified in risk for death categories as defined by European Society of Cardiology (ESC) guidelines based on clinical data, imaging, and laboratory results.

- The co-primary outcomes of the study were in-hospital death and 30-day death.

- The safety outcome was major bleeding according to International Society on Thrombosis and Haemostasis criteria, occurring up to 30 days from the index PE.

Results (I)

- Overall, 5,213 patients were included in the study; follow-up at 30 days was available in 5,203 patients (99.8%).

- The mean age of study patients was 70±16 years; active cancer was reported in 832 patients (16.8%), surgery or trauma was reported in less than 10% each, while the prevalence of bed rest longer than 3 days in the previous 4 weeks was 21.9%.

- In-hospital, 5,158 (99%) patients received anticoagulant treatment. During the hospital stay, 5.5% received reperfusion therapy. At discharge, 75.6 and 6.7% of patients received a direct oral anticoagulant (DOAC) or a vitamin K antagonist (VKA), respectively.

**Table 3** Anticoagulant treatment during hospital stay and at discharge

Anticoagulant treatment during hospital stay	Total population (n = 5,213)	Anticoagulant treatment at discharge	Patients discharged alive within 30 days (n = 4,786)
UFH, n (%)	1,228 (23.6)	UFH, n (%)	20 (0.4)
LMWH, n (%)	2,758 (52.9)	LMWH, n (%)	567 (11.9)
Fondaparinux, n (%)	1,424 (27.3)	Fondaparinux, n (%)	320 (6.7)
At least 1 parenteral anticoagulant, n (%)	4,801 (92.1)	*At least 1 parenteral anticoagulant, n (%)*	906 (18.9)
VKAs	280 (5.4)	VKAs	319 (6.7)
DOACs	2,597 (49.8)	DOACs	3,617 (75.6)
At least 1 oral anticoagulant, n (%)	2,860 (54.9)	*At least 1 oral anticoagulant, n (%)*	3,936 (82.2)
At least 1 anticoagulant, n (%)	5,158 (98.9)	*At least 1 anticoagulant, n (%)*	4,748 (99.2)
Contraindication for AC, n (%)	105 (2.0)	–	
Vena cava filter, n (%)	51 (1.0)	Vena cava filter, n (%)	22 (0.5)

Abbreviations: AC, anticoagulation; DOAC, direct oral anticoagulant; LMWH, low-molecular-weight heparin; UFH, unfractionated heparin; VKA, vitamin K antagonist.

Results (II)

- Out of 4,885 patients admitted to the emergency department due to acute PE, 1.2% were discharged from the emergency department, 5.8% were managed by early discharge (usually within 48 hours), and 93.0% by standard hospitalization.

- The overall crude in-hospital mortality was 3.4%; the main cause for in-hospital death was PE (49%); mortality at 30 days was 4.8%.

- After categorization of the patients by risk of death according to the ESC guidelines 2014, in-hospital death occurred in 20.3% of 177 high-risk patients (HR: 28.1, 95% CI: 13.0–60.6), in 4.0% of the 3,281 intermediate-risk (HR: 6.4, 95% CI: 3.1–13.0), and in 0.5% of 1,702 low-risk patients.

- Death at 30 days occurred in 22.6% high-risk (HR: 51.7, 95% CI: 25.1–106.5), 6.0% intermediate-risk (HR: 11.7, 95% CI: 6.0–22.8), and 0.5% low-risk patients, respectively.

Kaplan–Meier curve for time to all-cause death by category of risk according to ESC guidelines 2014
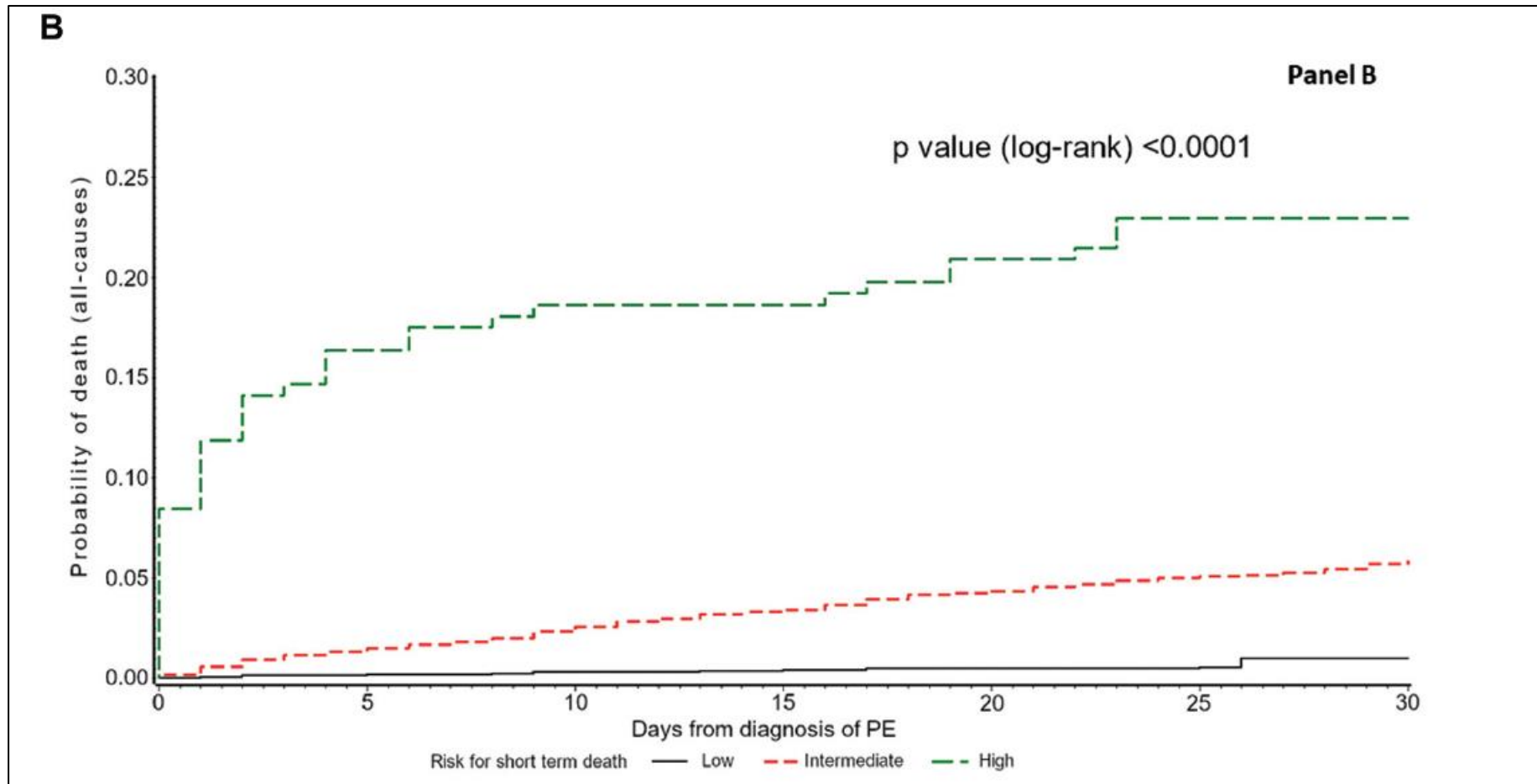
Results (III)

- Among intermediate-risk patients, the subgroup of those with sPESI>0, no RVD, and normal troponin (intermediate very low risk) had significantly lower mortality at 30 days compared to those with sPESI >0 and one among RVD or increased troponin and numerically but not significantly lower compared to intermediate-high risk patients (sPESI >0, RVD, and increased troponin).

- No difference emerged between intermediate-low and intermediate-high risk patients.

Kaplan–Meier curve for time to all-cause death with further categorization of intermediate-risk patients
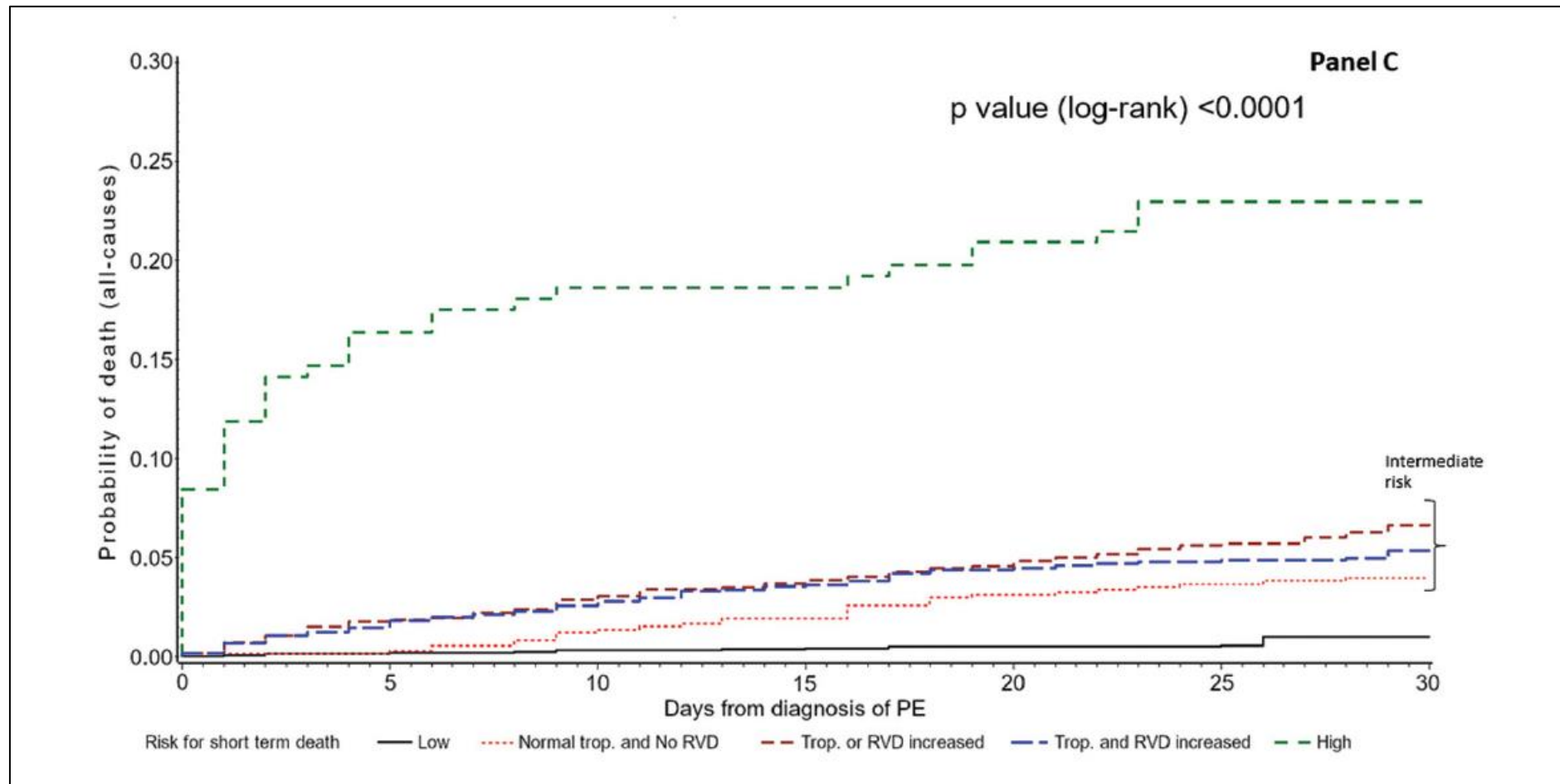
Conclusions

- This contemporary study, the largest registry ever specifically dedicated to patients with acute symptomatic PE, shows that these patients continue to require substantial resource commitment in the acute phase.

- Mortality remains elevated in patients classified at high or intermediate risk for death.

- Almost all patients with acute PE are admitted to the hospital and receive risk stratification assessments and prompt anticoagulation

- Direct anticoagulants are the most commonly used anticoagulants after discharge, while acute treatment includes parenteral anticoagulants in almost all patients.

- Identification of patients at very low risk of death using the model proposed by ESC guidelines can be clinically relevant (although not statistically significant) when the goal is safe discharge from the emergency department.

- Further studies are required to refine risk stratification in intermediate- risk patients.