Hospital-based palliative care referrals: determinants in older adults with cancer

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ABSTRACT

Objectives Early palliative care improves the quality of life of older patients with cancer. This work aimed to analyse the effect of sociodemographic, geriatric, and tumour-related determinants on hospital-based palliative care (HPC) referral in older patients with cancer, taking into account competing risk of death.

Methods Older adults with diagnosed cancer from 2014 to 2018 according to the general cancer registry of Gironde (French department) were identified in three population-based cohorts on ageing (PAQUID, 3C - Three City, AMI). Cause-specific Cox models focused on 10 usual determinants in geriatric oncology and palliative care: age, gender, living alone, place of residency, tumour prognosis, activities of daily living (ADL) and instrumental-ADL (IADL) limitations, cognitive impairment, depressive disorders, and polypharmacy.

Results 131 patients with incident cancer (mean age: 86.2 years, men: 62.6%, poor cancer prognosis: 32.8%) were included, HPC referral occurring for 26 of them. Unfavourable cancer prognosis was a key determinant for HPC referral (HR 7.02, 95% CI 2.86 to 17.23). An altered IADL score was associated with precocious (first year) referral (HR 3.21, 95% CI 1.20 to 8.64, respectively). Women had a higher rate immediately (first week) after diagnosis (HR 8.64, respectively). Cancer prognosis, functional decline and gender are independent factors of HPC referral in older patients with cancer. These findings may help for a better anticipation of the healthcare pathway.

BACKGROUND

The growing incidence of cancer associated with the ageing of the population lead to an increasing need for palliative care. This holistic care improves quality of life of patients and their families facing serious health-related suffering due to severe diseases such as cancer. European countries have developed specialised palliative care (SPC), provided at home or by hospital-based palliative care (HPC) teams. Current guidelines recommend early palliative care referral for patients with advanced cancer, high symptom burden or unmet psychosocial needs. However, the literature underlines that SPC referral may occur lately in disease course. A better understanding of the mechanisms involved in HPC referral would help to improve patient care pathway in palliative care and to guide public health actions.
Several factors such as advanced age, male gender, minority ethnicity, living alone or in rural areas and precariousness are reportedly HPC referral barriers for patients with cancer. However, the implications of tumourous and geriatric factors remain unexplored. Various age-related geriatric syndromes may affect older adults and pre-exist the cancer diagnosis. Among them, cognitive impairment, psychological disorders, functional decline and multimorbidity are frequently reported as indications for palliative care referral, even without cancer. Moreover, these conditions are frequently associated with lower access to and poorer tolerance of cancer treatments, as well as decreased survival. Thus, they may likely be associated with HPC referral.

Considering these hypotheses, this study primarily aimed to analyse the effect of sociodemographic, tumour-related and geriatric determinants on HPC referral in older patients with cancer, taking into account competing risk of death. Secondary stratified analysis specified the effect of sociodemographic and geriatric factors according to the initial tumour prognosis.

METHODS
Study population
The Personnes Âgées avec Cancer: recours aux soins PALliatifs hospitaliers study is an ancillary study of the INCAPAC project, where older adults with cancer were identified by merging the general cancer registry with three cohort studies conducted in geriatric population of the French department of Gironde: "Personnes âgées QUID" (PAQUID), "3C" (Three City) and "Agrica-Msa-Institut fédératif de recherche en santé publique - Aging Multidisciplinary Investigation" (AMI). These cohorts included patients aged 65 and over, with regular follow-up, and collected data at inclusion and every 2–3 years, related to lifestyle or clinical events. The general cancer registry provides an exhaustive identification of all new solid cancer cases. This study included subjects 1) aged 65+, from one of the three cohorts, 2) alive and resident in Gironde on 1 January 2014 and 3) with an incident cancer diagnosis recorded in the general cancer registry from 1 January 2014 to 31 December 2018. The study endpoint was 31 December 2020.

Outcome
The outcome was first HPC referral, identified among general cancer registry by the “Z515” coding, the specific code from the International Statistical Classification of Diseases and Related Health Problems 10th Revision (ICD-10) referring to hospital stays of patients receiving interdisciplinary palliative care.

Variables
Variables were obtained from cohorts and general cancer registry. Sociodemographic variables included age at diagnosis, gender, social isolation and place of residency. Initial tumour prognosis was a composite variable defined from tumour prognosis and metastasis status: unfavourable if 5-year tumour net survival <33% and/or synchronous metastasis at diagnosis, favourable otherwise. Geriatric factors were collected before cancer diagnosis, during cohort follow-up. Instrumental activities of daily living (IADL) and activities of daily living (ADL) scales assessed functional limitations. The Centre for Epidemiological Studies-Depression Scale detected depressive disorders. Mini-Mental State Evaluation assessed cognitive impairment. Finally, daily use of six or more drugs identified comorbid patients.

Statistical analysis
The main analysis estimated HPC HR through cause-specific Cox models, taking into account competing risk of death. Each of the ten Cox models (one per explanatory variable) included a specific adjustment set based on causal hypothesis analysis summarized by directed acyclic graphs (see online supplemental material). Secondary analysis stratified on initial tumour prognosis was performed to specify results from main analysis regarding sociodemographic and geriatric variables. The statistical relevancy of stratification was checked. Time from inclusion, to cancer diagnosis, was used as time axis. Analyses were case completed, considering missing data not at random. Cox model assumptions were tested. If significant non-proportional effect was found over time, a time interaction was introduced.

RESULTS
Population characteristics and survival
A total of 131 patients were included with a median age at cancer diagnosis of 85.8 years (IQR=82.3–91.6). More than half of the patients were male (62.6%), had an education level higher than primary school (55.7%), lived in urban areas (61.1%). Before cancer diagnosis, individuals were mostly married or cohabiting (59.5%), about one-third lived alone (32.1%) and less than 10% in nursing homes. Regarding prediagnosis geriatric data, almost half (41.2%) took more than six daily drugs, nearly a quarter presented a cognitive impairment (23.1%) and 10.7% a depressive disorder. Considering functional activity, 23.7% and 8.4% had limitations to IADL and ADL scales, respectively.

The four most frequent tumour locations were skin (28.2%), prostate (16.0%), colon (9.2%) and lung (8.4%), and near a quarter of cancer cases (25.2%) were metastatic at diagnosis. Nearly one-third (32.8%) of initial tumour prognosis remained unfavourable. Median follow-up time from cancer
Short report
diagnosis was 1.7 years (IQR = 0.42–3.73). Median overall survival was 2.9 years (95% CI 1.5 to 3.8).

**HPC referral**
During follow-up, 26 patients were referred to HPC (19.8%), 52 died without HPC (39.7%) and 53 were free of both events. Median time to first HPC referral was 3 months after diagnosis (IQR = 4–454 days). Almost all patients with HPC referral died during follow-up (n = 25). Probabilities varied differently over time for HPC referral and competing event of death without HPC, respectively, of 13% and 14% at 6 months, 19% and 27% at 2 years, and increasing at 20% and 39% at 5 years.

**Determinants of HPC referral**
Cancer prognosis was strongly associated with HPC referral all along follow-up, with estimated HR of 7.02 (95% CI 2.86 to 17.23) for patients with unfavourable prognosis, compared with those with favourable prognosis, adjusted on age at diagnosis, place of residence, lonely lifestyle, functional limitations at IADL or ADL, cognitive impairment and polypharmacy (table 1).

**Table 1**: Determinants associated with HPC referral for older patients followed in 3C, PAQUID, AMI cohorts with cancer diagnosis collected in general cancer registry of Gironde, PACPAL study, 2014–2018, France

<table>
<thead>
<tr>
<th>Determinant</th>
<th>Time period</th>
<th>n</th>
<th>HR</th>
<th>95% CI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adjusted for gender, SCP, place of residence, living alone, depressive disorder, functional limitations at IADL or ADL, cognitive impairment, polypharmacy</td>
<td>At all times</td>
<td>118</td>
<td>0.62</td>
<td>0.35 to 1.10</td>
<td>0.10</td>
</tr>
<tr>
<td>Female gender (ref=male)†</td>
<td>At all times</td>
<td>131</td>
<td>1.26</td>
<td>0.57 to 2.78</td>
<td>0.56</td>
</tr>
<tr>
<td>No adjustment needed</td>
<td>At all times</td>
<td>131</td>
<td>0.77</td>
<td>0.28 to 2.12</td>
<td>0.61</td>
</tr>
<tr>
<td>Living alone (ref=living surrounded)†</td>
<td>Within 7 days</td>
<td>10.55</td>
<td>2.13</td>
<td>0.91 to 4.97</td>
<td>0.08</td>
</tr>
<tr>
<td>Adjusted for gender, SCP, place of residence, functional limitations at IADL and ADL, cognitive impairment, polypharmacy</td>
<td>At all times</td>
<td>131</td>
<td>0.77</td>
<td>0.28 to 2.12</td>
<td>0.61</td>
</tr>
<tr>
<td>Poor initial tumour prognosis (ref=favourable prognosis)¶¶</td>
<td>At all times</td>
<td>118</td>
<td>7.02</td>
<td>2.86 to 17.23</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>IADL functional limitations (ref=no limitation)¶</td>
<td>At all times</td>
<td>131</td>
<td>2.13</td>
<td>0.91 to 4.97</td>
<td>0.08</td>
</tr>
<tr>
<td>ADL functional limitations (ref=no limitation)**</td>
<td>At all times</td>
<td>130</td>
<td>2.13</td>
<td>0.91 to 4.97</td>
<td>0.08</td>
</tr>
<tr>
<td>Cognitive impairment (ref=no impairment)††</td>
<td>At all times</td>
<td>118</td>
<td>0.46</td>
<td>0.05 to 3.85</td>
<td>0.47</td>
</tr>
<tr>
<td>Polypharmacy (ref=no polypharmacy)§§</td>
<td>At all times</td>
<td>131</td>
<td>0.61</td>
<td>0.27 to 1.40</td>
<td>0.24</td>
</tr>
</tbody>
</table>

Multivariate cause-specific Cox model.
*P value of tumour prognosis interaction=0.16.
†P value of tumour prognosis interaction <0.01.
‡P value of tumour prognosis interaction <0.01.
§P value of tumour prognosis interaction <0.01.
¶P value of tumour prognosis interaction <0.01.
**P value of tumour prognosis interaction <0.0001.
††Non-convergent estimation.
‡‡P value of tumour prognosis interaction=0.01.
§§P value of tumour prognosis interaction=0.03.
¶¶Initial tumour prognosis=unfavourable if 5-year net survival <33% and/or synchronous metastasis, favourable otherwise.
ADL, activities of daily living; AMI, Agriculture Mutuelle Institut fédératif de recherche en santé publique / Aging Multidisciplinary Investigation; 3C, Three City; HPC, hospital-based palliative care; IADL, instrumental ADL; PACPAL, Personnes Âgées avec Cancer: recours aux soins PALliatifs hospitaliers; PAQUID, Personnes Âgées QUID; SCP, socioprofessional category.

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the first year after diagnosis compared with non-altered patients. Stratified on tumour prognosis, estimated HR was slightly lower in the unfavourable group (unfavourable: HR 2.16 (95% CI 0.69 to 10.81), favourable: HR 3.92 (95% CI 0.90 to 17.22)).

Other significant results depended on time or subgroups of patients. Female gender was associated with a higher risk of HPC referral only the first week after cancer diagnosis. During that time, main analysis estimated a risk nearly 11 times greater for women compared with men (HR 10.55, 95% CI 1.27 to 87.67). Secondary stratified analysis estimated significant association only in the unfavourable prognosis subgroup (women/men: HR 8.64 (95% CI 1.01 to 74.00)), after adjustment. Patients living alone with favourable prognosis had an estimated HR at 0.14 (95% CI 0.01 to 1.66), after adjustment, while those with polypharmacy and unfavourable prognosis had HR at 0.56 (95% CI 0.10 to 1.09) in the unfavourable prognosis subgroup, after adjustment.

Significant statistical interaction was found between initial cancer prognosis and every explanatory variables, except for age.

DISCUSSION
This prospective study provides new data about the sociodemographic, tumour-related and geriatric factors involved in the HPC referral of older patients with cancer. Our analytical approach took into account competing risk of death and carefully selected each adjustment covariates. This methodology led to an accurate estimation of the proper effects of each studied determinants. Our secondary analysis also considered initial tumour prognosis as recommended in studies on HPC referral. In this population of patients with potentially high HPC needs due to tumour and/or geriatric factors, only one in five patients were referred to HPC facilities, a slightly higher rate than recent publications on the general adult population with cancer. The most strongly associated determinants being initial tumour prognosis and IADL limitations. The effect of other determinants mainly depended on the follow-up period or prognosis subgroup.

Consistent with the literature, this study confirms that cancer remains the main determinant for HPC referral, patients with most unfavourable prognosis having higher HPC needs. Advanced and evolving cancers frequently cause complex physical and psychological suffering. Unfavourable tumour prognosis (median survival ≤1 year) is thus a criteria retained by a 2016 international consensus to indicate SPC referral. Our study suggests that these guidelines may also apply to older adults.

Our findings also highlight how patients with IADL limitations had an increased early HPC referral during the first year of follow-up, especially for those with the most favourable tumour prognosis. Age-related functional decline is worsened by the natural history of cancer, depending on the tumour type. It strongly affects patients and family caregivers’ daily life, associated with adverse outcomes such as psychological and/or physical discomfort, falls or malnutrition. These quality of life impairments and resulting high levels of care explain the higher HPC needs, underlying how functional assessment at cancer diagnosis should be considered as an early predictor of HPC needs for this population.

The literature remains inconsistent about the influence of gender on HPC referral. Different gender-related perceptions about end of life could affect HPC referral. We rather hypothesise that gender influences HPC referral because of its impact on several intermediate factors, such as geriatric determinants, unmeasured sociodemographic factors or cancer prognosis. Cognitive impairment should be considered as such intermediate factor. Although non-significant in this report, it may lead to higher HPC needs, considering the associated physical and psychosocial suffering, and potentially delayed and advanced cancer diagnosis.

For other sociodemographic and geriatric factors, further research, based on larger samples, is necessary to specify uncertain or negative results and explore other clinical factors.

To conclude, these preliminary results are of value for geriatric oncology and palliative care practices by identifying older patients with cancer particularly requiring HPC referral. They support early and multidisciplinary HPC referral to improve patients’ quality of life and care pathway, particularly when facing an unfavourable tumour prognosis and/or functional decline. Finally, this study supports current public health research efforts for older patients with cancer, in order to better understand determinants of care pathway in palliative care in this specific population.

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