Diagnosis-related differences in the quality of end-of-life care: A comparison between cancer and non-cancer patients

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Abstract

Background
Cancer, chronic heart failure (CHF), and chronic obstructive pulmonary disease (COPD) in the advanced stages have similar symptom burdens and survival rates. Despite these similarities, the majority of the attention directed to improving the quality of end-of-life (EOL) care has focused on cancer.

Aim
To assess the extent to which the quality of EOL care received by cancer, CHF, and COPD patients in the last month of life is diagnosis-sensitive.

Methods
This is a retrospective observational study based on administrative data. The study population includes all Tuscany region residents aged 18 years or older who died with a clinical history of cancer, CHF, or COPD. Decedents were categorized into two mutually exclusive diagnosis categories: cancer (CA) and cardiopulmonary failure (CPF). Several EOL care quality outcome measures were adopted. Multivariable generalized linear model for each outcome were performed.

Results
The sample included 30,217 decedents. CPF patients were about 1.5 times more likely than cancer patients to die in an acute care hospital (RR 1.59, 95% C.I.: 1.54–1.63). CPF patients were more likely to be hospitalized or admitted to the emergency department (RR 1.09, 95% C.I.: 1.07–1.10; RR 1.15, 95% C.I.: 1.13–1.18, respectively) and less likely to use hospice services (RR 0.08, 95% C.I.: 0.07–0.09) than cancer patients in the last month of life. CPF patients had a four- and two-fold higher risk of intensive care unit admission or of undergoing life-sustaining treatments, respectively, than cancer patients (RR 3.71, 95% C.I.: 3.40–4.04; RR 2.43, 95% C.I.: 2.27–2.60, respectively).
Conclusion

The study has highlighted the presence of significant differences in the quality of EOL care received in the last month of life by COPD and CHF compared with cancer patients. Further studies are needed to better elucidate the extent and the avoidability of these diagnosis-related differences in the quality of EOL care.

Introduction

The majority of people in high-income countries die of chronic conditions other than cancer [1]. Chronic heart failure (CHF) and chronic obstructive pulmonary disease (COPD) are two prominent causes of death in high-income countries [1, 2], and their prevalence and burden are expected to grow as the populations are aging [2–5]. Although the focus on improving the quality of end-of-life (EOL) care was initially directed mainly to cancer patients [6–9], in recent years awareness of the importance of improving EOL care for patients with non-malignant diseases has increased [10, 11]. Nowadays, there is a general consensus that curative treatment should be integrated with the holistic approach provided by palliative care in the advanced stages of CHF and COPD [12–16].

Cancer, CHF, and COPD at the advanced stages have similar symptom burdens and illness experience [17–19]. They have similar survival rates too [20–22], although prognostication in CHF and COPD is difficult for the less-predictable functional trajectories of these conditions [10, 23]. Despite these similarities, the delivery of quality and comprehensive EOL care for CHF and COPD patients at the advanced stages seems more challenging than for cancer [24]. Indeed, cancer is more likely to be viewed as a terminal condition, whereas CHF and COPD, even in the advanced stages, tend to be treated as chronic conditions [25–28]. Consequently, CHF or COPD patients are less likely to be aware of their prognosis and of the need to provide a 'Do not resuscitate' order, and more likely to have unmet palliative care needs [29, 30, 31].

As far as the quality of EOL care is concerned, a few studies have compared patient outcomes across several malignant and non-malignant chronic conditions, with some showing a certain degree of consistency in the patterns of EOL care and treatment intensity provided across conditions [32] and others showing systematic and great diagnosis-related differences [33, 34]. Furthermore, previous studies have focused on treatment intensity outcomes [32] or have been limited to patients of a specific healthcare provider [33, 34].

In order to assess the quality of EOL care, major indicators from administrative data were initially developed and adopted in the context of cancer care [35, 36], and more recently, quality indicators were proposed and adapted to examine the EOL care provided in different serious illnesses and settings [37, 38].

The aim of the present study is to compare the pattern and intensity of EOL care received by cancer, CHF, and COPD patients in the last month of life in order to assess the extent to which the quality of EOL care is diagnosis-sensitive.

Materials and methods

This is a retrospective observational study of residents in Tuscany based on data extracted from the regional healthcare administrative data system (RHCADS). The RHCADS comprises several healthcare data sources and the following databases were used for the study: enrolment registry, regional census, inpatient hospitalizations, death registry, emergency department
In the RHCADS, each resident is represented by a unique encrypted identifier that enables complete record linkage at the level of the individual across databases and over time.

This study was conducted in accordance with the Helsinki Declaration. According to the Italian legislation (law 211/2003) and the regional procedures, the study does not need ethic approval as it is a purely observational study on routine collected anonymous data. Furthermore, because this was an observational retrospective study, patients had already been treated when the study protocol was written; therefore, it could not have modified their life-trajectories or care pathways in any way. Data were extracted from routinely collected administrative databases and there was no need to obtain additional data from individual residents. Data linkage to the patients was performed by using numerical codes, and researchers had access only to an anonymous dataset, which ensured residents’ privacy. For these reasons, no personal informed consent to the present analysis was requested for the study. The Tuscan Regional Health Agency is the authorized public entity (Regional Law n. 40/2005) entitled to perform research and analysis on the RHCADS data.

The study population includes all Tuscany region residents aged 18 years or older who died with a clinical history of cancer, CHF, or COPD in the years 2015 and 2016. More specifically, decedents who had at least one inpatient admission for cancer, CHF, or COPD in the last 36 months of life were included in the study. Because the inclusion criteria was based on inpatient admissions, the last 36-months of life time-frame was chosen in order to minimize the possibility of not including non-hospitalized decedents with cancer, CHF or COPD in the study population. Only decedents who have resided continuously in Tuscany for their last 36 months of life were included in the study as for this population it is possible to ensure complete information for the last 36 months of life. Both primary and secondary diagnosis codes associated with the hospital admissions were used. Table 1 shows in detail the ICD-9-CM inpatient diagnosis codes used.

Decedents who had hospital admissions associated with cancer and cardiopulmonary failure diagnosis codes in the same or in distinct hospitalization episodes were excluded from the study. ED deaths occurring as a consequence of a trauma or injury were excluded from the study; these criteria aimed at excluding people who could not be recognized as being near the end of life until the time of death.

According to the diagnosis codes of the hospitalizations occurred in the last 36 months of life (see Table 1), decedents were categorized into two mutually exclusive diagnosis categories: cancer (CA) and cardiopulmonary failure (CPF). The CPF group includes decedents who had hospital admissions solely associated with diagnoses codes of CHF and/or COPD. Decedents who had hospital admissions solely associated with cancer diagnosis codes were classified in the CA group. CHF and COPD decedents are frequently combined in one category in EOL studies [32, 34] as they have similar patterns of functional decline at the end of life [23].

All the covariates were captured at time of death. The following covariates were considered: age, sex, nationality, education level, comorbidity, and geographic region of residence.

Table 1. Cancer and Cardiopulmonary failure inpatients diagnosis codes (ICD-9-CM) included in the study.

| Diagnosis Category                  | ICD-9-CM Codes                                        |
|-------------------------------------|-------------------------------------------------------|
| Cancer                              | 140–209                                               |
| Chronic heart failure               | 398.91, 402.01, 402.11, 402.91, 404.01, 404.03, 404.11, 404.13, 404.91, 404.93, 428.XX |
| Chronic obstructive pulmonary disease| 491, 492, 493.2, 494, 496, 518.83, 518.84             |

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Comorbidity was measured using the Charlson comorbidity index (CCI) (Time Frame: last 36 months of life) [39].

The outcome measures adopted in the study were derived from indicators reported to be associated with poor quality of EOL care [35, 37]. Specifically, the outcome measures included: (i) death in an acute care hospital; (ii) one or more hospitalizations in the last month of life; (iii) one or more ED admissions in the last month of life; (iv) one or more intensive care unit (ICU) admissions in the last month of life; (v) use of one or more life-sustaining treatments (LSTs) in the last month of life; and (vi) access to hospice services in the last month of life. The following LSTs were considered: intubation, mechanical ventilation, gastrostomy, haemodialysis, cardiopulmonary resuscitation, pulmonary artery pressure monitoring, implantation of cardiac devices (pacemaker, cardioverter/defibrillator), cardiac catheterization, and surgical intervention.

A descriptive analysis with an $\chi^2$ test for categorical and ordinal data and an unpaired t-test for continuous data were performed in order to evaluate significant associations between outcome measures and all the variables considered. A multivariable generalized linear model for binomial distribution for each outcome was performed, including the statistically significant variables resulting from the univariate analyses. Margins for CA and CPF have been computed to estimate adjusted probabilities. For each analysis, an $\alpha$ level of 0.05 is considered as significant. The statistical software Stata 14 SE was used for the data analyses.

**Results**

A total of 30,217 decedents with cancer, CHF, and COPD met the eligibility criteria. The patients’ characteristics are presented in Table 2.

The mean age of the sample is 80.47 years (standard deviation of 11.50 years) and males represent 49.98% of the sample. The CPF cohort represents the 59.76% of the study sample. Upon comparing the characteristics of patients of the two cohorts, patients with CPF were found to be older than the CA patients. The CPF cohort had a higher percentage of patients with a CCI $\geq$3 compared to the CA cohort.

Approximately a third of the CA patients died in acute care hospitals (36.45%), compared with 52.31% of those registered as CPF patients. Among the patients hospitalized in the last month of life, the proportion of patients with one or more ICU admissions or who underwent one or more LSTs was significantly higher in the CPF cohorts (12.92% and 16.65%, respectively) than in the CA cohort (6.05% and 10.9%, respectively). CPF cohort showed a significantly higher proportion of patients with one or more hospital admissions (76.25%) and ED admissions (64.9%) and a lower proportion of patients resorting to hospice services (1.04%) in the last month of life than the CA cohort (72.79%, 55.32%, and 15.84%, respectively).

The variables significantly associated with each outcome of the univariate analyses were included in the multivariable generalized linear model (the univariate analyses for each of the outcome measures are presented in tables A-F in S1 File). Table 3 summarizes the results of multivariable analyses for the two diagnosis cohorts (the results of the full model of multivariable analysis for each outcome measure are reported in tables G-L in S2 File).

For all the outcomes, the CPF cohort differed significantly from the CA cohort. Specifically, CPF patients were about 1.5 times more likely than CA patients to die in an acute care hospital (RR 1.59, 95% C.I.: 1.54–1.63). Furthermore, in the last month of life, CPF patients were more likely to be hospitalized or admitted to the ED (RR: 1.09, 95% C.I.: 1.07–1.10; RR 1.15, 95% C. I.: 1.13–1.18, respectively) and less likely accessed to hospice services (RR 0.08, 95% C.I.: 0.07–0.09) than CA patients. Among the patients hospitalized in the last month of life, CPF patients have a risk of ICU admission or of undergoing LSTs that is about four- and two-fold higher.
than for CA patients, respectively (RR 3.71, 95% C.I.: 3.40–4.04; RR 2.43, 95% C.I.: 2.27–2.60, respectively).

### Discussion

The aim of this study was to evaluate whether the quality and treatment intensity of EOL care—measured by several established outcome measures [35–38]—differ significantly among the CA and CPF cohorts. In order to assess the extent to which EOL care is diagnosis-sensitive, several potential determinants and confounders were considered through multivariable analyses. According to the multivariable analyses, the CPF patients differed significantly from the CA patients in all the quality and treatment-intensity EOL care outcomes considered. Specifically, the study shows that patients with CPF had a higher risk of dying in acute care hospitals and considerably less access to hospice services in the last month of life than patients with CA, which is in line with the literature [33, 34, 40]. Dying in acute care hospitals is a widely recognized indicator of the low quality of EOL care as acute care hospitals are not generally designed to meet the needs of terminally ill patients in terms of symptom control and alleviation [35, 37, 38]. It may be argued that this difference in the place of death may reflect an underlying difference in EOL preferences by diagnosis; however, the literature reports that most CHF and COPD patients prefer to die at home or at non-acute-care care institutions and that these preferences seem to mirror those of patients suffering from malignant diseases.
In the last month of life, patients with CPF had a higher risk of hospitalization than patients with CA. In the literature, only a few studies have compared the hospitalization rates among cancer and non-cancer patients. In a large retrospective study conducted by Teno et al., a higher hospitalization rate in the last 90 days of life is reported among COPD patients [33]. Conversely, other studies, limited only to the comparison between COPD and lung cancer, have reported a higher hospitalization rate in the last six or 12 months of life among cancer patients [39, 45]. Besides the different patient populations considered in these studies, this apparent discrepancy in the literature may be due to the different time periods in which hospitalization rates are considered and the related potential causes of hospitalization. Indeed, in a more far-from-death period, hospitalization may be more frequently required in cancer patients for potentially appropriate causes (diagnosis establishment and management of chemotherapy and its complications). Conversely, in a period closer to death, these causes of hospitalization occur less frequently and the reasons for hospitalization among patients with different diagnoses potentially becomes more similar [17, 18]. Given the above considerations, the hospitalization rates estimated in a closer-to-death period may serve as a more appropriate indicator for assessing avoidable disparities in the quality of EOL care provided to different diagnosis cohorts.

As far as ED admissions are concerned, the study revealed that CPF groups have a higher risk of ED admission in the last month of life compared to the CA group. A similar result was reported previously [46], although the literature has not devoted much attention to this indicator, and further studies are needed to draw a definite conclusion on this potential disparity.

As for EOL treatment intensity, patients with CPF were at a higher risk of receiving LST or being admitted to the ICU than CA patients. In the literature, differences in EOL treatment
intensity between cancer and non-cancer patients have been reported, although there is no general consensus on the extent and magnitude of these differences. A study by Barnato et al. comparing the CA and CHF/COPD cohorts did not find a universally higher EOL treatment intensity in the CHF/COPD cohort [32]. Conversely, other studies reported a systematically lower EOL treatment intensity in CA patients for all the intensity measures analysed [33, 34].

Several factors may explain these differences in EOL care across conditions. First, patients with CHF or COPD may be less frequently involved in patient–physician discussions on EOL matters, in the decision-making process, and in advance care planning. Although the prognosis of COPD and CHF at the advanced stages is poor, physicians may be reluctant to pursue advance care planning with CHF or COPD patients as their illness trajectories are characterized by prognostic uncertainty [23, 47, 48, 49]. Second, advance care planning in the case of CHF and COPD may be hampered by the patient’s and their family’s perceptions of these diseases. Indeed, while cancer is often viewed as a terminal condition, COPD and CHF are generally thought of as chronic conditions that are not linked to dying [24, 50]. Lastly, limited clinician knowledge and misperceptions about palliative care as well as a lack of continuity and coordination in healthcare services for CHF or COPD patients may be additional explanations of the registered differences, especially of the lower access to palliative care services in patients with CHF or COPD [51, 52, 53]. For the above reasons, it may be more difficult to recognize impending death and to provide treatments that have aims other than life preservation in COPD or CHF patients.

Nevertheless, several prognostic models, care pathways, clinical guidelines, and recommendations of medical associations have been formulated to assist clinicians to overcome these barriers in patients with end organ failure [12, 14, 24, 47, 54]. In particular, the initiation of palliative care early in the course of the disease in conjunction with curative care is recommended to address patients’ needs holistically, and it may help patients, caregivers, and clinicians to be prepared for the impending death and the transition to less-aggressive treatments near the end of life [55, 56].

Considering that the study population is representative of the deaths occurring in the Tuscany region for CA, CHF, and COPD and that the CPF group represents the majority of the sample, the diagnosis differences in EOL care emerging from this study highlight a relevant issue as well as the need to strengthen EOL care pathways and future research for non-cancer chronic disease and multimorbidity patients. Furthermore, as the prevalence and burden of non-cancer chronic diseases and multimorbidity are expected to grow across many developed countries [2–5], the provision of quality EOL care for non-cancer chronic diseases and multimorbidity patients is an increasingly urgent issue that prompts a call for action.

The sample analysed represents virtually the whole population of an administrative region with around 3.7 million inhabitants and a wide and varied geographical area [57]. Furthermore, the data analysed could be considered as representative of almost all the EOL care that has been provided to the study population as the regional public health system provides healthcare free of charge for the entire population; private providers play a very marginal role in the healthcare system, especially in the provision of EOL care. The above considerations, together with the evaluation of various EOL outcomes measures and confounding factors, should be considered as the strengths of this study.

Nevertheless, the study has several limitations. Firstly, as the study is a retrospective analysis based on administrative data, it may suffer the recognized limitations of using this approach, such as the lack of control on data quality (i.e. underreporting or incorrect reporting of data). However, the quality of administrative data in terms of accuracy and reliability is very high as the data are audited each year. Second, it was not possible to identify and include in the study decedents with cancer or with CHF/COPD who were not hospitalized during the study time-
frame; this may have introduced a selection bias. However, it is possible to argue that the extent of this bias was limited as only a very small proportion of decedents with cancer or CHF/COPD was not hospitalized in the their last 36 months of life. Third, a retrospective analysis of administrative data does not allow consideration of important clinical data (e.g. disease severity) or patients’ preferences for care; this could have introduced a bias in the exposure-outcome relationship. Finally, it should be noted that the study relied on inpatients’ diagnosis codes to classify patients in the considered cohorts. This approach is widely adopted in research on EOL matters [23, 33, 34], as several studies have found that the cause of death reported in death certificates is often inaccurate and unreliable [58, 59, 60].

Conclusions
Cancer, CHF, and COPD in the advanced stages have similar symptom burdens and survival rates. Despite these similarities, the majority of the attention directed to improving the quality of end-of-life (EOL) care has focused on cancer. Although awareness of the quality and aggressiveness of EOL care in CHF and COPD patients has increased recently, research on these issues is still limited. The study has highlighted the presence of significant differences in the quality of EOL care received in the last month of life by COPD and CHF compared with cancer patients. These findings suggest the presence of potential diagnosis-sensitive determinants of the quality of EOL care. Further studies that take into account patients’ preferences of care and disease severity are needed to better elucidate the extent and the avoidability of these differences in the quality of EOL care provided to different diagnosis groups.

Supporting information
S1 File. Univariate analyses for each of the outcome measures.
(DOC)
S2 File. Full model of multivariable analysis for each outcome measure.
(DOC)
S1 Dataset. Full dataset of the study.
(XLS)

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