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ORIGINAL PAPER

Acute pulmonary embolism and cancer: findings from the COPE study

Cecilia Becattini[1] · Ludovica Anna Cimini[1] · Giorgio Bassanelli[2] · Aldo P. Maggioni[3] · Fulvio Pomero[4] · Ilaria Lobascio[5] · Iolanda Enea[6] · Daniela P. Pomata[7] · Maria Pia Ruggieri[8] · Beniamino Zalunardo[9] · Anna Novelli[10] · Stefania Angela Di Fusco[11] · Marco Triggiani[12] · Marco Marzolo[13] · Chiara Fioravanti[14] · Giancarlo Agnelli[1] · Lucio Gonzini[3] · Michele M. Gulizia[3,15] · on behalf of COPE Investigators

Background

- Venous thromboembolism (VTE), presenting either as deep vein thrombosis or pulmonary embolism (PE), is a common event in patients with cancer.
- In comparison to non-cancer patients, patients with cancer and VTE have an increased risk of recurrent VTE and major bleeding during anticoagulant treatment.
- For these reasons, the management of VTE in cancer patients is challenging and dedicated clinical studies have been conducted in this specific setting.
- However, the majority of the available evidence deals with the long-term phase or excludes specific groups of cancer patients and only limited data on the contemporary initial management and course of the disease in cancer patients with acute VTE are available.

AIM of the study

- To describe the clinical features, contemporary management, and short-term course of patients with acute PE, by the presence of active cancer, previous cancer, or no cancer.

Methods

- Data from patients enrolled in the COPE study.
- The COPE study is a prospective, multicentre cohort study of adult patients with acute, symptomatic, objectively diagnosed PE.
- Patients were evaluated at the time of diagnosis, at discharge, and at 30 days (±4) from the index PE.
- The co-primary outcomes of the study were in-hospital death and death at 30 days.
- The primary safety outcome was major bleeding according to ISTH criteria, occurring up to 30 days from the index PE.

Results (I)

- Data on cancer were available in 4956 out of 5213 patients included in the COPE study (95.1%); of these patients, 832 (16.8%), 464 (9.4%), and 3660 (73.8%) were classified as having active cancer, previous cancer, or no cancer, respectively.
- Patients with previous cancer were older than patients with active cancer or no cancer, with a higher proportion of patients aged over 80 years.
- Patients with active cancer had higher prevalence of recent surgery (surgery 8.5% vs. 4.3% vs. 6.7%) or recent hospitalization (17.2% vs. 13.2% vs. 13.3%) and lower prevalence of recent trauma (2.3% vs. 4.7% vs. 8.9%) and previous VTE (13.2% vs. 18.5% vs. 17.5%) compared to patients with previous cancer and to patients with no cancer.

Results (II)

- Patients with active cancer had about threefold higher prevalence of severe anemia at admission (17.8% vs. 6.1% vs. 6.1%) in comparison to other patient groups.
- Active cancer was associated with higher prevalence of contraindications for anticoagulation.
- The most prevalent primary sites of active cancer were urogenital (23.0%), gastrointestinal (21.0%), and lung (19.8%), with a high prevalence of patients with metastatic disease (57.6%) and on ongoing anticancer therapy.
- In almost all patients, the diagnosis of PE was obtained by computed tomography pulmonary angiogram.
- Patients with active cancer more frequently had the most proximal localization of PE at the segmental level and less commonly isolated subsegmental localization compared to patients with previous cancer and without cancer.

Results (III)

- According to ESC guidelines, the prevalence of intermediate–low-risk patients was about doubled among patients with active cancer in comparison to those with previous cancer or without cancer.
- During hospitalization, a lower proportion of patients with active cancer received oral anticoagulants in comparison to patients with previous cancer or no cancer.
- At discharge, 43.1% of patients with active cancer, 78.8% of those with previous cancer and 82.0% of those without cancer received a DOAC for the treatment of PE.

Results (IV)

- Rates of death in-hospital and at 30 days were higher in patients with active cancer compared to patients with previous cancer and no cancer.
- Major bleeding occurred in a higher proportion of patients with active cancer in comparison to those with previous cancer or without cancer, both during the in-hospital phase and at 30 days.
- Among patients with active cancer, lung or metastatic cancer were independent predictors of death; brain, hematological or gastrointestinal cancer had the highest risk of major bleeding.

Table 4 Clinical outcome by cancer status

	Total population ($n=4956$)	Cancer status			P
		Active ($n=832$)	Previous ($n=464$)	No cancer ($n=3660$)	
In-hospital death, n (%)	168 (3.4)	66 (7.9)	20 (4.3)	82 (2.2)	<0.0001
Death at 30 days, n (%)	235 (4.7)	115 (13.8)	24 (5.2)	96 (2.6)	<0.0001
In-hospital major bleeding, n (%)	131 (2.6)	35 (4.2)	10 (2.2)	86 (2.4)	0.008
Major bleeding at 30 days, n (%)	147 (3.0)	40 (4.8)	12 (2.6)	95 (2.4)	0.003

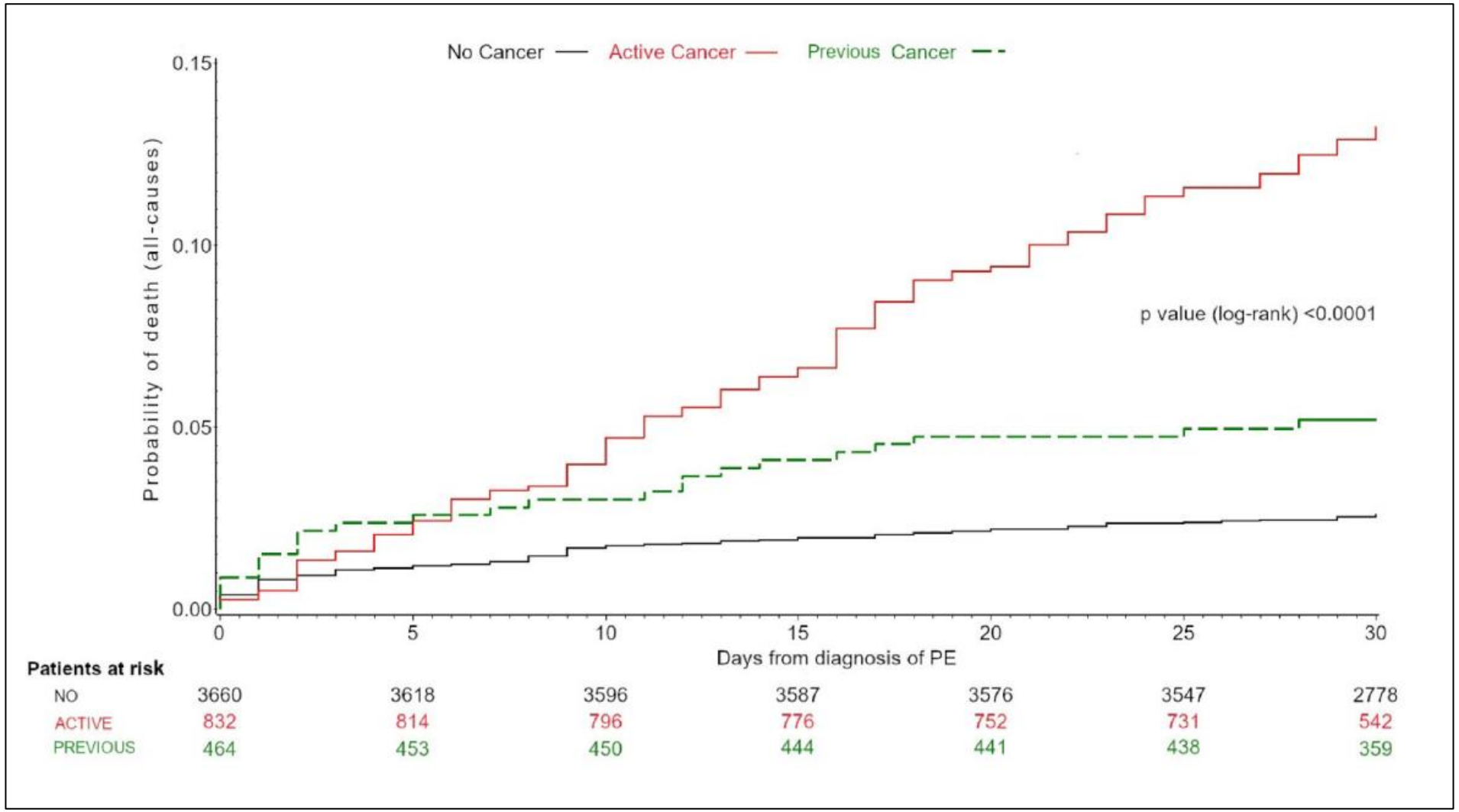
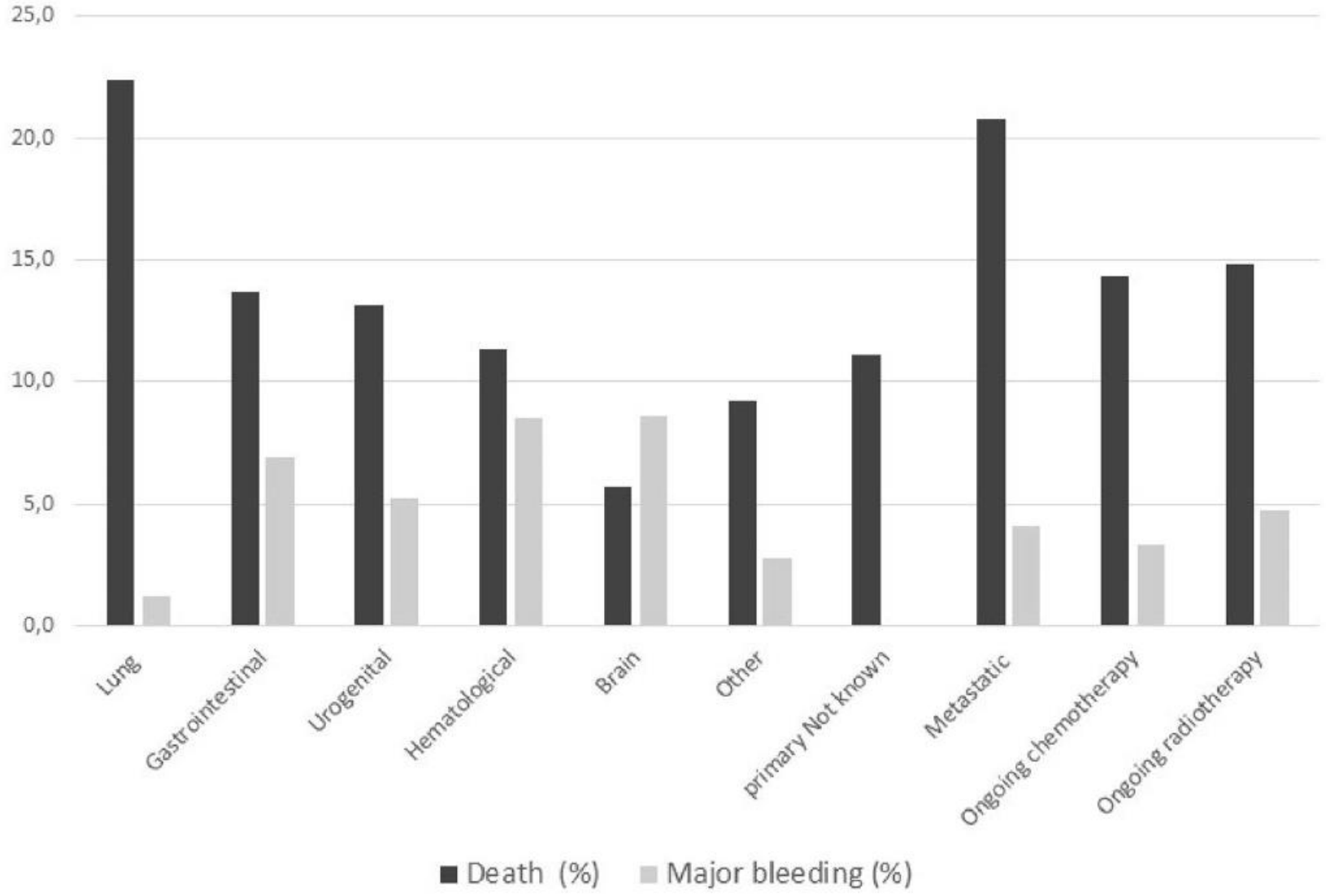

No Cancer
Active Cancer
Previous Cancer
Probability of death (all-causes)
0.15
0.10
0.05
0.00
p value (log-rank) <0.0001
0
5
10
15
20
25
30
Days from diagnosis of PE
Patients at risk
NO 3660 3618 3596 3587 3576 3547 2778
ACTIVE 832 814 796 776 752 731 542
PREVIOUS 464 453 450 444 441 438 359

Fig. 2 Clinical outcome at 30 days in patients with active cancer by site and stage of cancer



Conclusions

- The study shows that, since the initial phases of patient management, the risk for death and that for major bleeding after an acute PE are higher in patients with active cancer in comparison to patients with previous cancer or without cancer.
- Patients with active cancer have worse clinical outcome in comparison to patients with previous cancer or no cancer despite a higher prevalence of intermediate–low-risk PE according to the ESC stratification model.
- In patients with active cancer, cancer-related factors seem to be better predictors of death in comparison to some well-known hemodynamic or respiratory parameters.
- The study suggests that models for risk stratification in patients with acute symptomatic PE should be personalized based on the presence/absence of active cancer.