



HAL
open science

Chronic thromboembolic pulmonary hypertension suspicion after pulmonary embolism in cancer patients

J. Catella-Chatron, A. Merah, E. de Magalhaes, N. Moulin, S. Accassat, C. Duvillard, P. Mismetti, L. Bertoletti

► **To cite this version:**

J. Catella-Chatron, A. Merah, E. de Magalhaes, N. Moulin, S. Accassat, et al.. Chronic thromboembolic pulmonary hypertension suspicion after pulmonary embolism in cancer patients. *Respiratory Medicine and Research*, 2019, 76, pp.34 - 37. 10.1016/j.resmer.2019.08.002 . hal-03487678

HAL Id: hal-03487678

<https://hal.science/hal-03487678v1>

Submitted on 20 Jul 2022

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.



Distributed under a Creative Commons Attribution - NonCommercial 4.0 International License

Title page:

Title: Chronic thromboembolic pulmonary hypertension suspicion after pulmonary embolism in cancer patients

Short title: Do we screen CTEPH in cancer patients?

Authors :

Judith Catella-Chatron (1), Adel Merah (1,2), Elodie De Magalhaes (1,2), Nathalie Moulin (1), Sandrine Accassat (1,2), Cécile Duvillard (1), Patrick Mismetti (1,2,3), Laurent Bertoletti (1,2,3).

(1) Service de Médecine Vasculaire et Thérapeutique, Hôpital Universitaire de Saint Etienne, Faculté de Médecine de Saint Etienne

(2) INSERM, CIC1408, Saint-Etienne

(3) INSERM, SAINBIOSE U1059, Saint-Etienne

Corresponding author: Pr Laurent BERTOLETTI, Service de Médecine Vasculaire et Thérapeutique, Hôpital Nord, CHU de St-Etienne, 42055 St-Etienne Cedex, France.
+33477827771; fax: +33477820482

Abstract (223 words)

Introduction. Chronic thromboembolic pulmonary hypertension (CTEPH) is a severe condition which should be screened in patient with persistent dyspnea after pulmonary embolism (PE). After PE, CTEPH incidence was estimated between 0.1 and 9.1 % in overall patients. Although cancer is associated with an increased risk of CTEPH, CTEPH incidence is still unknown in cancer patients with PE. We aimed to estimate the frequency CTEPH-likely patients after PE, in cancer patients.

Materials. We individualized cancer patients of a monocentric prospective registry including consecutive patients with symptomatic PE. The primary outcome was the frequency of "CTEPH-likely" patients defined by the European Respiratory Society (ERS) guidelines (an accelerated tricuspid regurgitation more than 2.8m/s and at least 1–2 segmental or larger-sized defects, after more than 3 months of therapeutic anticoagulation).

Results. We included 129 cancer patients with PE. Colorectal cancer (19%), breast cancer (17%) and prostate cancer (15%) were the most frequent cancers. PE occurred after surgery or medical immobilization in 17% of patients, while 26% of patients had history of venous thromboembolism. During the follow-up, 2 patients (1.5%) had a clinical suspicion of CTEPH and only 1 patient with ovarian cancer (0.75% 95%CI [0.0%-2.2%]) was classified as "CTEPH-likely", 6 months after PE.

Conclusion. The frequency of screening for CTEPH seems negligible in PE patients with cancer. Concomitant cancer may affect the clinical suspicion of CTEPH.

Keywords : Chronic thromboembolic pulmonary hypertension, pulmonary embolism, cancer, epidemiology

Introduction

Chronic thromboembolic pulmonary hypertension (CTEPH) arise from one or multiple endothelialized pulmonary thrombi that do not resolve after pulmonary embolism (PE). CTEPH leads to chronic obstruction of the pulmonary artery tree, increased pulmonary vascular resistance, pulmonary hypertension (PH) and progressive right heart failure [1]. Untreated CTEPH has a very poor prognosis[2].

CTEPH diagnosis is a major clinical challenge because –if diagnosed- patients may be discussed for several treatments options. Pulmonary endarterectomy can potentially cure patients with CTEPH[3]. Pulmonary balloon angioplasty is becoming a more and more efficient option [4]. Beside these mechanical treatments, Riociguat has demonstrated its positive effect on exercise capacity [5]. Clinical symptoms and signs are non-specific or absent in early CTEPH, with signs of right heart failure only becoming evident in advanced disease. The mean diagnostic delay was 14 months in the European CTEPH registry[6] between the first symptoms and the diagnosis. Because of its low frequency after PE[7], diagnostic evaluation for CTEPH is not recommended for all PE survivors, but is suggested in case of clinical suspicion, for example in case of persistent dyspnea[8,9]. In case of clinical suspicion, the combination of a high or intermediate echocardiographic probability of PH with the presence of perfusion defects on V/Q lung scan defined CTEPH as “likely”, and may prompt the referral of the patients in a PH center [9].

This clinical challenge is upgraded in cancer patients. Venous thromboembolism (VTE) is a common complication of cancer and its therapy [10,11]. Approximately 20 % of all VTE cases are related to cancer[10] and cancer patients with VTE have a three-fold higher risk of recurrent VTE compared to patients without cancer[12,13]. Cancer symptoms may hide CTEPH symptoms or CTEPH symptoms may be interpreted as cancer symptoms.

A recent meta analyse estimates incidence of CTEPH of 3.21% (95% CI 2.0-4.4) after PE, considering only survivors patients, alive after an initial treatment period of 6 months[7]. Moreover, recurrent VTE was associated with a higher CTEPH incidence than after first PE (Odd Ratio 3.2, 95% CI 1.7-5.9)[7]. Whereas in survivors patients without major comorbidities, incidence was estimated at 2.78% (95% CI 1.5-4.1)[7], incidence of CTEPH after PE in patients with active cancer is currently unknown.

We aimed to assess the suspicion of CTEPH, after PE in patients with active cancer.

Methods

We conducted a post hoc analysis of consecutive patients with acute PE, prospectively included in the monocentric registry of Saint Etienne.

Registry design, patients and data collection

Consecutive patients with symptomatic acute PE and active cancer were included in our registry. PE was confirmed with high probability ventilation/perfusion (V/Q) scan, intermediate V/Q with proximal deep venous thrombosis or positive contrast-enhanced, pulmonary embolism-protocol, helical chest computerized tomography. Active cancer was defined according to ISTH definition [14]. Patients participating in a therapeutic clinical trial with a blind medication were excluded. All patients provided oral or written consent according to the requirements of the Ethics Committee of the hospital. The participating physicians ensured that eligible patients were consecutively enrolled.

Study variables

The parameters routinely recorded in the registry are: patient baseline characteristics; clinical status including any coexisting or underlying condition (like cancer); laboratory data; treatment received upon VTE diagnosis (drugs, doses and duration); outcome during the course of anticoagulant therapy (mainly recurrent symptomatic VTE, major bleeding, CTEPH clinical suspicion and death).

Among the patients in whom CTEPH was clinically suspected, patients were defined as "CTEPH likely" according to the definition of the European Respiratory Society (ERS) guidelines, with an accelerated tricuspid regurgitation more than 2.8 m/sec on TTE and at least 1-2 segmental or larger sized defects on pulmonary perfusion scan, after more than 3 months of therapeutic anticoagulation[8,9].

Treatment and follow up

Patients were managed according to the clinical practice of each clinician; therefore, there was no standardization of choice of drug treatment, dose or duration. Patients were followed-up for at least three months in the outpatient clinic of Saint Etienne. First visit was usually performed between 3 and 6 months after the diagnosis then following visits were provided every 6 or 12 months according the profile of each patient. During each visit, any signs or symptoms suggesting CTEPH complications were prospectively noted (dyspnea, weakness, fatigue, chest pain, palpitations, right heart failure signs, syncope, hemoptysis, cyanosis). During the follow-up, clinicians were free to suspect (or not) CTEPH, if patients presented with persistent dyspnea, and free to program (or not) transthoracic echocardiogram to assess for pulmonary hypertension, and pulmonary perfusion scan to assess for perfusion defects, in order to classify the patients as "CTEPH likely" or "unlikely".

Study design and outcomes

All patients recruited in our registry with active cancer were considered in our analysis. Our primary aim was to estimate the frequency of patients reported as "CTEPH-likely" during the follow-up.

Statistical analysis

Analyses were performed on all patients included in our registry between January 2008 and December 2016, with active cancer. Quantitative variables were presented as the number of case, mean (\pm standard deviation). Data were processed and analyzed using R package version 3.4.318 [15].

Results

Between January 2008 and December 2016, 129 patients with PE and active cancer were included among the 711 patients with PE (18.1%). Baseline patients characteristics are reported in *Table 1*. Of these, 68 patients (53 %) were male. The mean age was 72 years old with 77 patients (60%) above 70 years old. Initial pulmonary embolism presented with dyspnea for 99 patients (77%). Three patients (2.3%) presented with systemic hypotension. Among the 24 patients with TTE performed at PE diagnosis, 8 patients (6.2%) had systolic Pulmonary Arterial Pressure over 50 mmHg. Main risk factors of venous thromboembolism (VTE) were history of VTE for 33 patients (26%) and recent surgery for 18 patients (14%).

Cancer patient's characteristics are reported in *Table 2*. Main cancer site were colorectal (19.8%), breast (17%), prostate (16.5%), blood (9%), lung (8.5%). Cancer were metastatic for 41 patients (32%). Cancer treatments include chemotherapy (35%), radiotherapy (12%) and hormonal therapy (13%). Initially, 91% of patients were treated with low molecular weight heparin (LMWH), 7% of patients with unfractionated heparin and 2% of patients with direct oral anticoagulants (DOACS). As a long term therapy (after 6 months), 66% of patients were treated with LMWH, 26% of patients with vitamin K antagonist and 8% patients with DOACS. The median follow up was 190 days (\pm 240). The overall survival was 91.5 % at the end of follow-up.

During the follow-up, 2 patients (1.5%) were clinically suspected of CTEPH (none of them were those with elevated sPAP at baseline). One patient was classified as "CTEPH-likely", corresponding to an incidence of 0.75% (95% CI 0.0-2.2). This patient was a woman with a locally advanced ovarian cancer. CTEPH was suspected 6 months after PE diagnosis because of persistent dyspnea. TTE and lung scan were favorable to "CTEPH likely". No right heart catheterism (RHC) was performed to confirm CTEPH. The patient received conventional therapy consisting diuretics, oxygen on top of anticoagulant therapy. The patient is still alive 3 years after PE diagnosis.

Discussion

In 129 cancer patients prospectively followed after acute pulmonary embolism, a clinical suspicion of CTEPH was raised in 1.5% and the incidence of "CTEPH likely" (as defined by Europeans guidelines) was 0.75% (95% CI 0.0-2.2).

Compared to data recently aggregated in a meta-analysis[7], our incidence of "CTEPH likely" patients was near to the incidence of CTEPH after PE in all comers (0.56%), but lower than the incidence found in patient survivors 6 months after PE (3.21%)[7]. Of note, we included all patients with PE in the setting with active cancer, the median follow up was 6 months, and the survival rate was 91.5% at the end of the follow-up.

We know that cancer patients are at higher risk of venous thrombo embolism. As previously reported, almost 20% of our PE occurred in cancer patients[10] and 3.8% allow to discover cancer in the following year [16]. Moreover, this patients have a three-fold higher risk of recurrent VTE compared to those without cancer[12,13]. Recurrent VTE is associated with a higher CTEPH incidence than after first PE (Odd Ratio 3.2, 95% CI 1.7-5.9)[7]. Considering that, we expected an higher rate of CTEPH likely patients that thus we found. In a bicentric study of 146 patients followed for CTEPH incidence after acute PE, 17 were suffering from cancer [17], and only one was diagnosed for CTEPH, after a median time of 26 months of follow-up. Joined with our 129 patients, it seems that CTEPH is not frequently diagnosed after PE in patients with active cancer.

No previous study specifically assessed the incidence of CTEPH suspicion in cancer patients. Our low incidence may be explained by the non-specificity of the CTEPH clinical signs, like exercise intolerance, fatigue or low grade of dyspnea. Moreover, clinical suspicion of CTEPH may be decreased because symptoms being related to cancer or cancer treatment. Finally, it is possible that doctors may decide to not conduct any other investigation, because of the cancer status, despite overt clinical symptoms.

Our study has several limits. We conducted a monocentric study with an a posteriori analysis but our patients were included consecutively and prospectively. Only 24 TTE were performed at baseline, but none of the 8 patients with pulmonary hypertension at baseline were suspected of CTEPH during the follow-up. Our study population is small, considering the importance of cancer-associated thrombosis, but this is the first to point out the particularities of CTEPH suspicion in cancer patients. Our median follow up is limited to 6 months which may affect the rate of CTEPH suspicion especially since the survival of cancer patients is in constant progress and more and more concerns are currently raised on cardiovascular long-term complications[18]. Also, the number of patients include give no sufficient power to assess the risk according the type of cancer or the treatment. Of note, no right heart catheterism was done in the patient suspected of CTEPH.

Conclusion

The frequency of screening for CTEPH seems negligible in cancer patients after PE. Concomitant cancer may affect the clinical suspicion of CTEPH. CTEPH diagnosis and dedicated therapy may improve the prognosis of some cancer patients with PE. Better individualization of PE patients with cancer at good prognosis is needed.

Bibliography

- [1] I.M. Lang, M. Madani, Update on Chronic Thromboembolic Pulmonary Hypertension, *Circulation*. 130 (2014) 508–518. doi:10.1161/CIRCULATIONAHA.114.009309.
- [2] M. Riedel, V. Stanek, J. Widimsky, I. Prerovsky, Longterm Follow-up of Patients with Pulmonary Thromboembolism, *Chest*. 81 (1982) 151–158. doi:10.1378/chest.81.2.151.
- [3] I. Lang, G. Simonneau, J. Pepke-Zaba, E. Mayer, D. Ambrož, I. Blanco, A. Torbicki, S. Mellekjaer, A. Yaici, M. Delcroix, Factors associated with diagnosis and operability of chronic thromboembolic pulmonary hypertension, *Thromb. Haemost.* 110 (2013) 83–91. doi:10.1160/TH13-02-0097.
- [4] J.M. Moriarty, S.N. Khan, S.D. Kao, R. Saggar, Balloon Pulmonary Angioplasty for Chronic Thromboembolic Pulmonary Hypertension, *Cardiovasc. Intervent. Radiol.* 41 (2018) 1826–1839. doi:10.1007/s00270-018-2012-2.
- [5] H.-A. Ghofrani, A.M. D'Armini, F. Grimminger, M.M. Hoeper, P. Jansa, N.H. Kim, E. Mayer, G. Simonneau, M.R. Wilkins, A. Fritsch, D. Neuser, G. Weimann, C. Wang, Riociguat for the Treatment of Chronic Thromboembolic Pulmonary Hypertension, *N. Engl. J. Med.* 369 (2013) 319–329. doi:10.1056/NEJMoa1209657.
- [6] J. Pepke-Zaba, M. Delcroix, I. Lang, E. Mayer, P. Jansa, D. Ambroz, C. Treacy, A.M. D'Armini, M. Morsolini, R. Snijder, P. Bresser, A. Torbicki, B. Kristensen, J. Lewczuk, I. Simkova, J.A. Barberà, M. de Perrot, M.M. Hoeper, S. Gaine, R. Speich, M.A. Gomez-Sanchez, G. Kovacs, A.M. Hamid, X. Jaïs, G. Simonneau, Chronic Thromboembolic Pulmonary Hypertension (CTEPH), *Circulation*. 124 (2011) 1973–1981. doi:10.1161/CIRCULATIONAHA.110.015008.
- [7] Y.M. Ende-Verhaar, S.C. Cannegieter, A. Vonk Noordegraaf, M. Delcroix, P. Pruszczyk,

- A.T.A. Mairuhu, M. V. Huisman, F.A. Klok, Incidence of chronic thromboembolic pulmonary hypertension after acute pulmonary embolism: a contemporary view of the published literature, *Eur. Respir. J.* 49 (2017) 1601792. doi:10.1183/13993003.01792-2016.
- [8] S. Konstantinides, A. Torbicki, G. Agnelli, N. Danchin, D. Fitzmaurice, N. Galie, J.S.R. Gibbs, M. Huisman, M. Humbert, N. Kucher, I. Lang, M. Lankeit, J. Lekakis, C. Maack, E. Mayer, N. Meneveau, A. Perrier, P. Pruszczyk, L.H. Rasmussen, T.H. Schindler, P. Svitil, a. V. Noordegraaf, J.L. Zamorano, M. Zompatori, S. Achenbach, H. Baumgartner, J.J. Bax, H. Bueno, V. Dean, C. Deaton, C. Erol, R. Fagard, R. Ferrari, D. Hasdai, A. Hoes, P. Kirchhof, J. Knuuti, P. Kolh, P. Lancellotti, A. Linhart, P. Nihoyannopoulos, M.F. Piepoli, P. Ponikowski, P. a. Sirnes, J.L. Tamargo, M. Tendera, W. Wijns, S. Windecker, D. Jimenez, W. Ageno, S. Agewall, R. Asteggiano, R. Bauersachs, C. Becattini, H. Bounameaux, H.R. Buller, C.H. Davos, G.-J. Geersing, M. a. G. Sanchez, J. Hendriks, M. Kilickap, V. Mareev, M. Monreal, J. Morais, B. a. Popescu, O. Sanchez, a. C. Spyropoulos, N. Skoro-Sajer, R. Najafov, S. Sudzhaeva, M. De Pauw, F. Barakovi, M. Tokmakova, B. Skoric, R. Rokyta, M.L. Hansen, M. Elmet, V.-P. Harjola, G. Meyer, A. Chukhrukidze, S. Rosenkranz, A. Androulakis, T. Forster, F. Fedele, T. Sooronbaev, A. Maca, E. Ereminiene, J. Micallef, A. Andreasen, M. Kurzyna, D. Ferreira, a. O. Petris, S. Dzemeshevich, M. Asanin, I. Imkova, M. Anguita, C. Christersson, N. Kostova, H. Baccar, L.E. Sade, A. Parkhomenko, J. Pepke-Zaba, 2014 ESC Guidelines on the diagnosis and management of acute pulmonary embolism: The Task Force for the Diagnosis and Management of Acute Pulmonary Embolism of the European Society of Cardiology (ESC) * Endorsed by the European Respiratory Society (ERS), *Eur. Heart J.* (2014). doi:10.1093/eurheartj/ehu283.
- [9] N. Galiè, M. Humbert, J.-L. Vachiery, S. Gibbs, I. Lang, A. Torbicki, G. Simonneau, A. Peacock, A. Vonk Noordegraaf, M. Beghetti, A. Ghofrani, M.A. Gomez Sanchez, G.

- Hansmann, W. Klepetko, P. Lancellotti, M. Matucci, T. McDonagh, L. a Pierard, P.T. Trindade, M. Zompatori, M. Hoeper, V. Aboyans, A. Vaz Carneiro, S. Achenbach, S. Agewall, Y. Allanore, R. Asteggiano, L. Paolo Badano, J. Albert Barberà, H. Bouvaist, H. Bueno, R. a Byrne, S. Carerj, G. Castro, Ç. Erol, V. Falk, C. Funck-Brentano, M. Gorenflo, J. Granton, B. Iung, D.G. Kiely, P. Kirchhof, B. Kjellstrom, U. Landmesser, J. Lekakis, C. Lionis, G.Y.H. Lip, S.E. Orfanos, M.H. Park, M.F. Piepoli, P. Ponikowski, M.-P. Revel, D. Rigau, S. Rosenkranz, H. Völler, J. Luis Zamorano, 2015 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension: The Joint Task Force for the Diagnosis and Treatment of Pulmonary Hypertension of the European Society of Cardiology (ESC) and the European Respiratory Society (ERS): Endor, Eur. Heart J. 37 (2016) 67–119. doi:10.1093/eurheartj/ehv317.
- [10] J.F. Timp, S.K. Braekkan, H.H. Versteeg, S.C. Cannegieter, Epidemiology of cancer-associated venous thrombosis, *Blood*. 122 (2013) 1712–1723. doi:10.1182/blood-2013-04-460121.
- [11] C. Ay, I. Pabinger, A.T. Cohen, Cancer-associated venous thromboembolism : Burden , mechanisms , and management, (2017) 219–230.
- [12] P. Prandoni, A.W.A. Lensing, A. Piccioli, E. Bernardi, P. Simioni, B. Girolami, A. Marchiori, P. Sabbion, M.H. Prins, F. Noventa, A. Girolami, Recurrent venous thromboembolism and bleeding complications during anticoagulant treatment in patients with cancer and venous thrombosis, *J. Clin. Oncol.* 100 (2002) 3484–3488. doi:10.1182/blood-2002-01-0108.Reprints.
- [13] B.A. Hutten, M.H. Prins, M. Gent, J. Ginsberg, J.G.P. Tijssen, H.R. Büller, Incidence of Recurrent Thromboembolic and Bleeding Complications Among Patients With Venous Thromboembolism in Relation to Both Malignancy and Achieved International Normalized Ratio: A Retrospective Analysis, *J. Clin. Oncol.* 18 (2017) 3078–3083.

doi:10.1200/jco.2000.18.17.3078.

- [14] C. Kearon, W. Ageno, S.C. Cannegieter, B. Cosmi, G.J. Geersing, P.A. Kyrle, Categorization of patients as having provoked or unprovoked venous thromboembolism: guidance from the SSC of ISTH, *J. Thromb. Haemost.* 14 (2016) 1480–1483. doi:10.1111/jth.13336.
- [15] R Foundation for Statistical Computing., *R: a Language and Environment for Statistical Computing.*, (2016). <http://www.r-project.org>.
- [16] A. Delluc, J.C. Ianotto, C. Tromeur, C. De Moreuil, F. Couturaud, K. Lacut, E. Le Moigne, P. Louis, J. Thereaux, J.P. Metges, D. Mottier, Real-world incidence of cancer following a first unprovoked venous thrombosis: Results from the EPIGETBO study, *Thromb. Res.* 164 (2018) 79–84. doi:10.1016/j.thromres.2018.02.151.
- [17] L. Guérin, F. Couturaud, F. Parent, M.-P. Revel, F. Gillaizeau, B. Planquette, D. Pontal, M. Guégan, G. Simonneau, G. Meyer, O. Sanchez, Prevalence Of Chronic Thromboembolic Pulmonary Hypertension After Acute Pulmonary Embolism : A Prospective Multicenter Study, *Thromb. Haemost.* 112 (2013) 598–605. doi:10.1164/ajrccm-conference.2010.181.1_meetingabstracts.a1947.
- [18] B. Mery, J.-B. Guichard, J.-B. Guy, A. Vallard, J.-C. Barthelemy, A. Da Costa, N. Magné, L. Bertoletti, Atrial fibrillation in cancer patients: Hindsight, insight and foresight, *Int. J. Cardiol.* 240 (2017) 196–202. doi:10.1016/j.ijcard.2017.03.132.

Table legend:

Table 1. Baseline patients characteristics.

PE, Pulmonary Embolism; VTE, Venous Thrombo Embolism; CTPA, CT pulmonary angiogram;

Patients, N	129
<i>Clinical characteristics</i>	
Male gender	68 (52.7%)
Mean age (years \pm SD)	72.0 \pm 12.9
Age > 70yr	77 (59.7%)
Body weight (mean kg \pm SD)	73.6 \pm 18.3
BMI \leq 18 kg/m ²	6 (4.7%)
BMI > 30 kg/m ²	20 (15.5%)
<i>Acute PE index</i>	
Syncope	13 (10.1%)
Dyspnea	99 (76.7%)
Fever	15 (11.6%)
Temperature less than 36°C	2 (1.6%)
SBP < 100 mmHg	3 (2.3%)
Heart Rate > 110 bpm	8 (6.2%)
Sat O ₂ levels < 90% (Blood gases) n=38	9 (7.0%)
Inverted T wave (ECG)	18 (14.0%)
Right Branch Block (ECG)	11 (8.5%)
Central Thrombi (CTPA) n=23	1
PA main branches thrombi (CTPA) n=23	3
Segmental thrombi (CTPA) n=34	27
PAP levels > 50 mmHg (TTE baseline) n=24	8
<i>Risk factors for PE</i>	
Surgery < 2 months	18 (14.0%)
Immobilization \geq 4 days	4 (3.1%)
Estrogen use	16 (12.4%)
Varicose veins	17 (13.2%)
Prior VTE	33 (25.6%)
<i>Underlying diseases</i>	
Atrial fibrillation	4 (3.1%)
Systemic arterial hypertension	57 (44.2%)
Diabetes mellitus	14 (10.9%)
Thyroid diseases	6 (4.7%)
Depression	5 (3.9%)
Use of psychotropic drugs	12 (9.3%)
Use of antiplatelets drugs	28 (21.7%)
Use of anticoagulants drugs	4 (3.1%)
Follow-up (mean days)	260.1 \pm 240.0
Follow-up (median days\pmSD)	190.0 \pm 240.0
<i>Cancer site</i>	
Colorectal	25 (19.4%)
Breast	24 (18.6%)
Prostate	19 (14.7%)
Hematological	12 (9.3%)
Lung	11 (8.5%)
Kidney	6 (4.7%)
Uterus	6 (4.7%)
Skin	5 (3.9%)
Stomach	5 (3.9%)
Ovary	4 (3.1%)
Bladder	4 (3.1%)

Pancreas	1 (0.8%)
Peritoneum	2 (1.6%)
ENT (pharynx/larynx + tong)	2 (1.6%)
Others (unknown, sarcome, thyroid)	3 (2.3%)
Metastasis	41 (31.8%)
Cancer treatment	
Radiotherapy	15 (11.6%)
Chemotherapy	45 (34.9%)
Hormonal therapy	17 (13.2%)

(continued)