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Brief title: Cardiogenic shock and active cancer

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Abstract

Aims

Characteristics, management, and outcomes of patients with active cancer admitted for cardiogenic shock remain largely unknown. This study aimed to address this issue and identify the determinants of 30-day and 1-year mortality in a large cardiogenic shock cohort of all etiologies.

Methods and results

FRENSHOCK is a prospective multicenter observational registry conducted in French critical care units between April and October 2016. "Active cancer" was defined as a malignancy diagnosed within the previous weeks with planned or ongoing anticancer therapy. Among the 772 enrolled patients (mean age 65.7 ± 14.9 years; 71.5% male), 51 (6.6%) had active cancer. Among them, the main cancer types were solid cancers (60.8%), and hematological malignancies (27.5%). Solid cancers were mainly urogenital (21.6%), gastrointestinal (15.7%), and lung cancer (9.8%). Medical history, clinical presentation, and baseline echocardiography were almost the same between groups. In-hospital management significantly differed: patients with cancers received more catecholamines or inotropes (norepinephrine 72 vs 52%, p=0.005 and norepinephrine-dobutamine combination 64.7 vs 44.5%, p=0.005), but had less mechanical circulatory support (5.9 vs 19.5%, p=0.016). They presented similar 30-day mortality rate (29 vs 26%) but a significantly higher mortality at one-year (70.6 vs 45.2%, p<0.001). In multivariable analysis, active cancer was not associated with 30-day mortality but was significantly associated with 1-year mortality in 30-day survivors (HR 3.61 [1.29 - 10.11], p=0.015).

Conclusion

Active cancer patients accounted for almost 7% of all cases of cardiogenic shock. Early mortality was the same regardless active cancer or not, whereas long-term mortality was significantly increased in patients with active cancer.

Keywords: heart failure; cardiogenic shock; cancer; cardio-oncology; prognosis

Abbreviation list

CPs: cancer patient

CRP: C-reactive protein

CS: cardiogenic shock

IABP: intra-aortic balloon pump

ICCU: intensive cardiac care unit

ICU: intensive care unit

MI: myocardial infarction

MCS: mechanical circulatory support

PCI: percutaneous coronary intervention

VA-ECMO: venoarterial-extracorporeal membrane oxygenation

Introduction

Cardiovascular diseases and cancers are the most prevalent diseases and the leading causes of death worldwide [1]. Through medical progress, the mortality rate among cancer patients (CPs) has decreased dramatically over the last three decades [2]. Consequently, an increased number of CPs, who also share many cardiovascular risk factors, such as age [3], may develop acute heart disease such as cardiogenic shock (CS) [4].

CS caused by severe impairment of myocardial performance is a life-threatening condition defined as persistent low cardiac output, without hypovolemia, resulting in organ hypoperfusion and multi-organ failure [5]. Although recent progress has been made in the field of CS, notably regarding diagnosis but also organ support, mortality remains >40% which makes this condition a major challenge in intensive cardiac care units (ICCU) and intensive care units (ICU) [6].

The interconnection between cancer and cardiovascular diseases has led to the development of the field of cardio-oncology [7], which distinguishes two main types of cardio-oncology syndromes in CPs [8]. CS belongs to the type 1 cardio-oncological syndrome when the etiology comes from cancer itself, directly or indirectly through an increase in coronary risk, thromboembolic events, tamponade, or paraneoplastic syndrome. And CS belongs to type 2 cardio-oncological syndrome when it results from side effects of cancer treatments such as chemotherapy, radiotherapy, targeted therapy, or immunotherapy.

There is currently a critical lack of data regarding cardio-oncology, indeed due to the lack of large-scale, randomized trials, only 3% of the recommendations are level of evidence A and 21% are level of evidence B in the very first cardio-oncology guidelines published in 2022 [9]. This lack of data is even more critical regarding CS in CPs. Indeed, most scientific evidence comes from case reports or large retrospective cohorts with very limited clinical data [10]. This

paucity of data makes it difficult for clinicians to know whether CS foreshadows the end of life of CPs who might benefit from palliative care or whether these CPs might benefit from intensive management strategies, including mechanical circulatory support (MCS).

The main objective of this study based on the largest European prospective cohort of CS to date, was to assess characteristics and outcomes of CS according to the presence of active cancer. The secondary objective was to determine prognostic factors of CS in CPs.

Methods

Patient population

FRENSHOCK is a prospective multicenter observational registry conducted in metropolitan France during six months between April and October 2016 in ICU and ICCU (NCT02703038). The methods used for this registry have been previously described [11]. Briefly, the primary objective was to evaluate the characteristics, management, and outcomes of CS patients, with a new modified definition of CS as seen in routine clinical practice, on a nationwide scale.

All adult patients (≥18 years old) with CS were prospectively included in this registry if they met at least one criterion of (i) hemodynamic criteria, (ii) left and/or right heart overload; and (iii) signs of organ malperfusion. Patients could be included regardless of CS etiology, and whether CS was primary or secondary.

"Active cancer" was defined as a malignancy diagnosed within the previous weeks with planned treatment or patients with ongoing cancer treatment such as chemotherapy, radiation therapy, surgery, targeted therapy, or immunotherapy. The distinction between solid cancers and hematological malignancies has been individually verified by an oncologist.

All institutions were invited to participate in the study, including university teaching hospitals, general and regional hospitals, and public and private hospitals that manage CS patients (ICCUs, surgical ICUs, medical ICUs, and general ICUs).

The study was conducted in accordance with the guidelines for good clinical practice and French law. Written consent was obtained for all the patients. The data recorded and their handling and storage were reviewed and approved by the CCTIRS (French Health Research Data Processing Advisory Committee) (n° 15.897) and the CNIL (French Data Protection Agency) (n° DR-2016-109).

Data collection

Data on baseline characteristics, including demographics (age, gender, body mass index (BMI)), risk factors (hypertension, diabetes, current smoking, hypercholesterolemia), and medical history [cardiomyopathy, myocardial infarction (MI), stroke, peripheral artery disease, chronic kidney disease, active cancer, chronic obstructive lung disease], were collected as previously mentioned. Clinical, biological, and echocardiographic data were collected within the first 24 h after admission. Up to three CS triggers were determined for each patient by the local investigator, that is, ischemic (Type 1 or Type 2 acute MI according to European guidelines); ventricular and supraventricular arrhythmia; conduction disorder; infectious disease; non-compliance (poor compliance with medical treatment or hygiene and diet rules); or iatrogenesis. Iatrogenesis is defined as unintended consequences, complications, or adverse effects associated with medical procedures, medications, or interventions performed during the management of a patient. Investigators could also note other existing factors or etiologies which were indicated as 'other'. Information regarding the use of cardiac procedures, that is, coronary angiography and/or percutaneous coronary intervention (PCI); right heart catheterization; the need for medications (inotropes, vasopressors, diuretics, and fibrinolysis) and organ replacement therapies such as mechanical ventilation (invasive or non-invasive); temporary MCS [intra-aortic balloon pump (IABP); extracorporeal membrane oxygenation or Impella® (Abiomed, Danvers, MA, USA)]; and renal replacement therapy (continuous or intermittent) were collected. In-hospital complications were noted, such as stroke, bleeding and transfusions, hemolysis, thrombocytopenia, nosocomial infections, vascular complications, and death. Information on mortality was obtained directly by the local investigators (cause and date).

Statistical analysis

Continuous variables were reported as means (SD) or medians and interquartile ranges when appropriate. Discrete variables were described in numbers and percentages. Groups (30-day survivors and non-survivors) were compared by analysis of variance for continuous variables and $\chi 2$ or Fisher's exact test for discrete variables. Odds ratios (ORs) were presented with their 95% confidence intervals (CIs). To determine independent predictors of in-hospital all-cause mortality, binary logistic regression analyses were used, with a threshold <0.10 for variable elimination. Variables included in the final models were selected ad hoc based on their physiological relevance and potential to be associated with outcomes. Two multivariable analyses were conducted. The first included only variables available on admission: age, gender, type of institution, risk factors, comorbidities, and causes of CS. A sensitivity analysis was performed, and lactate peak was added to the covariates in the main analysis. The second model added in-hospital management variables (first place of admission; respiratory, circulatory, or renal support; use of inotropes, vasopressors, diuretics, and fibrinolysis in the first 24 h; and myocardial revascularization). This analysis was repeated on the subset of patients with ischemic CS. Analyses were repeated using forward stepwise analysis to assess the consistency of results. Collinearity was assessed by calculating variance inflation factors. Statistical analyses were performed using IBM SPSS 23.0 (IBM SPSS Inc.). For all analyses, two-sided P values <0.05 were considered significant.

Results

Study population

A total of 772 CS patients were included in 49 centers. Among these patients, 51 had active cancer (6.6%). Clinical characteristics between non-CPs and CPs are presented in Table 1. The mean age of the CPs population was 68.6 (±12.3) years with a predominance of men (76.5%), not significantly different compared to non-CPs. Employment status was similar between the two groups. The rate of main cardiovascular risk factors was the same in both groups. In CPs, a medical history of cardiac disease was reported in 51% (31.4% coronary artery disease), previous PCI in 29.4%, previous ischemic stroke in 9.8%, peripheral artery disease in 13.7%. Although, there was also no difference in terms of medical history, except for a higher rate of cardiac toxicity among CPs (p=0.02). There was no difference in previous cardiac treatments. Besides cardiovascular diseases, 5.9% of CPs had chronic obstructive pulmonary disease and 25.5% had chronic kidney disease.

Among CPs, main cancer types were solid cancers (60.8%) and hematological malignancies accounted for 27.5% (Table 2). Solid cancers were mainly urogenital (21.6%), gastrointestinal (15.7%), and lung cancer (9.8%).

At admission, in CPs, the mean heart rate was 102 (±27) bpm (60.8% with sinus rhythm), and SBP was 102 (±25) mmHg (Table 3). Clinical signs of left and right heart failure were significantly more frequent in CPs compared to non-CPs with 84% (versus 71%, p=0.042) and 69% (versus 48%, p=0.004) respectively and mottling was reported in 48.8% of the cases.

The main triggers of CS (not mutually exclusive) in CPs were ischemic (31.4%), infectious disease (25.5%), and iatrogenic (19.6%) (Table 1). Infectious disease and iatrogenic triggers were significantly more frequent compared to non-CPs. Cardiac arrest was the trigger of CS for 3 CPs (5,9%) patients. Most patients in both groups had multiple organ failure as evidenced by

kidney dysfunction, hepatic cytolysis and cholestasis, and lactate elevation (Table 3). Lactate level and C-reactive protein (CRP) at admission were significantly increased in CPs compared to non-CPs. Hemoglobin level was significantly lower in CPs with more anemia in CPs (78.4 vs 48.7%, $p < 0.001$).

Baseline echocardiography at admission showed a mean left ventricular ejection fraction (LVEF) of 28.2% (±13.5) which was not different between groups.

In-hospital management

In-hospital management is reported in **Table 4**. Most CPs were directly admitted in ICCU (60%); 40% were admitted in ICU, and before admission, the first medical contact occurred most often within the hospital, as CPs were more often already hospitalized ($p= 0.035$).

Medical management was relatively similar between the two groups, except for the administration of norepinephrine and norepinephrine plus dobutamine combination, which was significantly higher in CPs (respectively 72 vs. 52%, $p=0.005$ and 64.7 vs 44.5%, $p=0.005$). Another major difference was the use of MCS, which was much less frequent in CPs (5.9 vs 19.5%, p=0.016). There was slightly less coronary angiography performed in CPs, although not significant. However, the number of diseased vessels and the rate of PCI were similar in both groups. There was no difference between groups regarding the need for respiratory support or renal replacement therapy. The median length of stay in ICU and/or ICCU was significantly higher in CPs compared to non-CPs, with 16 vs. 11 days ($p=0.041$). There was no difference between groups regarding discharge mode after hospitalization.

Thirty-day and one-year outcomes and correlates

The mortality rate at 30 days was similar in CPs compared to the overall CS population (26% vs. 29.4%). In-hospital mortality was also similar between the two groups, although it was

numerically higher in cancer patients (42.9 vs. 32.8%), but not statistically significantly. The mortality rate at one-year was significantly increased in CPs, with 45.2% mortality in the overall population and 70.6% in CPs (Crude HR=1.85 [1.31 – 2.62], p<0.001) (**Structured graphical abstract**).

In CPs, the multivariable analysis identified three independent factors at admission (a low BMI (HR: 0.79; *p*=0.009), admission in ICU (HR: 7.05; *p*=0.007), and ASAT ≥ 180 IU/L (HR: 4.43; *p*=0.004)) associated with higher mortality at 30 days, and two with 1 year mortality (diastolic blood pressure (HR: 0.97; *p*=0.012) and lactate ≥ 4 mmol/L at admission (HR: 3.17; *p*=0.003)) (**Supplementary table 1 and 2**).

Figure 1 shows the Kaplan-Meier Landmark analysis of 30-day CS survivors. Using a multivariable cox regression among CS patients who were still alive at 30 days, age, active cancer, low hemoglobin, hyponatremia, low estimated glomerular filtration rate at admission, volume expansion during the first 24h, furosemide, levosimendan and amiodarone use, transfusion and renal replacement therapy requirement during in-hospital management were negatively associated with 1 year mortality although any PCI realization during hospitalization was protective (**Supplementary table 3**).

Discussion

To date, this post hoc analysis of a large prospective, observational multicenter registry of unselected CS, is the first study aiming at describing characteristics, management, and outcomes of CS among CPs.

The first results show that CPs represent almost 7% of patients in CS. CPs' medical history, but also clinical presentation, and baseline echocardiography were comparable whether the patient with CS had active cancer or not. However, in-hospital management significantly differed since catecholamines, or inotropes were more often used for CPs while on the contrary, CPs had less MCS. The main result remains that CPs presented similar 30-day mortality rate (about 30%), but a significantly higher mortality at one-year (70% versus 43%, hence Crude HR=1.85 [1.31 – 2.62], p<0.001)

During the last decade, a continuous increase in cancer incidence, accompanied by a stable decrease in cancer mortality has been observed [2]. Early diagnosis and more efficient treatments are the most likely explanations for this epidemiological and clinical shift, which has led to an increase in the life expectancy of CPs. Thus, although still relatively uncommon, the rate of CS among CPs is likely to increase steadily over time. Moreover, patients with cancer were often excluded from most of the large cardiology studies and registries [12].

Some shreds of evidence are slowly emerging and in 2021 and 2022, the first consensus document for "Evaluation and management of cancer patients presenting with acute cardiovascular disease" was published by a Task Force including the Association of Acute CardioVascular Care and the Council of Cardio-Oncology of the European Society of Cardiology [13,14]. Besides, the very first cardio-oncology guidelines were published only very recently, in 2022, but CS issue is not specifically addressed [9].

The prevalence of active cancers among patients with CS is about 7% in our study. Puymirat et al. also reported a prevalence between 7 and 8% of CPs among CS in the CUB-Réa database, a retrospective registry collecting data during 15 years (between 1997 and 2012) in 32 ICUs in France [15]. In the international ESC-HF-LT Registry, the prevalence of cancer in the subgroup of patients admitted with CS (n=195) in more than 200 centers between 2011 and 2015 was around 5% [16].

As expected, anemia was significantly more frequent in CPs than in non-CPs. Cancer-related anemia is a common comorbidity in CPs that is partly a consequence of concomitant antineoplastic therapy and a result of chronic inflammation associated with cancer [17]. Indeed, in the present study, inflammation appeared to be more important in the CPs, as suggested by the significantly higher CRP level. However, this higher inflammation in CPs may also be explained by more associated infectious CS triggers.

Although difficult to confirm, differences in terms of patient management (more vasopressors used in CPs), might likely be attributed to multiple factors, including different triggers (with infections being more frequent in CPs), distinct hemodynamic profiles (with CPs displaying a higher prevalence of vasoplegic syndrome due to underlying inflammation), and potential paraneoplasia syndromes in CPs.

In the present study, 30-day mortality was 29.4% in CPs and cancer was not an independent variable associated with 30-day mortality. Among, the independent factors at admissions associated with higher 30-day mortality, a low BMI might be the most pragmatic and helpful for clinician to help him/her choose the intensity of care in the best interest of the patient. As expected, admission to ICU rather than ICCU was also an independent factor of 30-mortality due to the difference in severity between patients.

In contrast, at 1 year, CPs have an almost twice excess of mortality (70 vs 43%). Independent factors identified in multivariable analysis seem too imprecise to use them as parameters to guide further support. These results are in line with those of the few previous studies. In the administrative Nationwide Inpatient Sample Database which includes around 500,000 patients hospitalized for CS between 2004 and 2011, cancer was independently associated with poor outcomes. Having a solid tumor represented an extremely unfavorable prognostic factor with an odds ratio (OR) of 1.50 for CPs without metastases and an OR of 2.05 for CPs with metastases [18].

These results suggest that cancer has a limited influence on the early mortality of CS. While 1-year mortality is probably more related to cancer, although the lack of data in this study makes it impossible to confirm this issue. Another hypothesis may be that CS and its consequences had impeded the continuation or implementation of cancer treatment for CPs.

According to a recent experts review on critically ill oncology and hematology patients, no predefined criteria or prognostic scores of ICU or ICCU triage for admission should be used [19]. Indeed, our data thereby support these recent expert positions on critically ill CPs and cancer should not be seen as a limiting factor in the short-term period. Each situation being different and challenging, the benefit-risk assessment must be discussed in an urgent multidisciplinary manner based on multiple criteria such as performance status and Clinical Frailty Scale [20].

Experts also suggest that time-limited trials should be used for CPs, meaning unlimited ICU management with a full-code status for a limited period before a re-evaluation of the clinical situation [19]. The appropriate length of time for full-code status (doing everything that can be done, including cancer chemotherapy and acute MCS) appears to be around 5 to 7 days for solid tumors but possibly for up to 14 days for hematologic malignancies [21]. To be noted, in case of multiple organ failure, full-code management for four to five days leads to similar outcomes as unlimited aggressive care [22]. Although cancer is not mentioned in this expert consensus, our

results suggest that acute MCS for refractory CS should be implemented before the onset of multi-organ failure in selected patients as a strategy to buy time for cardiac recovery (bridge-to-recovery strategy) or bridge-to-other therapies (bridge-to-decision strategy) [23].

The 2016 International Society for Heart and Lung Transplantation listing criteria for heart transplantation advises that the use of MCS support should be considered for patients with potentially reversible or treatable comorbidities, such as cancer, with subsequent reevaluation to establish candidacy (Class IIb, Level of Evidence: C) [24]. These guidelines also state that in patients with preexisting cancers, the risk of tumor recurrence should be stratified with a cardio-oncology collaboration. And that cardiac transplantation should be considered when risk of tumor recurrence is low based on tumor type, response to therapy, and negative metastatic workup. The specific amount of time to wait to transplant after neoplasm remission will depend on the aforementioned factors, and no arbitrary time period for observation should be used (Class of Recommendation I, Level of Evidence: C) [24]. Thus, even though in our current study the use of MCS was lower in CPs, by showing no difference between CPs and non-CPs in terms of 30-day survival, the criteria for MCS implementation should be based on other parameters than cancer alone. In the very special case of CS due to immune checkpoint inhibitors-associated fulminant myocarditis, the latest ESC Guidelines on cardio-oncology recommend an optimal cardiovascular treatment including mechanical support (Class I, level C) [9].

In contrast, if intensive therapy seems unreasonable given the patient's medical history and characteristics, then palliative care, often underused in CS [25], should be considered. Indeed, the most recent American Heart Association guidelines recommend the involvement of a multidisciplinary team, including palliative care, for all complex cardiovascular patients [26].

Limitations

As in any observational study, there are limitations to our analysis, such as missing data. The number of CPs represents a small sample size, even if it appears still enough to highlight significant, and original data. Data for patients who died before informed consent was obtained were not collected and recorded in the database because of administrative regulations. So, it cannot be excluded that the most severe patients i.e., with several comorbidities, frailty or multiple end-stage organ failure, could not have been admitted in ICU/ICCU for futility or have been deceased before inclusion. This could be a source of bias resulting in an underestimation of mortality. This addressing bias may possibly be greater for CPs with an associated risk of underestimating cancer prevalence among the CS population, but this further reinforces the message in our view. Indication bias for aggressive therapies among CPs such as MCS is possible. The existence of metastasis was not recorded. Another limitation to mention is that SCAI SHOCK Stage Classification was not used for the CS severity classification, nor the classification of cardio-oncological syndrome for the CPs, given that these scores were not still available at the time of the study [27]. Then, the factors associated with 30-day mortality should be interpreted with caution as an exploratory analysis since it is based on a low number of 30-day deaths (n = 15) in CPs. Finally, while general and more particularly cardiovascular data are important, cancer-specific data are relatively limited or even missing for some patients. Although, in the present study, the high proportion of iatrogenic triggers of CS among CPs suggests that there were numerous type 2 cardio-oncological syndromes but even more type 1 cardio-oncological syndromes.

Strengths

Our study highlights the absolute lack of difference in early mortality between CPs and non-CPs. Thus, providing evidence that the management of patients with active cancer and CS is not futile. Our study could partly help clinicians in triage decisions of CPs with CS and limit

delay ICU admission which may increase mortality [28]. Further studies are needed to collect more cancer-related data and better identify patients who might benefit from long-term intensive management.

Conclusion

In this first, prospective, observational multicenter study describing characteristics, management, and outcomes of CS among CPs, CPs represent nearly 7% of patients in CS. Besides cancer status, no difference was found in medical history and initial presentation between groups. In-hospital management however significantly differs with higher catecholamine and less MCS use in CPs. The main finding was that early mortality was not significantly different between CPs and non-CPs, whereas a marked excess of mortality was noted at 1-year in CPs, which means that therapeutic nihilism should be avoided for well-selected CPs with CS for whom a more aggressive management might be beneficial.

CLINICAL PERSPECTIVES

COMPETENCY IN MEDICAL KNOWLEDGE: Active cancer patients with cardiogenic shock had no difference in 30-day mortality compared to patients without cancer. Whereas a marked excess of mortality was noted at 1-year in active cancer patients.

COMPETENCY IN PATIENT CARE: Cardiologists, intensivists, and oncologists should be aware that therapeutic nihilism should be avoided for well-selected active cancer patients with cardiogenic shock for whom a more aggressive management might be beneficial.

TRANSLATIONAL OUTLOOK: Further studies are needed to develop algorithms to better predict patients who have the best survival rates among active cancer patients with cardiogenic shock and also determine the optimal therapeutics intensity and regimen in this population.

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Conflict of interest

The authors declare no competing interests.

Declarations

- Ethics approval and consent to participate: The data recorded and their handling and storage were reviewed and approved by the CCTIRS (French Health Research Data Processing Advisory Committee) (n° 15.897) and the CNIL (French Data Protection Agency) (n° DR-2016-109).
- Consent for publication: All authors hereby consent to the publication.
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    - Coordination and supervision of the FRENSHOCK registry: CD
    - Funding acquisition: FR, ME, and EB
    - Project administration: FR, ME, EB and CD
    - Data acquisition: all authors
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- Conceptualization, HM, JG, and CD
- Statistical analysis: VB
- Writing-original draft: HM and CD
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Figure legends

Figure 1. Early (30-day) and long-term (1-year) all-cause mortality by Kaplan-Meier landmark analysis according to the cancer status of the patients.

Graphical abstract. Characteristics, management, and outcomes of cancer patients with cardiogenic shock: An analysis of the FRENSHOCK prospective multicenter registry.

Kaplan-Meier Landmark analysis of failure rate (all-cause death) of 30-day survivors

aMCS. Acute mechanical circulatory support, CRP. C reactive protein, CS. Cardiogenic shock, CCU. Critical care unit, LOS. Length of stay in hospital.

Tables

Table 1 - Clinical characteristics at admission according to the cancer status of the patients.

	Overall (n=772)		No cancer (n=721)		Active Cancer (n=51)		P value
Male gender. n/total n (%)	552/772	(71.5)	513/721	(71.2)	39/51	(76.5)	0.416
Age (years). mean +/- SD	65.7	+/- 14.9	65.5	+/- 15.1	68.6	+/- 12.3	0.146
BMI (kg/m²). mean +/- SD	25.8	+/- 5.5	25.9	+/- 5.4	24.8	+/- 6.8	0.182
n	*744*		*695*		*49*		
Risk factors. n/total n (%)							
Current smoker	206/740	(27.8)	196/693	(28.3)	10/47	(21.3)	0.300
Diabetes mellitus	217/770	(28.2)	204/719	(28.4)	13/51	(25.5)	0.658
Arterial hypertension	364/771	(47.2)	340/720	(47.2)	24/51	(47.1)	0.982
Dyslipidaemia	277/771	(35.9)	258/720	(35.8)	19/51	(37.3)	0.838
Medical history. n/total n (%)							
History of cardiac disease	433/771	(56.2)	407/720	(56.5)	26/51	(51.0)	0.440
Ischaemic	230/771	(29.8)	214/720	(29.7)	16/51	(31.4)	0.803
Hypertrophic	11/771	(1.4)	10/720	(1.4)	1/51	(2.0)	0.531
Idiopathic	78/771	(10.1)	75/720	(10.4)	3/51	(5.9)	0.468
Toxic	34/771	(4.4)	28/720	(3.9)	6/51	(11.8)	0.020
Multisite pacing	63/771	(8.2)	60/720	(8.3)	3/51	(5.9)	0.791
Defibrillator	127/771	(16.5)	123/720	(17.1)	4/51	(7.8)	0.086
CABG	62/771	(8.0)	59/720	(8.2)	3/51	(5.9)	0.790
PCI	166/771	(21.5)	151/720	(21.0)	15/51	(29.4	0.156
Peripheral artery disease	91/771	(11.8)	84/720	(11.7)	7/51	(13.7)	0.660
Ischemic stroke	62/771	(8.0)	57/720	(7.9)	5/51	(9.8)	0.594
Chronic renal failure	164/771	(21.3)	151/720	(21.0)	13/51	(25.5)	0.446
Dialysis	11/771	(1.4)	11/720	(1.5)	0/51	(0.0)	1.000
COPD	50/771	(6.5)	47/720	(6.5)	3/51	(5.9)	1.000
Previous medications							
Aspirin	288/772	(37.4)	268/721	(37.3)	20/51	(39.2)	0.782
P2Y12 inhibitor	126/772	(16.4)	118/721	(16.4)	20/51	(39.2)	0.892
Statins	286/772	(37.1)	269/721	(37.4)	17/51	(33.3)	0.560
Betablockers	316/772	(41.0)	297/721	(41.3)	19/51	(37.3)	0.570
Vitamin K antagonist	165/772	(21.4)	155/721	(21.6)	10/51	(19.6)	0.743
Direct oral anticoagulant	56/772	(7.3)	54/721	(7.5)	2/51	(3.9)	0.573
ACE inhibitor or ARB	292/772	(37.9)	272/721	(37.8)	20/51	(39.2)	0.844
Sacubitril / Valsartan	18/772	(2.5)	18/721	(2.7)	0/51	(0.0)	0.630
Furosemide	376/772	(48.8)	345/721	(48.0)	31/51	(60.8)	0.077
Aldosterone antagonist	108/772	(14.0)	100/721	(13.9)	8/51	(15.7)	0.724
Amiodarone	132/772	(17.6)	121/721	(17.3)	11/51	(21.6)	0.435
Proton pump inhibitor	276/772	(36.4)	253/721	(35.7)	23/51	(45.1)	0.179
Triggers. n/total n (%)							
Ischaemic	291/772	(37.7)	275/721	(38.1)	16/51	(31.4)	0.335

Mechanical	24/772	(3.1)	23/721	(3.2)	1/51	(2.0)	1.000
Ventricular arrhythmia	98/772	(12.7)	93/721	(12.9)	5/51	(9.8)	0.521
Atrial arrhythmia	108/772	(14.0)	103/721	(14.3)	5/51	(9.8)	0.373
Conductive disorders	18/772	(2.3)	17/721	(2.4)	1/51	(2.0)	1.000
Infectious	96/772	(12.4)	83/721	(11.5)	13/51	(25.5)	0.003
Non compliance	30/772	(3.9)	28/721	(3.9)	2/51	(3.9)	1.000
Iatrogenic	61/772	(7.9)	51/721	(7.1)	10/51	(19.6)	0.004
Other	102/772	(13.2)	91/721	(12.6)	11/51	(21.6)	0.068
None / undefined	111/772	(14.4)	103/721	(14.3)	8/51	(15.7)	0.783

ACE : Angiotensin-Converting Enzyme. ARB : Angiotensin-Receptor Blocker. BMI : Body Mass Index. CABG : Coronary Artery Bypass Graft. COPD : Chronic Obstructive Pulmonary Disease. PCI : Percutaneous Coronary Intervention. SD : Standard Deviation.

Table 2 – Cancer type and localization in the CPs population (n=51)

n = 51	n	%
Type of cancer		
Solid	31	60.8
Hematological malignancies	14	27.5
Unknown	6	11.8
Cancer's localization		
Hematological malignancies	14	27.5
Urogenital (incl. Prostate)	11	21.6
Gastrointestinal	8	15.7
Unknown	7	13.7
Lung	5	9.8
Otorhinolaryngeal	3	5.9
Sarcoma	1	2.0

Table 3 - Clinical, echographic, and biological presentation according to the cancer status of the patients.

	Overall (n=772)	No cancer (n=721)	Active Cancer (n=51)	P value
First medical contact. n/total n (%)				0.035
Emergency department	257/769 (33.4)	242/718 (33.7)	15/51 (29.4)	
Mobile emergency unit	229/769 (29.8)	215/718 (29.9)	14/51 (27.5)	
Hospital (already hospitalized)	147/769 (19.1)	129/718 (18.0)	18/51 (35.3)	
General practitioner	68/769 (8.8)	67/718 (9.3)	1/51 (2.0)	
Cardiologist	68/769 (8.8)	65/718 (9.1)	3/51 (5.9)	
Admission unit. n/total n (%)				0.145
ICCU	414/590 (70.2)	390/550 (70.9)	24/40 (60.0)	
ICU	176/590 (29.8)	160/550 (29.1)	16/40 (40.0)	
Clinical presentation at admission				
Heart rate (bpm). mean +/- SD	95.6 +/- 29.6	95.2 +/- 29.7	102.3 +/- 26.6	0.097
n	*769*	*718*	*51*	
SBP (mmHg). mean +/- SD	101 +/- 25	101 +/- 25	102 +/- 25	0.812
n	*770*	*719*	*51*	
DBP (mmHg). mean +/- SD	63 +/- 17	63 +/- 17	62 +/- 19	0.694
n	*769*	*718*	*51*	
Sinus rhythm. n/total n (%)	399/768 (52.0)	368/717 (51.3)	31/51 (60.8)	0.191
Cardiac arrest. n/total n (%)	79/771 (10.3)	76/720 (10.6)	3/51 (5.9)	0.288
Mottling. n/total n (%)	256/660 (38.8)	235/617 (38.1)	21/43 (48.8)	0.162
Blood tests at admission				
Sodium (mmol/l). mean +/- SD	135 +/- 6	135 +/- 6	136 +/- 6	0.057
n	*760*	*709*	*51*	
eGFR (mL/min/1.73 m²). mean +/- SD	49.6 +/- 26.6	50.0 +/- 26.9	43.5 +/- 21.9	0.096
n	*751*	*701*	*50*	
Bilirubin (mg/L). median (IQR)	16 (9 - 29)	16 (10 - 29)	13 (8 - 23)	0.211
n	*544*	*502*	*42*	

Hemoglobin (g/dL). mean +/- SD	12.5 +/- 2.3	12.6 +/- 2.3	11.2 +/- 2.4	< 0.001
n	*754*	*703*	*51*	
Anemia*. n/total n (%)	361/754 (47.9)	321/703 (45.7)	40/51 (78.4)	< 0.001
Arterial blood lactates (mmol/l). median (IQR)	3.0 (2.0- 4.7)	3.0 (2.0 - 4.6)	3.0 (2.0 - 5.3)	0.040
n	*684*	*639*	*45*	
ASAT (IU/L). median (IQR)	90 (39 - 301)	91 (39 - 293)	80 (33 - 482)	0.817
n	*547*	*502*	*45*	
ALAT (IU/L). median (IQR)	59 (27 - 183)	60 (28 - 181)	59 (21 - 208)	0.674
n	*559*	*514*	*45*	
Nt proBNP (pg/mL). median (IQR)	9277 (4052 - 23256)	9277 (3900 - 22149)	33000.0	0.139
n	*224*	*210*	*14*	
BNP (pg/mL). median (IQR)	1150 (477 - 2768)	1153 (468 - 2788)	1025 (484 - 2595)	0.927
n	*264*	*245*	*19*	
Troponin I (µi/L)	0.76 (0.15 – 14.2)	0.68 (0.15 – 14.0)	2.20 (0.35 – 43.0)	0.236
n	*164*	*151*	*13*	
Troponin I-hs (ng/mL)	2.79 (0.11 – 60.0)	3.0 (0.11 – 62.5)	0.52 (0.20 – 10.9)	0.770
n	*207*	*195*	*12*	
Troponin T-hs (ng/mL)	145 (31 – 2174)	156 (33 – 2607)	90 (7 – 300)	0.132
n	*260*	*238*	*22*	
CRP (mg/L). median (IQR)	28 (9 - 69)	27 (9 - 65)	57 (25 - 166)	0.006
n	*406*	*377*	*29*	
Baseline echography				
LVEF (%). mean +/- SD	26.3 +/- 13.4	26.1 +/- 13.3	28.2 +/- 13.5	0.300
n	*763*	*712*	*51*	

TAPSE (mm). mean +/- SD	13.4	+/- 5.0	13.4	+/- 5.1	13.6	+/- 4.6	0.851
n	*259*		*237*		*22*		
PSVtdi (cm/s). median (IQR)	8 (6 - 11)		8 (6 - 11)		10 (7 - 14)		0.228
n	*206*		*194*		*12*		
Severe mitral regurgitation. n/total n (%)	107/733	(14.6)	100/683	(14.6)	7/50	(14.0)	0.901
Severe aortic stenosis. n/total n (%)	36/759	(4.7)	34/708	(4.8)	2/51	(3.9)	1.000
Severe aortic regurgitation. n/total n (%)	10/755	(1.3)	9/704	(1.3)	1/51	(2.0)	0.505

* Men : haemoglobin < 13 g/dL. Women : haemoglobin < 12 g/dL.

ALAT : ALanine AminoTransferase. ASAT : ASpartate AminoTransferase. ICCU : intensive cardiac care unit. ICU : intensive care unit. CRP : C-Reactive Protein. DBP : Diastolic Blood Pressure. eGFR : estimated glomerular filtration rate. IQR : InterQuartile Range. LVEF : Left Ventricular Ejection Fraction. PSVtdi : Peak Systolic Velocity Tissue Doppler Imaging. SBP : Systolic Blood Pressure. SD : Standard Deviation. TAPSE : Tricuspid Annular Plane Systolic Excursion.

Table 4 - In-hospital management / discharge according to the cancer status of the patients.

	Overall (n=772)		No cancer (n=721)		Active Cancer (n=51)		P value
Medications used, n (%)							
Diuretics	633/768	(82.4)	590/717	(82.3)	43/51	(84.3)	0.713
Volume expander	321/767	(41.9)	298/716	(41.6)	23/51	(45.1)	0.627
Dobutamine	632/768	(82.3)	586/717	(81.7)	46/51	(90.2)	0.126
If yes, Maximum dose (mg/kg/min):							0.905
5-10	405/632	(63.7)	377/586	(63.9)	28/46	(60.9)	
10-15	136/632	(21.4)	126/586	(21.4)	10/46	(21.7)	
>15	47/632	(7.4)	43/586	(7.3)	4/46	(8.7)	
Unknown	44/632	(7.5)	40/586	(7.5)	4/46	(8.7)	
Norepinephrine	410/768	(53.4)	373/717	(52.0)	37/51	(72.6)	0.005
If yes, Maximum dose (mg/h):							0.272
< 1	86/410	(21.0)	81/373	(21.7)	5/37	(13.5)	
1-5	215/410	(52.4)	197/373	(52.8)	18/37	(48.6)	
>5	75/410	(18.3)	64/373	(17.2)	11/37	(29.7)	
Unknown	34/410	(8.3)	31/373	(8.3)	3/37	(8.1)	
Epinephrine	95/768	(12.4)	90/717	(12.6)	5/51	(9.8)	0.565
If yes, Maximum dose (mg/h):							0.089
< 1	34/95	(35.8)	31/90	(34.4)	3/5	(60.0)	
1-5	40/95	(42.1)	40/90	(44.4)	0/5	(0.0)	
>5	14/95	(14.7)	12/90	(13.3)	2/5	(40.0)	
Unknown	7/95	(7.4)	7/90	(7.8)	0/5	(0.0)	
Norepinephrine + dobutamine combination	352/768	(45.8)	319/717	(44.5)	33/51	(64.7)	0.005
Levosimendan	57/768	(7.4)	55/717	(7.7)	2/51	(3.9)	0.576
Dopamine	2/717	(0.3)	1/717	(0.1)	1/51	(2.0)	0.128
Isoprenaline	32/768	(4.2)	32/717	(4.5)	0/51	(0.0)	0.262
Antiarrhythmic	298/768	(38.8)	277/717	(38.6)	21/51	(41.2)	0.719
Transfusion	128/767	(16.7)	116/716	(16.2)	12/51	(23.5)	0.175
Fibrinolysis	13/767	(1.7)	13/716	(1.8)	0/51	(0.0)	1.000

Organ replacement therapies, n (%)							
Respiratory support							
Invasive	291/768	(37.9)	268/717	(37.4)	23/51	(45.1)	0.272
Non invasive	199/768	(25.9)	187/717	(26.1)	12/51	(23.5)	0.688
Mechanical circulatory support	143/770	(18.6)	140/719	(19.5)	3/51	(5.9)	0.016
IABP	48/141	(34.0)	48/138	(34.8)	0/3	(0.0)	0.551
Impella	26/141	(18.4)	26/138	(18.8)	0/3	(0.0)	1.000
VA-ECMO	85/141	(59.9)	82/138	(59.0)	3/3	(100.0)	0.274
Renal replacement therapy	122/771	(15.8)	113/720	(15.7)	9/51	(17.7)	0.712
Invasive cardiology, n (%)							
CAG	399/772	(51.7)	379/721	(52.6)	20/51	(39.2)	0.065
CAG result							0.158
Normal	74/772	(18.5)	71/721	(18.7)	3/51	(15.0)	
1 - Mono	80/772	(20.1)	79/721	(20.8)	1/51	(5.0)	
2 - Bi	91/772	(22.8)	85/721	(22.4)	6/51	(30.0)	
3 - Tri	87/772	(21.8)	79/721	(20.8)	8/51	(40.0)	
Unknown	67/772	(16.8)	65/721	(17.2)	2/51	(10.0)	
Culprit lesion	256/318	(80.5)	241/301	(80.1)	15/17	(88.2)	0.408
Any PCI	217/772	(28.1)	204/721	(28.3)	13/51	(25.5)	0.667
Any PCI (even in a second time)	226/772	(29.3)	212/721	(29.4)	14/51	(27.5)	0.767
Right heart catheterisation	121/768	(15.8)	111/717	(15.5)	10/51	(19.6)	0.434
Pace-maker implantation	35/733	(4.8)	31/685	(4.5)	4/48	(8.3)	0.232
Automatic Defibrillator implantation	37/733	(5.1)	36/685	(5.3)	1/48	(2.1)	0.504
Radiofrequency ablation	17/733	(2.3)	17/685	(2.5)	0/48	(0.0)	0.619
Discharge							
LVEF (%), mean +/- SD	35.0	+/- 14.5	34.9	+/- 14.5	35.6	+/- 13.5	0.828
n	*439*		*415*		*24*		
LVEF variation *, mean +/- SD	+ 8.5	+/- 14.2	+ 8.4	+/- 14.2	+ 8.5	+/- 14.4	0.986
n	*436*		*412*		*24*		
Length of stay in ICCU or ICU (days), median (IQR)	11 (7 - 21)		11 (7 - 20)		16 (10 - 28)		0.041
n	*440*		*412*		*28*		

Length of stay in hospital (days), median (IQR)	17 (11 - 28)		17 (11 - 27)		18 (13 - 40)		0.156
n	*436*		*412*		*24*		
Discharge							0.165
Home	171/649	(26.3)	164/607	(27.0)	7/42	16.7	
Rehabilitation	44/649	(6.8)	42/607	(6.9)	2/42	4.8	
Transfered (other center/other department)	214/649	(33.0)	200/607	(32.9)	14/42	(33.3)	
Death	217/649	(33.4)	199/607	(32.8)	18/42	(42.9)	
Other	3/649	(0.5)	2/607	(0.3)	1/42	(2.4)	
Registration on transplant waiting list	40/622	(6.4)	39/585	(6.7)	1/37	(2.7)	0.502

* at discharge compared with admission.

IABP: intra-aortic balloon pump. VA-ECMO: venoarterial-extracorporeal membrane oxygenation. CAG: coronary angiogram. PCI: PCI, percutaneous coronary intervention; LVEF: left ventricular ejection fraction. ICCU: intensive cardiac care unit. ICU: Intensive care unit.

Figure 1. Early (30-day) and long-term (1-year) all-cause mortality by Kaplan-Meier landmark analysis according to the cancer status of the patients