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par

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La mortalité liée à l'insuffisance cardiaque est-elle plus importante que celle liée aux cancers ? Étude française rétrospective sur 5 ans

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RESUME

INTRODUCTION. L'insuffisance cardiaque et les cancers sont des pathologies grevées d'une importante morbi-mortalité. Une étude réalisée il y a vingt ans avait mis en évidence que le diagnostic d'insuffisance cardiaque était associé à une mortalité aussi importante que celui d'une pathologie cancéreuse. Le but de notre étude est d'évaluer, à la lumière des avancées thérapeutiques, si ce constat est toujours d'actualité vingt ans après.

METHODE. Nous avons réalisé une étude française rétrospective, basée sur les données de l'ensemble de la population de patients hospitalisés dans les hôpitaux français en 2013. Parmi ces patients, nous avons étudiés ceux pris en charge pour une insuffisance cardiaque ou un cancer. Nous nous sommes intéressés aux différences de mortalité cardiovasculaire et toutes causes chez ces patients, que le diagnostic d'insuffisance cardiaque ou de cancer ait été établi moins de 6 mois avant l'inclusion (nous avons alors qualifié la pathologie d'active ou aigüe) ou non.

RESULTATS. Parmi les 5,123,193 patients hospitalisés en 2013, 292,335 ont été admis pour une poussée d'insuffisance cardiaque et 442,285 pour un cancer parmi les cancers gastro-intestinaux, pulmonaires, urologiques, gynécologiques, hématologiques et du sein. Les patients insuffisants cardiaques étaient plus comorbides et plus âgés que les patients atteints de cancer. Qu'il s'agisse de pathologies aigues ou chroniques, la mortalité cardiovasculaire des patients insuffisants cardiaques était significativement plus élevée que pour tous les types de cancers pour lesquels elle demeure néanmoins élevée. En termes de mortalité toutes causes, les cancers ont un pronostic significativement moins bon que l'insuffisance cardiaque à l'exception des cancers de la prostate et de la vessie chez l'homme et du cancer du sein chez la femme.

CONCLUSION. Notre étude montre une amélioration du pronostic en termes de mortalité toutes causes dans l'insuffisance cardiaque comparativement aux pathologies cancéreuses. L'insuffisance cardiaque reste cependant grevée d'un pronostic sombre en termes de mortalité cardiovasculaire, de même que les cancers pour lesquels ce mode de décès reste fréquent.

Mots clés. Insuffisance cardiaque, cancer, mortalité cardiovasculaire, mortalité toutes causes, pronostic

ABSTRACT

BACKGROUND. Heart failure (HF) and cancers are two diagnoses associated with a bad prognosis. Some data reported two decades ago that HF was as malignant as cancer. Whether this is still the case remains unknown. The aim of our study was to investigate, twenty years after the first study, the prognosis of heart failure compared to the most common types of cancer in the French population.

METHODS. This French nationwide retrospective study considered all patients hospitalized in French hospitals in 2013 using the PMSI database based on an administrative hospital-discharge system. Among these patients we included all patients admitted for an episode of HF or cancer. We investigated whether there was a difference in cardiovascular and all-cause mortality in patients diagnosed for a recent HF or cancer, defined by a disease diagnosed in the last 6 months. We also studied patients with a non-recent diagnosis.

RESULTS. Of the 5,123,193 patients hospitalized during 2013, 292,335 had an admission for HF and 442,285 for cancer with the most common being gastrointestinal, lung, urologic, breast, gynecologic and hematologic. HF patients had more comorbidities compared to the cancer population and were older. In active (i.e. recent) and chronic diseases, cardiovascular mortality rates were higher in HF compared to any type of cancer. Regarding all-cause mortality, the only cancers that had greater survival rates compared to HF were prostatic and bladder cancers in men and breast cancers in women.

CONCLUSION. Our data show an improvement in the prognosis of heart failure compared to cancers regarding all-cause death. Nevertheless, cardiovascular mortality remains high in both heart failure and cancers.

Keywords. Heart failure, cancer, cardiovascular mortality, all cause deaths, prognosis.

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SERMENT D'HIPPOCRATE

En présence des Maîtres de cette Faculté,
de mes chers condisciples
et selon la tradition d'Hippocrate,
je promets et je jure d'être fidèle aux lois de l'honneur
et de la probité dans l'exercice de la Médecine.

Je donnerai mes soins gratuits à l'indigent,
et n'exigerai jamais un salaire au-dessus de mon travail.

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ne verront pas ce qui s'y passe, ma langue taira
les secrets qui me seront confiés et mon état ne servira pas
à corrompre les mœurs ni à favoriser le crime.

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je rendrai à leurs enfants
l'instruction que j'ai reçue de leurs pères.

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et méprisé de mes confrères
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TABLE DES MATIERES

ABBREVATIONS

ACEi : Angiotensin Converting Enzyme inhibitors

BB : Beta-Blocker

CI : Confidence interval

CNIL : Commission Nationale de l'Informatique et des Libertés

ESC : European Society of Cardiology

HF : Heart Failure

HR : Hazard Ratio

ICD : International Classification of Disease

INCA : Institut National du Cancer

IR : Incidence Rates

LVEF : Left Ventricular Ejection Fraction

MRa : Mineralocorticoid Receptor Antagonist

NYHA : New York Heart Association scale

PEF : Preserved Ejection Fraction

PMSI : Programme de Médicalisation des Systèmes d'Information

REF : Reduced Ejection Fraction

INTRODUCTION

Nowadays in high-income level countries, ageing population and effective treatment of the major acute pathologies led to an increase in the prevalence of chronic diseases such as heart failure. The incidence of heart failure (HF) is increasing in the overall population, mainly in the elderly; this is also the case for most types of cancers. However, the prognostic impact of HF compared most type of cancers at a whole population scale is poorly known.

While heart failure is saw as the Cinderella syndrome, i.e. a diagnosis with a heavy morbi-mortality burden but often underestimated by patients, cancers keep the strong reputation of being one of the worst diseases someone could ever get. Some data[(1)] reported two decades ago that HF was as "malignant" as most common types of cancer (except for lung cancer) and was associated with a similar number of expected life-years loss. Whether this is still the case remains unknown and this is the reason why we decided to lead this study.

I- Heart Failure

A- Definition

HF is defined as the association of symptoms with echocardiography results and biological parameters. The main echocardiography criterion remains the left ventricular ejection function (LVEF). According to the 2012 ESC criterion : LVEF below 35% identified HF with reduced ejection fraction (HF-REF) while LVEF above 50% corresponded to HF with preserved ejection fraction (HF-PEF). LVEF values between 35-50% represented a "grey area" in which most patients had a systolic dysfunction.

The definition of HF according to the LVEF criterion evolved in 2021 with the most recent ESC guidelines that introduced the notion of mildly reduced ejection fraction between 41 and 49 %, reduced if below 40 % and preserved above 50 % .

B- Prevalence

In 2012, approximatively 1-2 % of the adult population in high-income level countries had HF, the prevalence among 70 years old subjects or older rising up to ≥ 10 %. In France, the prevalence of HF in the overall population in 2008 was of 2,3 % representing 1,130,000 persons (CI 95%, 1,039,000 – 1,224,000) [(2)], and increased with age, reaching 15 % in the >85 years old class age. Between 2000 and 2010, HF represented the third cause of mortality (after stroke and myocardial infarction), with a prevalence of 2,3 % of the overall French adult population and 11,9 % among patients over 60 years old.

C- Etiologies

The incidence of HF is increasing every year because of the increase in life expectancy and the prevalence of cardiovascular diseases in these ageing populations, which are precursors of HF.

At least half of the patients with HF have reduced ejection fraction and the main etiologies are: coronary artery diseases (representing two third of patients), myocarditis mainly due to viral infection, alcohol abuse, chemotherapy for cancer and idiopathic dilated cardiomyopathy.

Conversely, HF-PEF population is more heterogenic as it includes HF resulting from valve diseases, pericarditic pathologies, hypertrophic cardiomyopathy, storage disease (cardiac amyloidosis, Fabry disease)... HF-PEF is more common in women of higher age, long history of arterial hypertension, atrial fibrillation and with more comorbidities. The prevalence of HF-PEF remains uncertain because of probably significant levels of underdiagnosis.

It is easy to understand that HF is a major public health issue: patients with HF are generally old and with comorbidities, and thus require multiple types of care (medical visits with several specialists, need for paramedics). But mostly it may be associated with recurrent episodes of acute decompensation, requiring unplanned hospitalization sometimes in intensive

care units. The incidence of hospitalization for HF between 60 and 95 years old was multiplicated by 3 in from 2004 to 2008 [(2)].

HF benefits from regular therapeutic progresses due to important research and the European Society of Cardiology (ESC) guidelines are regularly updated.

D- 2012 ESC guidelines

In France, cares for HF are based on the ESC guidelines. The last edition of HF guidelines was published in 2021, yet in this work, we will discuss 2012 guidelines are they correspond to the guidelines followed for the population of the study.

Beta-Blockers (BB) and Angiotensin Converting Enzyme inhibitors (ACEi) were the first-line therapies for all patients with HF-REF independently of symptoms. An implantable cardioverter-defibrillator was recommended to prevent sudden death in patients with LVEF ≤ 35 % and a life expectancy > 1 year.

The novelty of these 2012 guidelines were the introduction of mineralocorticoid blockers (aldosterone receptor antagonists), ivabradine and mechanical treatments such as resynchronization therapy. Details about the recommendations and their treatment algorithm can be seen in figure 1.

II- Cancer

The French national institute of cancerology named INCA (Institut National du Cancer)[(3-6)] made in 2012 a statement on each cancer in France. The aim was to make a point on the incidence, the prevention and the management of cancer disease. In terms of treatment, it is important to keep in mind that cancer treatment is based on surgery. The main question at the beginning of a treatment is to know if the cancer is localized or diffuse. If a cancer is

accessible for a surgery, the main treatment is a curative surgical resection. If it's not accessible, a neo-adjuvant treatment can be given in order to reduce tumor size and make it eligible for surgery. Radiotherapy is used either as a neo-adjuvant treatment or after surgery to avoid local invasion. The only exceptions are hematologic cancers.

The beginning of the 21th century was marked by the development of new treatments: immunotherapies. Thanks to them, cancer can be seen as a genomic disease characterized by an accumulation of DNA alterations due to mutations. Based on these premises, tumor antigens, which could be recognized as non-self by the immune system, could be used as targets to halt tumor progression. Immunotherapy aims on eradicating malignant cells by using the own defense mechanism. The innate and adaptative immune systems are used for immunotherapy: Natural Killers (NK) cells, eosinophils, basophils and phagocytic cells (including dendritic cells (DCs), neutrophils, macrophages, etc.) for the innate part, and B and T lymphocytes for the adaptative part. The innate immune systems can either kill directly tumor cells or trigger adaptative immune responses.

Several types of immunotherapies successively emerged: the first antitumoral virus against sarcoma was developed in 1863 by Virchow; cancer vaccines-like in melanoma were described by Kawakami and al. in 1995; cytokines therapies were developed in patients with pulmonary metastatic cancers; activation of B cells and production of CD20 cells were used in lymphoma and in ovarian cancers... These few examples show the multiple ways to target tumor cells though activation of the immune system.

This also shows the complexity and the heterogenic situations that can lead to resistance in malignant cells. In 2018, Jerby-Arnon et al. discovered the capacity of melanoma cells to resist to immunotherapy by using T-cells exclusion and immune evasion. This is an example of the complexity of the interaction between the immune system and the tumor, and it demonstrates that the response to a treatment can vary between patients.

The early 2010 was marked by the arrival of a new panel of treatments for most cancers. In the following paragraphs, we will explore these new therapeutic options for the most common cancers in each sex: lung, large bowel and prostate cancer for men; breast, lung, large bowel for women.

A- Lung cancer

a. Epidemiology

The incidence of lung cancer is globally constantly increasing because of the consumption of tobacco, its main risk factor. The incidence in France in 2012 remained high with 39,500 new cases per year with a majority of men: 52.7 for 100,000 persons per year in men and 20.7 for 100,000 in women. The median age was 65 years in each sex.

Lung cancer represents 11% of the overall cancer in French population: in men it ranks second (13% of all cancers) and third in women (8% of all cancers) in terms of incidence.

This cancer remains the first cause of mortality by cancer among all types of cancer (29,100 deaths due to lung cancer, 17,500 due to large bowel cancer and 11,500 due to breast cancer in France in 2011). Death rates increased with age and mostly for men: at the age of 65 years old, mortality rate was four times more important in men compared to women. One-year survival was low, 13% for men and 18% for women.

b. Treatment

There are two categories of lung cancers: small cell or non-small cell cancers. For non-small cells lung cancers, chemotherapies are based on a platinum-based doublet therapy associated with an immune therapy. The choice depends on molecular anomalies such as the expression of PDL-1 or on some genetic mutations (EGFR, ALK and ROS1).

For small cells lung cancer, the prognostic is very low due to a rapid progression of the disease, even under chemotherapy, and the development of chemoresistance. The chemotherapy consists in an association of two platine salts.

In 2012, new oral immunotherapy appeared such as Crizotinib, Afatinib with ASMR levels (Amélioration du Service Rendu) of III and IV respectively.

B- Large Bowel cancer

a. Epidemiology

In 2011, 40,500 new cases of large bowel cancer were diagnosed in France, mostly in men (53 %) with a rate of 36.3 per 100,000 persons per year for men and 24.7 for 100,000 in women. Mean age at the time of diagnosis was 70 years for men and 75 for women. It ranked third between all cancers in men and women (first was prostate and second breast cancer).

In terms of mortality, rates remained high (second cause of death by cancer after lung cancer): 14.4 deaths for 100,000 in men and 8,3 deaths in 100 000 in women with a median age of 75 years for men and 80 for women. Five-year survival was linked with patients' age and the extent of disease.

The incidence remains stable and the mortality is likely decreasing over time due to improvements in screening, treatment and lower surgical mortality rates.

b. Treatment

A chemotherapy by Oxaliplatine, 5-Fluorouracile and folinic acid is generally used. This chemotherapy is even used in patients with local invasion. In 2012, immune therapy by Regorafinib and Aflibercep appeared.

C- Breast cancer

a. Epidemiology

In term of incidence, breast cancer is the most frequent cancer among women in Europe, USA and in France with 53,000 new cases in 2011 representing 33 % of all women cancers and 15% of all cancers whatever the gender. The mean age at diagnosis was 61 years in 2005, with >60 % of women aged between 50 and 74 years. The INCA epidemiologic data concern only extensive cancers.

The prognosis of breast cancer remained good and may vary with age (higher the age, lower the prognosis) and the invasion grade. While the incidence of breast cancer is increasing, its mortality rate decreases over time.

b. Treatment

Chemotherapy includes an anthracycline agent and Paclitaxel. If HER2 receptors are present, Trastuzumab can be used. Hormonotherapy is indicated if hormonal receptors are expressed by the tumor.

Oral immunotherapy appeared in late 2010 with drugs such as Lapatinib, Trastuzumab, Pertuzumab and Everolimus.

D- Prostate cancer

a. Epidemiology

Prostate cancer is the most frequent cancer among men in France and it ranks first in terms of incidence (before lung cancer). In 2011, 71,000 new cases of prostate cancer were diagnosed in France, which represents 34% of the overall incidence of cancers among men. More than 69% patients are diagnosed after 65 years.

Prostate cancer ranked third in terms of mortality due to cancer in men (10% of the deaths due to cancer in men, 6% of deaths due to cancer whatever the gender). Its prognosis was good

with survival rates of 94 and 80% at 1 and 5 years respectively, and may vary with age (increased survival in younger patients).

b. Treatment

Several treatments can be proposed such as surgery, radiotherapy, curie-therapy (considered as internal radiotherapy), cryotherapy and androgenic suppression (surgically or by oral drugs).

METHODS

I- Study design

This French nationwide retrospective study was based on the French data base called « Programme de Médicalisation des Systèmes d'Information » (PMSI). This database contains more than 98% of the French population (67 million people) from birth or immigration to death. It regroups data from hospitalizations in all French healthcare centers, public or private since 2004.

Administrative and medical information such as gender, age, date of admission and discharge, main and associated diagnosis, events during hospitalization and complications are recorded. All the medical procedures are standardized and have a unique code according to the tenth revision of the International Classification of Disease (ICD-10).

Every patient has a unique identifier that guarantees the anonymity of the data and prevents the risk of duplicates. The reliability of PMSI data base has already been assessed in previous studies[7-8].

II- Study population

All patients over 18 years old hospitalized in French hospitals between the 1st of January until the 31st of December 2013 were screened for the study. We analyzed patients admitted for an episode of heart failure or cancer. Each patient included had at least 5 years of follow-up or less if they died within this 5-years period. We aimed to study the difference in cardiovascular and all-cause mortality between HF and the most common cancers, and between recently diagnosed HF, i.e. HF diagnosed within the last 6 months, and active cancer. Based on the AMPLIFY trial[9], we defined a cancer as being active when it has been diagnosed within 6 months and without a previous diagnosis of cancer in the last 18 months before inclusion.

We used ICD-10 codes for each diagnosis. Heart failure is associated with codes I50, I11.0, 13.0, I13.2, J81, R570. LVEF data weren't available by that time in the PMSI database. Myocardial infarction (I21-I23), pulmonary edema (R570, J81), coronary diseases (Z951, Z955) and smoking status (Z72.0, F17) were also collected.

We analyzed the most frequent cancers for each gender: gastrointestinal including colorectal, liver, pancreatic and stomach cancers (ICD-10 codes C16, C8, C19, C20, C22, C25), lung cancers (C34), urologic cancers including prostate and kidney cancers (C61, C64, C65, C67) and hematologic cancers including lymphoma, leukemia, and myeloma (C81, C82, C83, C85, C91, C92, C93, C94, C95, C88, C90) in men; gastrointestinal, lung, gynecologic including ovaries, breast and uterus cancers (C50, C56, C57, C53, C54, C55), breast cancers alone (C50) and hematologic cancers in women. For both genders, we also analyzed metastatic cancer (C77- C80) independently of the primitive cancer.

Comorbidities were defined as the main cardiovascular risk factors and diseases, and organ impairments such as arterial hypertension (I10-I15), diabetes mellitus (E10-E14), obesity (E65, E66), chronic kidney disease (N17-N19), lung disease (J40-J70, J96.1), sleep apnea syndrome (G47.3) and liver diseases (K70-K77).

Patients' information such as demographics, medical history, comorbidities, events during follow-up or hospitalization were obtained at discharge for each hospitalization.

III- Endpoints

Patients were followed until December 31st 2018 for the occurrence of cardiovascular or all-cause death. The endpoints were assessed during follow-up starting from the date of first admission in 2013 until the date of death or last follow-up in the absence of the outcome. Information on outcomes were obtained from the PMSI database.

IV- Statistical analysis

Continuous data were described as mean ± standard deviation. Qualitative variables were described as percentage and frequencies. We used parametric or nonparametric tests as appropriate: the Wilcoxon W and Kruskal-Wallis tests were used for comparing values between two independent groups and the Chi-square test for comparing categorical data.

For the outcome analysis in the cohort, the incidence of death rate (%/year) was estimated using hazard ratios (HRs) with confidence interval (CI) of 95 %. Univariate and multivariate analyses with Cox model were used to identify potential predictors of all-cause death and cardiovascular death. In all analyses, a p value <0.05 was considered statistically significant. All analyses were performed using Stat v 16.0 (Stata Corp).

V- Ethics

All the data are anonymous and protected by professional confidentiality. Since the study was conducted retrospectively, patients weren't involved and, as there was no impact on patients' care, there was no need for ethical approval. The access to PMSI database is controlled and the allowance depends on the "Commission Nationale de l'Informatique et des Libertés" (CNIL). The CNIL is an independent institution in charge of the protection of the freedom in the digital universe, in compliance with the Declaration of Helsinki (authorization number 1897139).

RESULTS

I- Baseline characteristics

A- Overall HF and cancers

Between January the 1st, 2013 and December the 31st, 2018, 5,123,193 patients were screened for this study; 734,620 patients had either an admission for HF or cancer: 292,335 (39.8 %) for HF and 442,285 (60.2 %) for cancer. Flow chart is available in Figure 2.

Baseline characteristics of patients are available in Table 1. In the HF group, mean age was 75.8 ± 13.5 years with a majority of men (56.3 %). We identified fourteen types of cancer, all presented in Table 2 and their prevalence is shown in Figure 3. For convenience, we organized them by most common types and their prevalence is shown Table 3. In the cancer group, mean age varied according to the type of cancer, with a younger age for breast cancers (63.2 ± 13.8 years) and older patients for urologic cancers (71.5 ± 10.5 years). The proportion of men remained higher for the cancers usually found in both genders, i.e. gastro-intestinal, lung and hematologic cancers, except for metastatic cancers (47.4%).

In terms of comorbidities, patients with HF had a substantially greater overall comorbidity burden including arterial hypertension (71.7 % vs 35.4 %, $p < 0.001$), diabetes mellitus (33.6 % vs 13.6%, $p<0.0001$), history of ischemic stroke (4.8 % vs 1.4 %, $p<0.0001$), inflammatory diseases (8.25 % vs 4.58 %, $p<0.0001$) and cognitive impairment (9.18 % vs 2.56 %, $p<0.0001$).

B- Recent HF and active cancers

A total of 313,037 patients were enrolled with either a first diagnosis of HF (119,851 patients, 38,3 %) or a first diagnosis of cancer in the last 6 months (193,186 patients, 61,7%). Flowchart is available Figure 4.

According to Table 4, patients were younger in the cancer group: 68.0 ± 12.8 years versus 73.4 ± 13.7, p < 0,0001 in men, with similar proportion of women. Compared to the cancer group, HF patients had significantly more comorbidities such as arterial hypertension (62.1 % vs 29.6 %, p < 0,0001), diabetes mellitus (27.6 % vs 11.5 %, p < 0,0001), history of ischemic stroke (4.1 % vs 1.1 %, p < 0,0001), inflammatory diseases (5.5 % vs 2.8 %, p < 0,0001) and major organ impairment such as lung disease (21 % vs 8,8 %, p < 0,0001).

The proportions of cancer between the active and the overall cancers populations were similar, as shown in Table 2. In the two groups, the most frequent cancer was colorectal cancer, followed by breast and prostatic cancer.

II- Mortality rates in overall cancers and HF

In terms of cardiovascular death in the overall study population, after adjustment on age, all types of cancers had lower mortality rates in comparison to HF. These results were similar in both genders. Data are presented Table 5.

Regarding all-cause mortality, in men, prostate and bladder cancers were the only cancers displaying lower mortality rates compared to HF: HR 0.775 (0.764 - 0.786), p < 0.0001 in prostate and 0.904 (0.880 – 0.920), p < 0.0001 in bladder cancers. In women, breast and bladder cancers had lower mortality rates compared to HF. No statistical difference was found for lymphoma. Otherwise, as observed in men, all the other types of cancers had higher mortality rates. Survival rates of cancers compared to HF during the five years of follow up can be seen in Figure 5.

In both genders, pancreatic and lung cancers had the highest mortality rates and metastatic cancers ranked third.

III- Mortality rates in active cancers and recent HF

The rates of cardiovascular mortality were lower for all types of cancer compared to HF, after adjustment on age (data are available in Table 6). In both gender, lung cancer had a lower CV mortality rate compared to HF: HR 0. 390 (0.358 – 0.425), p < 0,0001 in men; HR 0.363 (0.317 – 0.416), p < 0,0001 in women. The same results were observed for all other types of cancers, including metastatic cancers, with an HR of 0.310 (0.288 – 0.335), p < 0,001 in men and 0.220 (0.203 – 0.239), p < 0.0001 in women. The most important difference in cardiovascular mortality was observed with colorectal cancers, which had the lowest rate with a HR of 0.182 (0.165 – 0.200), p < 0.0001 in men and of 0.158 (0.141-0.178), p < 0.0001 in women.

Regarding all-cause mortality, after adjustment on age, two cancers had lower mortality rates compared to HF in men: prostate cancer with a HR 0.679 (0.663 – 0.696), p < 0.0001 and bladder cancer with a HR 0.883 (0.857 – 0.910), p < 0,0001. No significant difference was found regarding the mortality rate of breast cancer in men. Otherwise, all the other types of cancers had higher all-cause mortality rates compared to HF.

In women, breast cancer was the only cancer with a lower all-cause mortality rate (HR 0.745 (0.726 – 0.764), p < 0.0001. No statistic difference was found for bladder, myeloma and lymphoma cancers. All the other types of cancers had higher all-cause mortality rates compared to HF.

DISCUSSION

Our nationwide study indicates that in terms of cardiovascular mortality, HF has a lower prognosis than any type of cancer even metastatic ones. However, regarding all-cause mortality, most types of cancers have a higher rate of mortality compared to HF. These results are similar when the disease, i.e. HF or cancer, is considered recent/active.

Our data are comparable to the ones reported by Stewart and al. twenty years earlier[1]. This study had population baseline characteristics and a methodology equivalent to ours. It was led in Scotland and enrolled patients admitted for HF or cancer in 1991 with 5 years of follow-up using data collected in a nationwide database. Besides the differences in gender, i.e. more women with HF in the Scottish study (53 % versus 44 % in our study), patients had a similar age (71 years old of median age in men with HF in the Scottish study versus 73.4 years old in our, 62 years old in women with breast cancer in the previous study versus 63.2 years old in our) and the more frequent cancers were the same than in our population. Further information about comorbidities or associated diseases weren't available (probably because they were not displayed at discharge by that time) but as the baseline characteristics are similar, we can compare the evolution of the prognosis of these diseases in terms of all-cause mortality (as cardiovascular mortality was not studied)

It is interesting to note that twenty years ago, because of high mortality rates in HF, it was qualified "more malignant" that any cancer, with the exception of lung cancer for both genders and ovarian for women. In light of our results, this is no longer the case. Survival curves can be seen Figure 6.

This study shows that HF patients are older but also likely more comorbid than cancer patients, with higher rates of arterial hypertension, diabetes mellitus, dyslipidemia, chronic lung disease, chronic kidney disease and inflammatory diseases. Some comorbidities can be

linked to a higher age, such as poor nutritional status and cognitive impairment, but others are independent such as smoking status or alcohol-related diagnoses. The two populations are different with, in one hand, HF patients that are likely older and with several pathologies and, in the other hand, cancer patients that are younger and without other associated diseases. Thus, the prognosis might be linked, at least partly, to the burden of this multi-pathogenic state in HF patients and more to the prognosis of cancer itself in cancer patients. Even so, the cardiovascular status in cancers patient can't be ignored.

If we take the example of a cancer developing in patients at cardiovascular risk, e.g. lung cancer, cardiovascular mortality was lower than in HF patients but still remarkable. This leads to the conclusion that mortality in lung cancer may be explained mostly by the aggressive development of the tumor with all its consequences (such as respiratory failure, general deterioration status, thromboembolism complications, among others) but also by the cardiovascular status. Even if the cardiovascular mortality rate is lower, the number of cardiovascular deaths is far to be negligible (18 414 deaths). Indeed, by having some cardiovascular risk factors and by being at risk of developing cardiovascular disease due to those risk factors but also from the side-effect of some chemotherapies, the cancer population can be considered at high cardiovascular risk and the screening of cardiovascular disease should be a part of the routine care.

As shown in our study, the prognosis of HF patients is improving with time. This questions directly the impact of therapeutic strategies. In cancers, treatments are given in hospital: most of chemotherapies can only be administered intravenously and have to be displayed by the hospitals pharmacies, and radiotherapy is only possible in a health structure. In such conditions, management of treatments and patients' compliance are under medical control. With HF, the situation is completely different. With the exception of acute events, patients are managed out of office, and most of treatments are drugs that need to be taken

daily, supervised by regular medical follow-ups aiming at checking drug tolerance and the eventual onset of symptoms.

In 2015, a French national observational study[10] investigated the rate of healthcare utilization in HF patients diagnosed between 2011 and 2014. Based on the PMSI database, 499 296 HF patients were included in the study. In terms of healthcare utilization, 95% of the patients had at least one annual medical visit with their general practitioner and only 42% with a cardiologist. Regarding the medical treatment, 64% had at least once a loop diuretic, 44% an angiotensin-converting enzyme inhibitor, 65% a beta-blocker and 68 % a renin-angiotensin system inhibitor (RASI). Approximately one half of the patients had a beta-blocker and a RASI combination, for another third of patients an aldosterone antagonist was added. This means that according to the 2012 ESC guidelines, only 50 % of the French HF patients were considered correctly treated based on the recommendations for the treatments in HF-REF. These findings are consistent with another French study[11] that aimed at studying the use of recommended medications in myocardial infarction patients in 2015 in French hospitals, and also similar to a study led in UK[12]. The latter study showed that, though less than half of HF patients had at least one visit with a cardiologist in the year, more than 95 % had one with a general practitioner.

By being followed by a general practitioner and also by others healthcare practitioners, patients can benefit from a holistic approach such as the screening of cancers or early stages diagnoses which can lead to the decrease of the overall mortality in the HF population.

Of note, we conducted our study based on data from 2013, before the arrival of new major therapeutics in HF such as glifozins and the Sacubitril/ Valsartan association that are now recommended in first line therapy of HF patients with reduced LVEF (recommendation class I in the 2021 ESC guidelines). It would be interesting to lead a new study in few years in order to study the evolution of prognosis of HF following the arrival of such therapies.

Even if the prognosis of HF is improving with time, it still remains poor and the diagnosis of HF continues to be associated with a heavy burden. Public health policies are developed for the prevention and screening of cancers and information of the general population is improving. HF could also benefit from such policies.

The main strength of our study is that it is a real-world observational nationwide study with a very large sample size. Reliability of PMSI database has already been assessed in multiple previous studies. Yet, it has also several limitations. By being a retrospective cohort study, missing information may be an important confounding factor.

First, we included cancer patients with no information about their stage, except when the cancer was metastatic. In this particular case, we didn't know neither the original localization of the tumor nor the localization of the metastases. We didn't have data regarding the LVEF in HF patients and only little information regarding the etiology of HF (e.g. in the HF group more than 60% of the patients had coronary artery disease but it may not always be the cause of HF).

Second, PMSI database does not include any information on treatment, neither for cancer (medical, surgical, radiation) nor for HF (medical, resynchronization therapy, implantable cardioverters). Of note, cancer treatments can affect the risk of HF, e.g left ventricular function impairment due to platine salts.

Last, our study only included in-hospital events so patients with HF diagnosed outside of French hospitals and only treated by general practitioners or cardiologists were not included, though the number of these patients may be limited. The same applies for out-of-hospital deaths. This could lead to an underestimation of the incidence of HF and of its mortality rate. Yet, as more than 86 % of the French population die in-hospital or in a healthcare center we

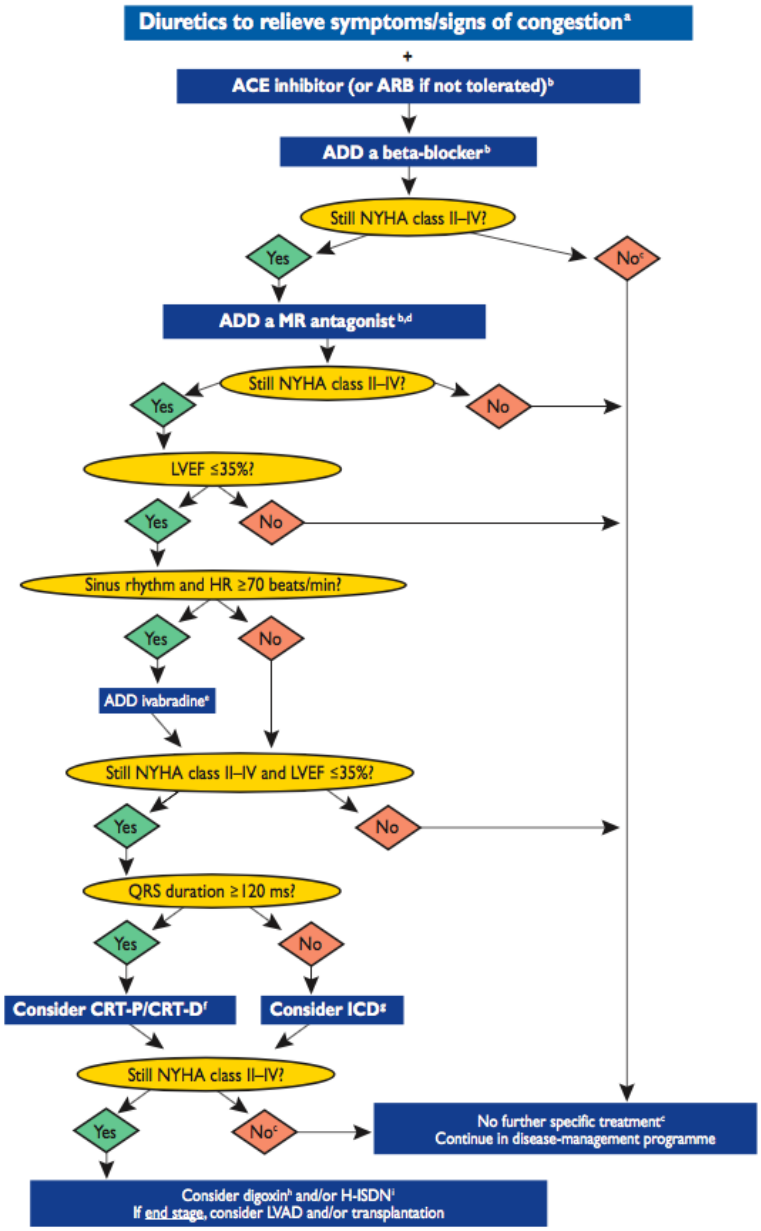
considered the part of missing data negligible. Misclassification of the diagnosis based on the ICD code is also possible, but any misclassification can be considered negligible and the French PMSI database has already been used and validated for similar studies.

CONCLUSION

This nationwide study showed that HF is more “malignant” than all cancers in terms of cardiovascular mortality. Yet, regarding all-cause mortality, the situation changed within twenty years with a higher mortality rate in nearly all cancers with the exception of prostate and bladder in men and breast in women. The prognosis in HF patients improved with time suggesting an improvement of the efficacy of therapies despite a well-described insufficient application of recommended guidelines. In cancer patients, cardiovascular mortality is not negligible, advocating an improvement in the screening of cardiovascular diseases that might be underestimated in this population.

TABLE AND FIGURES

Figure 1. 2012 ESC guidelines for treatment of chronic heart failure with systolic dysfunction



ACE = angiotensin-converting enzyme; ARB = angiotensin receptor blocker; CRT-D = cardiac resynchronization therapy defibrillator; CRT-P = cardiac resynchronization therapy pacemaker; H-ISDN = hydralazine and isosorbide dinitrate; HR = heart rate; ICD = implantable cardioverter-defibrillator; LBBB = left bundle branch block; LVAD = left ventricular assist device; LVEF = left ventricular ejection fraction; MR antagonist = mineralocorticoid receptor antagonist; NYHA = New York Heart Association

The 2012 guidelines introduced a therapeutic intensification strategy based on LVEF and patients' symptoms (using NYHA scale). All HF patient's should receive an ACE inhibitors (ACEi) and a beta-blocker (BB). If the patient remains symptomatic (NYHA ≥ 2) on BB and ACEi therapies and has LVEF ≤ 35%, a mineralocorticoid/ aldosterone receptor antagonists (MRa) needs to be added. These recommendations extend the use of MRa as the second line of treatment. If the patient remains symptomatic (NYHA ≥ 2) on BB, ACEi and MRa therapies and has sinus rhythm with a heart rate ≥ 70 bpm, Ivabradine should be added.

If the patient is still symptomatic despite of all the previous therapies, a mechanical treatment such as a cardiac resynchronization therapy should be considered depending on QRS morphology and duration, heart rhythm (sinus rhythm or atrial fibrillation) and LVEF.

In case of HF-PEF, the same drugs can be used but with a lower level of evidence

Figure 2. Flow chart of the study patients for the analysis of the incidence of cardiovascular or all cause deaths according to history of cancer or heart failure during all the follow up period.

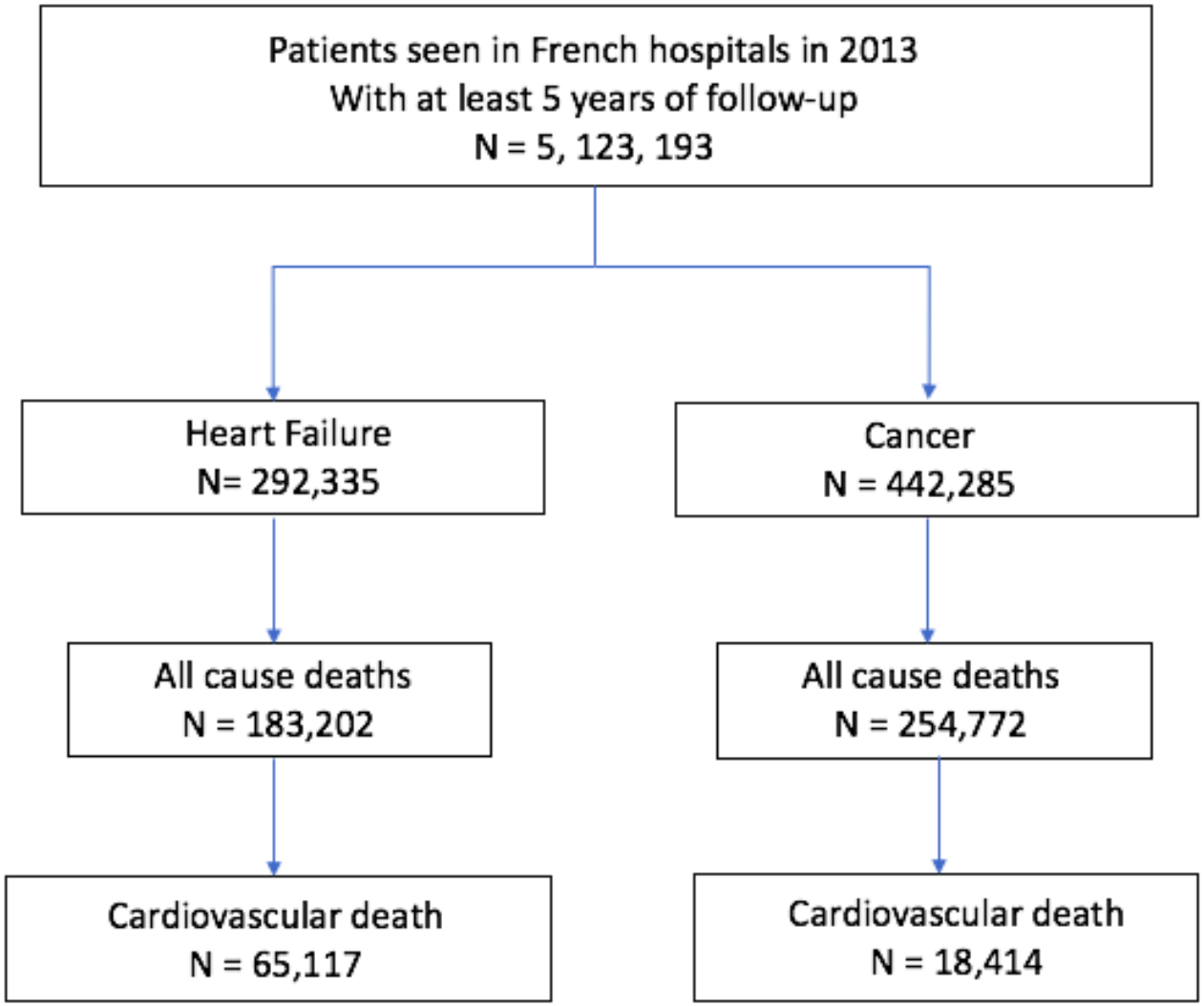


Table 1. Characteristics of all the patients admitted for HF or cancer according to gender in France in 2013

	Men				Women			
	Heart failure (n=164601)	**Previous cancer (n=244609)**	**p**	**Total (n=409210)**	**Heart failure (n=127734)**	**Previous cancer (n=197676)**	**p**	**Total (n=325410)**
Age (years), mean±SD	73.4±13.7	68.0±12.8	<0.0001	70.0±13.4	79.3±13.0	66.1±14.7	<0.0001	72.7±15.7
Arterial hypertension, n (%)	114460 (69.5)	93606 (38.3)	<0.0001	208066 (50.8)	95109 (74.5)	63225 (32.0)	<0.0001	158334 (48.6)
Diabetes mellitus, n (%)	58656 (35.6)	39153 (16.0)	<0.0001	33734 (23.9)	39726 (31.1)	20967 (10.6)	<0.0001	60693 (18.6)
History of pulmonary edema, n (%)	5063 (7.8)	0 (0.0)	<0.0001	5063 (1.2)	9485 (7.4)	0 (0.0)	<0.0001	9485 (0.3)
Valve disease, n (%)	30225 (24.7)	5594 (2.3)	<0.0001	35819 (8.7)	28118 (22.0)	3787 (1.9)	<0.0001	31905 (9.8)
Aortic stenosis, n (%)	12934 (7.9)	2359 (1.0)	<0.0001	15293 (3.7)	12365 (9.7)	1203 (0.6)	<0.0001	13568 (4.1)
Aortic regurgitation, n (%)	5798 (3.5)	1188 (0.5)	<0.0001	6986 (1.7)	4722 (3.7)	780 (0.4)	<0.0001	5502 (1.7)
Mitral regurgitation, n (%)	14199 (8.6)	1850 (0.8)	<0.0001	16049 (3.9)	13080 (10.2)	1474 (0.7)	<0.0001	14554 (4.5)
Dilated cardiomyopathy, n (%)	40705 (24.7)	0 (0.0)	<0.0001	40705 (9.9)	23927 (18.7)	19 (0.0)	<0.0001	23946 (7.3)
Coronary artery disease, n (%)	100797 (61.2)	21801 (8.9)	<0.0001	122598 (29.9)	53144 (41.6)	6493 (3.3)	<0.0001	59637 (18.3)
Previous MI, n (%)	17136 (10.4)	2255 (0.9)	<0.0001	19391 (4.7)	10163 (8.0)	771 (0.4)	<0.0001	10934 (3.4)
Previous PCI, n (%)	26800 (16.3)	4459 (1.8)	<0.0001	31259 (7.6)	10223 (8.0)	916 (0.5)	<0.0001	11139 (3.4)
Previous CABG, n (%)	5597 (3.4)	484 (0.2)	<0.0001	6081 (1.4)	1544 (1.2)	80 (0.0)	<0.0001	1624 (0.5)
Vascular disease, n (%)	63808 (38.8)	25382 (10.4)	<0.0001	89190 (21.8)	31295 (24.5)	6701 (3.4)	<0.0001	12574 (8.9)
Atrial fibrillation, n (%)	69632 (42.3)	23003 (9.4)	<0.0001	92635 (22.7)	59684 (46.7)	10948 (5.5)	<0.0001	70632 (21.7)
Previous pacemaker or ICD, n (%)	31823 (19.3)	5855 (2.4)	<0.0001	37678 (9.2)	16408 (12.8)	2251 (1.1)	<0.0001	18659 (5.7)
Ischemic stroke, n (%)	7647 (4.6)	4172 (1.7)	<0.0001	11819 (2.8)	6414 (5.0)	2215 (1.1)	<0.0001	8629 (2.6)
Intracranial bleeding, n (%)	3209 (1.9)	2459 (1.0)	<0.0001	5668 (1.4)	2394 (1.9)	1339 (0.7)	<0.0001	3733 (1.1)
Smoker, n (%)	26232 (15.9)	28770 (11.8)	<0.0001	83772 (20.5)	6424 (5.0)	11707 (5.9)	<0.0001	18131 (5.5)
Dyslipidemia, n (%)	60573 (36.8)	39236 (16.0)	<0.0001	99809 (24.4)	34505 (27.7)	23176 (11.7)	<0.0001	57681 (17.7)
Obesity, n (%)	35798 (21.7)	20933 (8.6)	<0.0001	56731 (13.8)	28098 (22.0)	18628 (9.4)	<0.0001	46726 (14.3)
Alcohol related diagnoses, n (%)	18390 (11.2)	22989 (9.4)	<0.0001	41379 (10.1)	4134 (3.2)	5449 (2.8)	0.98	9580 (2.9)
Chronic kidney disease, n (%)	24415 (14.8)	8522 (3.5)	<0.0001	32937 (8.0)	18524 (14.5)	4352 (2.2)	<0.0001	22876 (7.0)
Lung disease, n (%)	47932 (29.1)	35048 (14.3)	<0.0001	82980 (20.3)	32641 (25.6)	16186 (8.2)	<0.0001	48827 (15.0)
Sleep apnea syndrome, n (%)	20014 (12.2)	9487 (3.9)	<0.0001	29501 (7.2)	8105 (6.3)	3341 (1.7)	<0.0001	11446 (3.5)
COPD, n (%)	33748 (20.5)	24027 (9.8)	<0.0001	57775 (14.1)	16874 (13.2)	7755 (3.9)	<0.0001	24629 (7.5)
Liver disease, n (%)	11444 (7.0)	15067 (6.2)	<0.0001	26511 (6.5)	6185 (4.8)	6824 (3.5)	<0.0001	13009 (3.9)
Thyroid diseases, n (%)	11541 (7.0)	7501 (3.1)	<0.0001	19042 (4.6)	23207 (18.2)	18856 (9.5)	<0.0001	42063 (12.9)
Inflammatory disease, n (%)	12850 (7.8)	11291 (4.6)	<0.0001	24141 (5.9)	11281 (8.8)	9005 (4.6)	<0.0001	20286 (6.2)
Anemia, n (%)	28290 (17.2)	40007 (16.4)	<0.0001	68297 (16.7)	28082 (22.0)	32784 (16.6)	<0.0001	60866 (18.7)
Poor nutrition, n (%)	11947 (7.3)	20288 (8.3)	<0.0001	32235 (7.8)	15270 (12.0)	15147 (7.7)	<0.0001	30417 (9.3)
Cognitive impairment, n (%)	11177 (6.8)	6348 (2.6)	<0.0001	17525 (4.3)	15678 (12.3)	4986 (2.5)	<0.0001	20664 (6.3)
Illicit drug use, n (%)	577 (0.4)	743 (0.3)	0.01	1320 (0.3)	277 (0.2)	339 (0.2)	0.004	616 (0.2)
Death during follow-up, n (%)	95265 (57.8)	150316 (61.4)	<0.0001	245581 (60)	87937 (68.8)	104456 (52.8)	<0.0001	192393 (59.1)
Cardiovascular death, n (%)	33861 (20.6)	21251 (8.7)	<0.0001	55112 (13.5)	31256 (24.5)	7550 (3.8)	<0.0001	38806 (11.9)

Values are n (%) or mean ± SD. CI = confidence intervall ; COPD = chronic obstructive pulmonary disease; HR = hazard ratio ; ICD = implantable cardioverter defibrillator ; IQR = interquartile range ; MI = myocardial infarction ; PCI = percutaneous coronary intervention ; CABG = Coronary Artery Bypass Graft ; COPD = Chronic Obstructive Pulmonary Diseas

Table 2. Type of cancers seen in patients in French hospitals in 2013

	Active cancers (n= 193,186)	Overall population with cancer (n = 442,285)
Age, years	67.3±13.28	67.4±13.6
Gender (male)	106,415 (55.08)	244,609 (55.31)
Breast cancer	26,612 (13.78)	66,105 (14.95)
Ovarian cancer	3419 (1.77)	10,313 (2.33)
Uterine cancer	4603 (2.38)	11,217 (2.54)
Prostatic cancer	18,532 (9.59)	49,250 (11.14)
Renal cancer	4608 (2.39)	12,628 (2.86)
Bladder cancer	10,886 (5.63)	31,375 (7.09)
Gastric cancer	4255 (2.20)	9444 (2.14)
Colorectal cancer	38,081 (19.71)	92,118 (20.83)
Liver cancer	5462 (2.83)	12,219 (2.76)
Pancreas cancer	6661 (2.1)	12,530 (2.83)
Lung cancer	21,436 (11.10)	44,059 (9.96)
Lymphoma	6301 (3.26)	19,165 (4.33)
Leukemia	6351 (3.29)	16,716 (3.78)
Myeloma	4198 (2.17)	13,119 (2.97)
Metastatic cancer	47,900 (24.79)	131,121 (29.65)

Values are n (%) or mean±SD.

Figure 3. Prevalence of cancer types seen in patients with active cancer and in the overall population of cancer

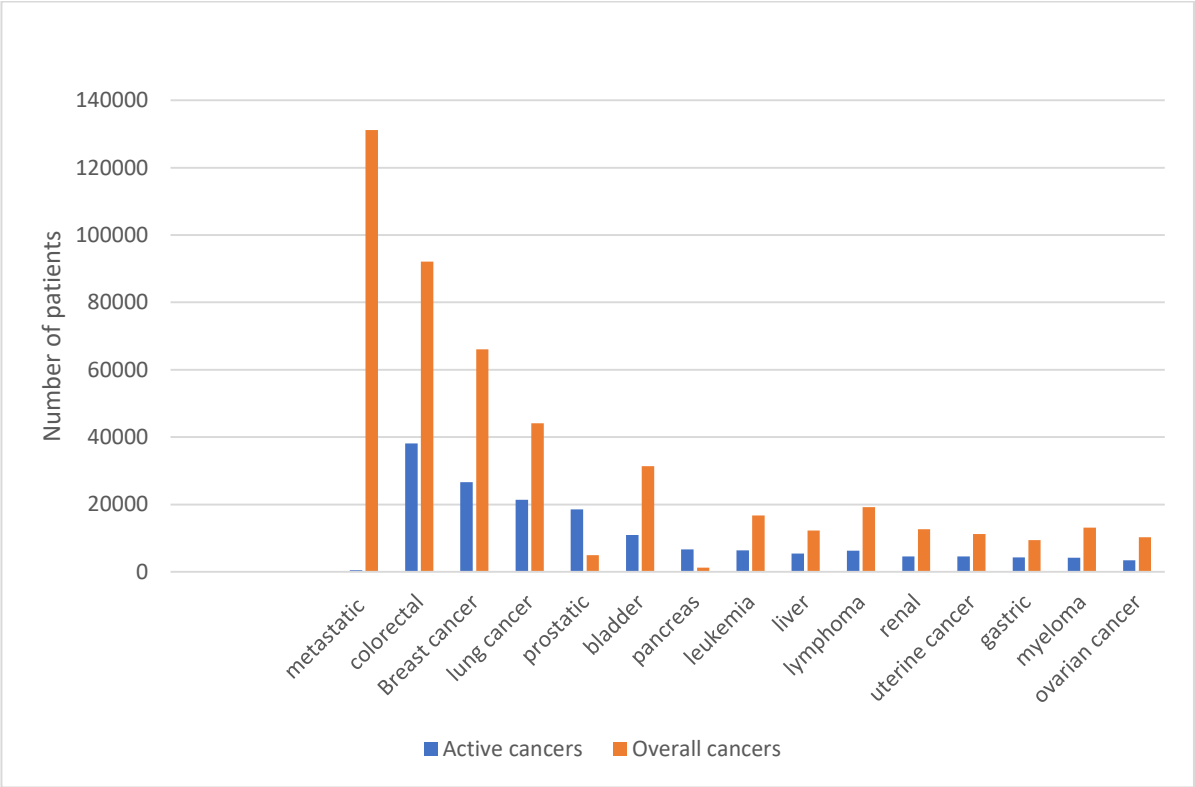


Table 3. Demographic profile of all patients admitted for HF or the most common types of cancers in French hospitals in 2013

	Number of cases	Age (years)	Men
Heart failure	292,335	75.8±13.5	56.3 %
Gastrointestinal cancer	92,118	68.4±12.1	60.1 %
Lung cancer	44,059	65.4±10.8	69.5 %
Urologic cancer	88,667	71.5±10.5	90 %
Breast cancer	66,105	63.2±13.8	1.3%
Gynecologic cancer	83,367	63.6±13.7	1 %
Hematologic cancer	45,631	67.8±15.2	56.9 %
Metastatic cancer	131,121	65.3±13.0	47.4 %

Values are number or mean ±SD.

Figure 4. Flow chart of the study patients for the analysis of the incidence of cardiovascular or all cause deaths according to history of active cancer or HF

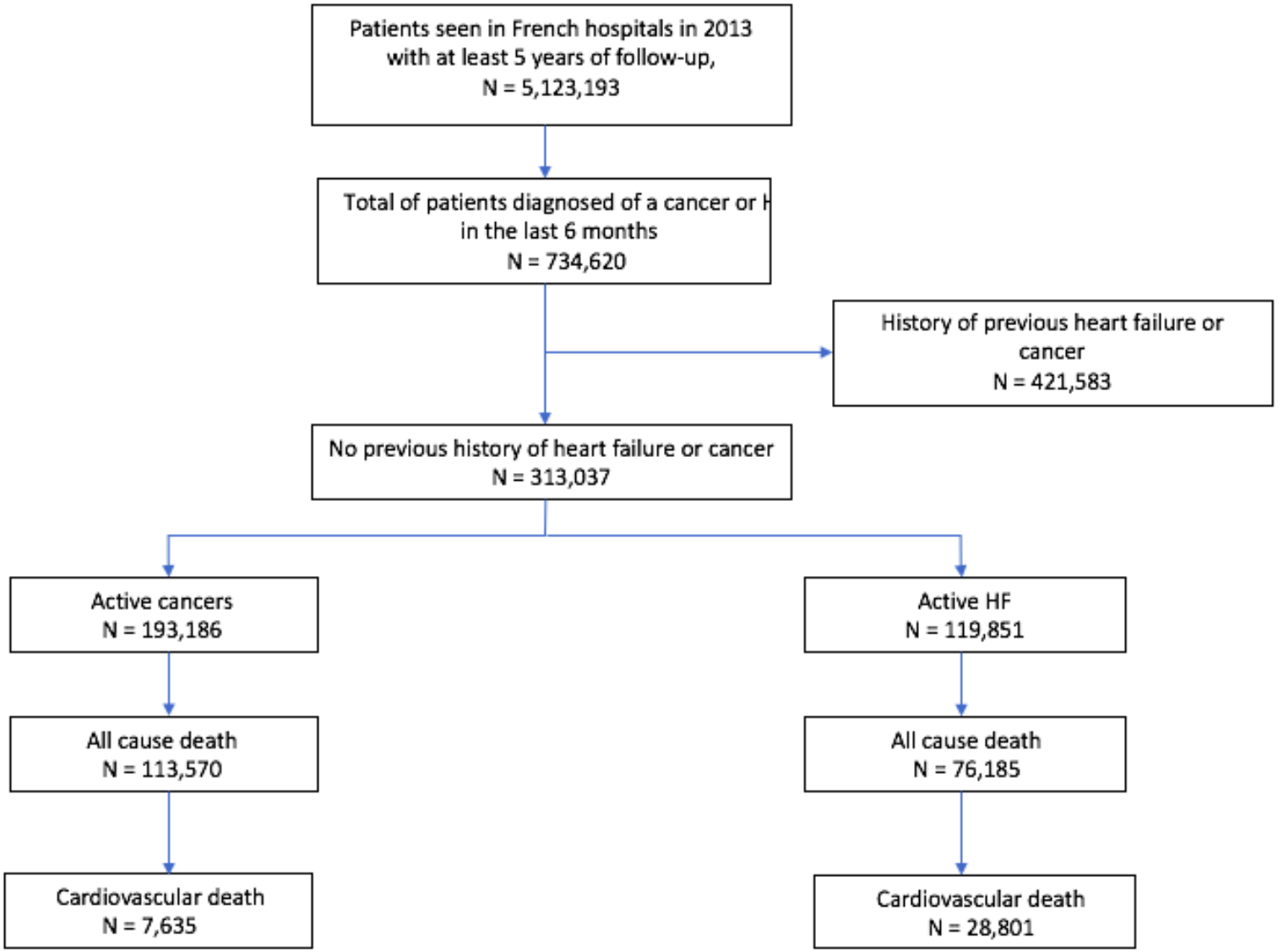


Table 4. Characteristics of the patients diagnosed for recent HF or cancer according to gender in France in 2013

	Men				Women			
	Heart failure (n=65253)	**Previous cancer (n=106415)**	**p**	**Total (n=171668)**	**Heart failure (n=54598)**	**Previous cancer (n=86771)**	**p**	**Total (n=141369)**
Age (years), mean±SD	73.4±13.7	68.0±12.8	<0.0001	70.0±13.4	80.1±12.8	66.4±15.0	<0.0001	71.7±15.7
Arterial hypertension, n (%)	38799 (59.5)	33115 (31.1)	<0.0001	71914 (41.9)	35636 (65.3)	24145 (27.8)	<0.0001	59781 (42.3)
Diabetes mellitus, n (%)	19435 (29.8)	14299 (13.4)	<0.0001	33734 (19.7)	13709 (25.1)	7912 (9.1)	<0.0001	21621 (15.3)
History of pulmonary edema, n (%)	5063 (7.8)	0 (0.0)	<0.0001	5063 (2.9)	4185 (7.7)	0 (0.0)	<0.0001	4185 (3.0)
Valve disease, n (%)	9579 (14.7)	1741 (1.6)	<0.0001	11320 (6.6)	9598 (17.6)	1280 (1.5)	<0.0001	10878 (7.7)
Aortic stenosis, n (%)	4342 (6.7)	775 (0.7)	<0.0001	5117 (3.0)	4427 (8.1)	398 (0.5)	<0.0001	4825 (3.4)
Aortic regurgitation, n (%)	1631 (2.5)	358 (0.3)	<0.0001	1989 (1.2)	1396 (2.6)	251 (0.3)	<0.0001	1647 (1.2)
Mitral regurgitation, n (%)	3888 (6.0)	548 (0.5)	<0.0001	4436 (2.6)	3997 (7.3)	494 (0.6)	<0.0001	4491 (3.2)
Dilated cardiomyopathy, n (%)	12173 (18.7)	0 (0.0)	<0.0001	12173 (7.1)	7367 (13.5)	6 (0.0)	<0.0001	7373 (5.2)
Coronary artery disease, n (%)	34613 (53.0)	7194 (6.8)	<0.0001	41807 (24.4)	18314 (33.5)	2266 (2.6)	<0.0001	20580 (14.6)
Previous MI, n (%)	6698 (10.3)	699 (0.7)	<0.0001	7397 (4.3)	4180 (7.7)	250 (0.3)	<0.0001	4430 (3.1)
Previous PCI, n (%)	9007 (13.8)	1456 (1.4)	<0.0001	10463 (6.1)	3514 (6.4)	335 (0.4)	<0.0001	3849 (2.7)
Previous CABG, n (%)	1180 (1.8)	181 (0.2)	<0.0001	1361 (0.8)	368 (0.7)	26 (0.0)	<0.0001	394 (0.3)
Vascular disease, n (%)	19822 (30.4)	8423 (7.9)	<0.0001	28245 (16.5)	10326 (18.9)	2248 (2.6)	<0.0001	12574 (8.9)
Atrial fibrillation, n (%)	23781 (36.4)	7825 (7.4)	<0.0001	31606 (18.4)	22646 (41.5)	4213 (4.9)	<0.0001	26859 (19.0)
Previous pacemaker or ICD, n (%)	8352 (12.8)	1981 (1.9)	<0.0001	10333 (6.0)	4601 (8.4)	809 (0.9)	<0.0001	5410 (3.8)
Ischemic stroke, n (%)	2548 (3.9)	1406 (1.3)	<0.0001	3954 (2.3)	2334 (4.3)	771 (0.9)	<0.0001	3105 (2.2)
Intracranial bleeding, n (%)	1032 (1.6)	820 (0.8)	<0.0001	1852 (1.1)	829 (1.5)	430 (0.5)	<0.0001	1259 (0.9)
Smoker, n (%)	8059 (12.4)	10856 (10.2)	<0.0001	18915 (11.0)	2081 (3.8)	4550 (5.2)	<0.0001	6631 (4.7)
Dyslipidemia, n (%)	17780 (27.2)	12965 (12.2)	<0.0001	30745 (17.9)	10858 (19.9)	8155 (9.4)	<0.0001	19013 (13.4)
Obesity, n (%)	10201 (15.6)	6821 (6.4)	<0.0001	17022 (9.9)	8504 (15.6)	6495 (7.5)	<0.0001	14999 (10.6)
Alcohol related diagnoses, n (%)	5821 (8.9)	9001 (8.5)	0.001	14822 (8.6)	1328 (2.4)	2112 (2.4)	0.98	3440 (2.4)
Chronic kidney disease, n (%)	6124 (9.4)	2212 (2.1)	<0.0001	8336 (4.9)	5252 (9.6)	1205 (1.4)	<0.0001	6457 (4.6)
Lung disease, n (%)	14690 (22.5)	11587 (10.9)	<0.0001	26277 (15.3)	10494 (19.2)	5459 (6.3)	<0.0001	15953 (11.3)
Sleep apnea syndrome, n (%)	4928 (7.6)	2954 (2.8)	<0.0001	7882 (4.6)	1920 (3.5)	988 (1.1)	<0.0001	2908 (2.1)
COPD, n (%)	9654 (14.8)	8089 (7.6)	<0.0001	17743 (10.3)	4954 (9.1)	2655 (3.1)	<0.0001	7609 (5.4)
Liver disease, n (%)	3638 (5.6)	5477 (5.1)	0.0001	9115 (5.3)	2135 (3.9)	2256 (2.6)	<0.0001	4391 (3.1)
Thyroid diseases, n (%)	3017 (4.6)	2234 (2.1)	<0.0001	5251 (3.1)	7420 (13.6)	6399 (7.4)	<0.0001	13819 (9.8)
Inflammatory disease, n (%)	3364 (5.2)	2980 (2.8)	<0.0001	6344 (3.7)	3273 (6.0)	2399 (2.8)	<0.0001	5672 (4.0)
Anemia, n (%)	7361 (11.3)	11723 (11.0)	0.09	19084 (11.1)	8177 (15.0)	9488 (10.9)	<0.0001	17665 (12.5)
Poor nutrition, n (%)	3442 (5.3)	6333 (6.0)	<0.0001	9775 (5.7)	4999 (9.2)	4643 (5.4)	<0.0001	9642 (6.8)
Cognitive impairment, n (%)	3807 (5.8)	2254 (2.1)	<0.0001	6061 (3.5)	5968 (10.9)	1974 (2.3)	<0.0001	7942 (5.6)
Illicit drug use, n (%)	163 (0.2)	261 (0.2)	0.85	424 (0.2)	72 (0.1)	104 (0.1)	0.53	176 (0.1)
Death during follow-up, n (%)	39136 (60.0)	66898 (62.9)	<0.0001	106034 (61.8)	37049 (67.9)	46672 (53.8)	<0.0001	83721 (59.2)
Cardiovascular death, n (%)	14175 (21.7)	4676 (4.4)	<0.0001	18851 (11.0)	14626 (26.8)	2959 (3.4)	<0.0001	17585 (12.4)

Values are n (%) or mean ± SD. CI = confidence intervalle ; COPD = chronic obstructive pulmonary disease; HR = hazard ratio ; ICD = implantable cardioverter defibrillator ; IQR = interquartile range ; MI = myocardial infarction ; PCI = percutaneous coronary intervention ; CABG = Coronary Artery Bypass Gr

Table 5. Age-adjusted HR for all-cause death and cardiovascular mortality according to gender (vs HF as reference) in the overall cancer population

	Cardiovascular death				All-cause death			
	Men		Women		Men		Women	
	Age-adjusted HR (95%CI)	p	Age-adjusted HR (95%CI)	p	Age-adjusted HR (95%CI)	p	Age-adjusted HR (95%CI)	p
Recent cancer	0.282 (0.276-0.288)	<0.0001	0.242 (0.235-0.249)	<0.0001	1.157 (1.148-1.167)	<0.0001	0.998 (0.989-1.008)	0.76
Previous lung cancer	0.417 (0.394-0.442)	<0.0001	0.379 (0.344-0.417)	-	3.115 (3.071-3.160)	<0.0001	3.175 (3.107-3.246)	<0.0001
Previous gastric cancer	0.271 (0.236-0.311)	<0.0001	0.245 (0.202-0.297)	<0.0001	2.280 (2.214-2.347)	<0.0001	1.884 (1.806-1.966)	<0.0001
Previous liver cancer	0.429 (0.388-0.474)	<0.0001	0.349 (0.286-0.428)	<0.0001	3.082 (3.010-3.155)	<0.0001	3.327 (3.194-3.465)	<0.0001
Previous colorectal cancer	0.211 (0.199-0.223)	<0.0001	0.190 (0.177-0.204)	<0.0001	1.142 (1.124-1.159)	<0.0001	1.074 (1.054-1.095)	<0.0001
Previous pancreas cancer	0.334 (0.290-0.384)	<0.0001	0.264 (0.224-0.311)	<0.0001	3.608 (3.512-3.706)	<0.0001	3.365 (3.267-3.466)	<0.0001
Previous prostatic cancer	0.245 (0.235-0.255)	<0.0001	-	<0.0001	0.775 (0.764-0.786)	<0.0001	-	-
Previous renal cancer	0.275 (0.249-0.304)	<0.0001	0.240 (0.204-0.282)	<0.0001	1.220 (1.185-1.255)	<0.0001	1.145 (1.095-1.197)	<0.0001
Previous bladder cancer	0.250 (0.236-0.264)	<0.0001	0.189 (0.164-0.218)	-	0.904 (0.888-0.920)	<0.0001	0.911 (0.876-0.947)	<0.0001
Previous myeloma	0.271 (0.243-0.302)	<0.0001	0.288 (0.257-0.322)	<0.0001	1.276 (1.238-1.314)	<0.0001	1.228 (1.188-1.270)	<0.0001
Previous leukemia	0.339 (0.311-0.370)	<0.0001	0.302 (0.270-0.336)	<0.0001	1.450 (1.414-1.487)	<0.0001	1.382 (1.340-1.426)	<0.0001
Previous lymphoma	0.254 (0.232-0.279)	<0.0001	0.230 (0.206-0.257)	<0.0001	1.153 (1.123-1.184)	<0.0001	0.971 (0.940-1.003)	0.08
Previous breast cancer	0.304 (0.226-0.408)	<0.0001	0.208 (0.198-0.218)	<0.0001	1.303 (1.198-1.417)	<0.0001	0.964 (0.950-0.979)	<0.0001
Previous ovarian cancer	-	-	0.209 (0.183-0.237)	<0.0001	-	-	2.345 (2.288-2.404)	<0.0001
Previous uterine cancer	-	-	0.242 (0.218-0.268)	<0.0001	-	-	1.514 (1.476-1.554)	<0.0001
Previous metastatic cancer	0.333 (0.318-0.348)	<0.0001	0.252 (0.240-0.265)	<0.0001	2.946 (2.914-2.979)	<0.0001	2.192 (2.165-2.220)	<0.0001

HR (Hazard Ratio); CI (Confidence Interval)

Figure 5. Five-year survival for all cause death for HF and most common types of cancer according to gender, in the overall population

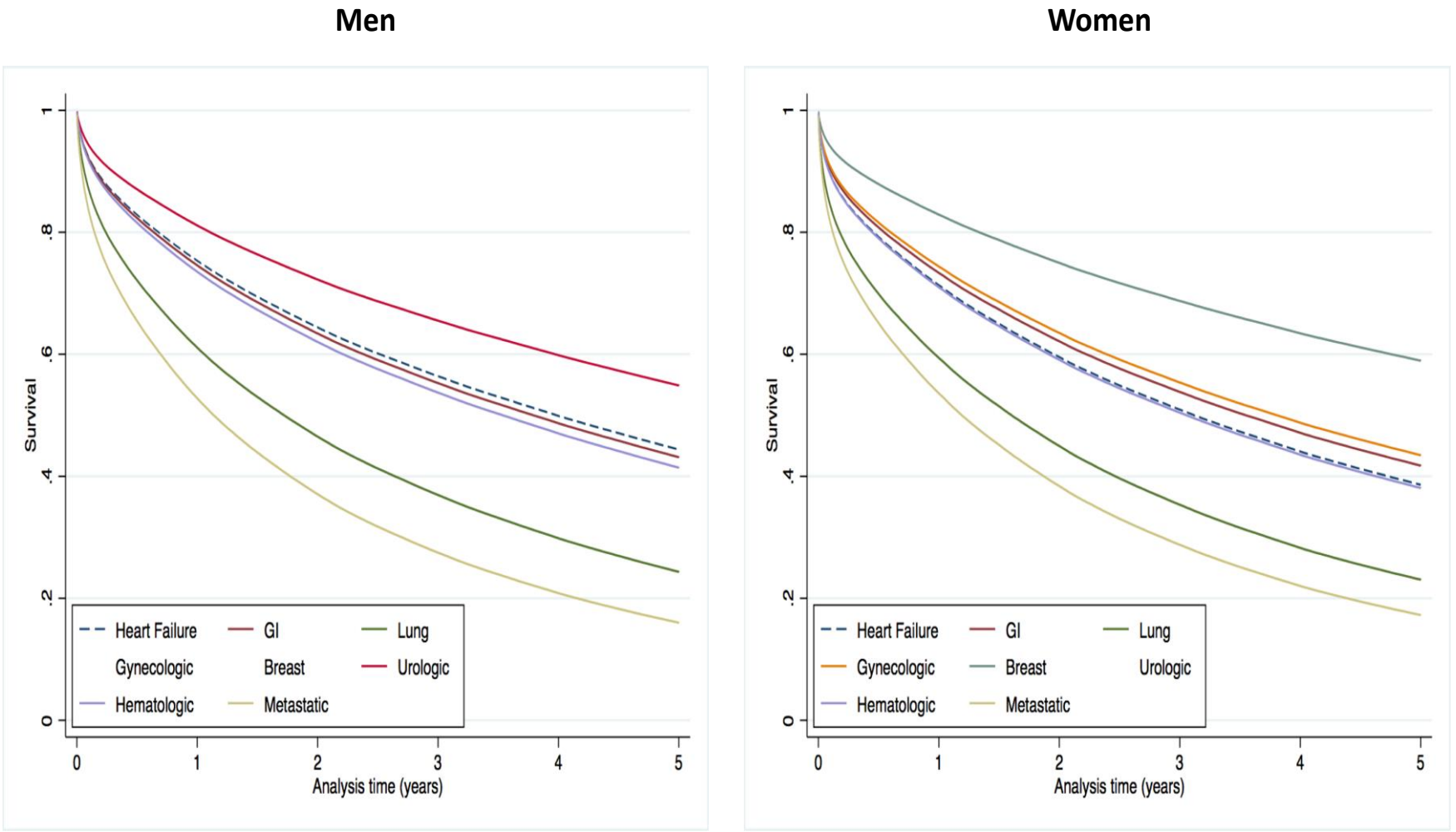
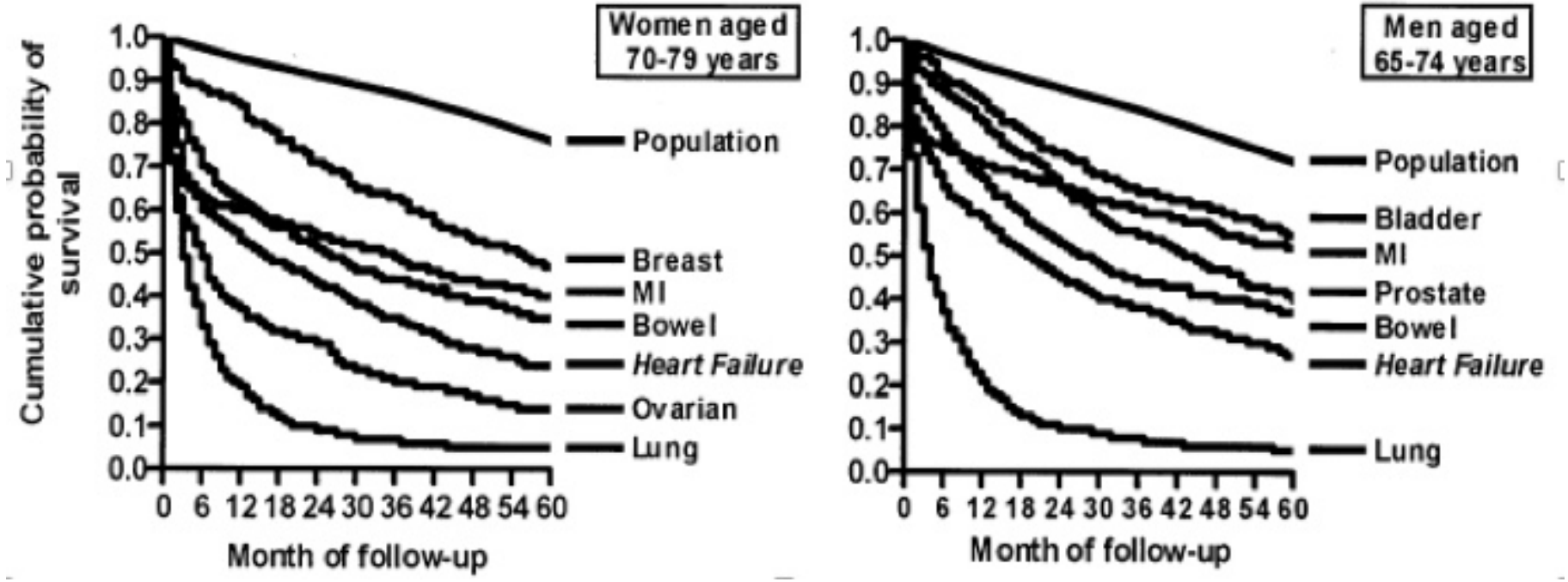


Table 6. Age-adjusted HR for all-cause death and cardiovascular mortality according to gender (vs HF as reference) in patients diagnosed for an active cancer

	Cardiovascular death				All-cause death			
	Men		Women		Men		Women	
	Age-adjusted HR (95%CI)	p	Age-adjusted HR (95%CI)	p	Age-adjusted HR (95%CI)	p	Age-adjusted HR (95%CI)	p
Previous lung cancer	0.390 (0.358-0.425)	<0.0001	0.363 (0.317-0.416)	-	3.516 (3.443-3.591)	<0.0001	3.300 (3.196-3.408)	<0.0001
Previous gastric cancer	0.231 (0.186-0.288)	<0.0001	0.199 (0.146-0.271)	<0.0001	2.676 (2.566-2.791)	<0.0001	2.143 (2.018-2.276)	<0.0001
Previous liver cancer	0.395 (0.339-0.461)	<0.0001	0.338 (0.254-0.449)	<0.0001	3.462 (3.344-3.585)	<0.0001	3.463 (3.266-3.673)	<0.0001
Previous colorectal cancer	0.182 (0.165-0.200)	<0.0001	0.158 (0.141-0.178)	<0.0001	1.119 (1.091-1.148)	<0.0001	1.057 (1.025-1.090)	<0.0001
Previous pancreas cancer	0.294 (0.241-0.359)	<0.0001	0.240 (0.194-0.297)	<0.0001	4.002 (3.856-4.154)	<0.0001	3.424 (3.292-3.562)	<0.0001
Previous prostatic cancer	0.218 (0.204-0.233)	<0.0001	-	<0.0001	0.679 (0.663-0.696)	<0.0001	-	-
Previous renal cancer	0.239 (0.201-0.285)	<0.0001	0.220 (0.169-0.286)	<0.0001	1.213 (1.156-1.274)	<0.0001	1.177 (1.096-1.264)	<0.0001
Previous bladder cancer	0.221 (0.201-0.243)	<0.0001	0.168 (0.132-0.213)	-	0.883 (0.857-0.910)	<0.0001	0.955 (0.896-1.018)	0.16
Previous myeloma	0.230 (0.190-0.279)	<0.0001	0.247 (0.203-0.300)	<0.0001	1.103 (1.045-1.164)	<0.0001	1.032 (0.972-1.096)	0.30
Previous leukemia	0.340 (0.295-0.391)	<0.0001	0.269 (0.226-0.321)	<0.0001	1.601 (1.537-1.667)	<0.0001	1.502 (1.433-1.575)	<0.0001
Previous lymphoma	0.225 (0.190-0.265)	<0.0001	0.202 (0.167-0.245)	<0.0001	1.152 (1.101-1.206)	<0.0001	0.972 (0.920-1.027)	0.32
Previous breast cancer	0.275 (0.166-0.456)	<0.0001	0.170 (0.158-0.184)	<0.0001	1.002 (0.853-1.176)	0.98	0.745 (0.726-0.764)	<0.0001
Previous ovarian cancer	-	-	0.179 (0.144-0.221)	<0.0001	-	-	1.893 (1.812-1.978)	<0.0001
Previous uterine cancer	-	-	0.187 (0.158-0.222)	<0.0001	-	-	1.352 (1.298-1.409)	<0.0001
Previous metastatic cancer	0.310 (0.288-0.335)	<0.0001	0.220 (0.203-0.239)	<0.0001	3.398 (3.337-3.460)	<0.0001	2.175 (2.130-2.220)	<0.0001

HR (Hazard Ratio); CI (Confidence Interval)

Figure 6. Five year survival following first admission for heart failure or cancer in Scottish hospital in 1991



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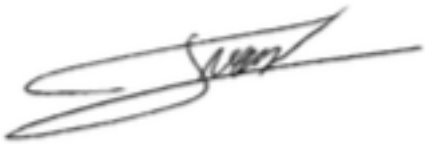
Vu, le Directeur de Thèse



Vu, le Doyen
De la Faculté de Médecine de Tours
Tours, le

CHAHID Sihame 50 pages – 6 tableaux – 6 figures

Résumé :
INTRODUCTION. L'insuffisance cardiaque et les cancers sont des pathologies grevées d'une importante morbi-mortalité. Une étude réalisée il y a vingt ans avait mis en évidence que le diagnostic d'insuffisance cardiaque était associé à une mortalité aussi importante que celui d'une pathologie cancéreuse. Le but de notre étude est d'évaluer, à la lumière des avancées thérapeutiques, si ce constat est toujours d'actualité vingt ans après.

METHODE. Nous avons réalisé une étude française rétrospective, basée sur les données de l'ensemble de la population de patients hospitalisés dans les hôpitaux français en 2013. Parmi ces patients, nous avons étudiés ceux pris en charge pour une insuffisance cardiaque ou un cancer. Nous nous sommes intéressés aux différences de mortalité cardiovasculaire et toutes causes chez ces patients, que le diagnostic d'insuffisance cardiaque ou de cancer ait été établi moins de 6 mois avant l'inclusion (nous avons alors qualifié la pathologie d'active ou aigüe) ou non.

RESULTATS. Parmi les 5,123,193 patients hospitalisés en 2013, 292,335 ont été admis pour une poussée d'insuffisance cardiaque et 442,285 pour un cancer parmi les cancers gastro-intestinaux, pulmonaires, urologiques, gynécologiques, hématologiques et du sein. Les patients insuffisants cardiaques étaient plus comorbides et plus âgés que les patients atteints de cancer. Qu'il s'agisse de pathologies aigues ou chroniques, la mortalité cardiovasculaire des patients insuffisants cardiaques était significativement plus élevée que pour tous les types de cancers pour lesquels elle demeure néanmoins élevée. En termes de mortalité toutes causes, les cancers ont un pronostic significativement moins bon que l'insuffisance cardiaque à l'exception des cancers de la prostate et de la vessie chez l'homme et du cancer du sein chez la femme.

CONCLUSION. Notre étude montre une amélioration du pronostic en termes de mortalité toutes causes dans l'insuffisance cardiaque comparativement aux pathologies cancéreuses. L'insuffisance cardiaque reste cependant grevée d'un pronostic sombre en termes de mortalité cardiovasculaire, de même que les cancers pour lesquels ce mode de décès reste fréquent.

Mots clés. Insuffisance cardiaque, cancer, mortalité cardiovasculaire, mortalité toutes causes, pronostic

Jury :

Président du Jury :	Professeur Laurent FAUCHIER
Directeur de thèse :	Professeur Fabrice IVANES
Membres du Jury :	Professeur Dominique BABUTY
	Professeur Laurent PLANTIER

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