

Prevalence and intensity of dyspnea, pain, and agitation among people dying with late stage dementia compared with people dying with advanced cancer: a single-center preliminary study in Brazil

Luiz Guilherme L. Soares¹, André M. Japiassu², Lúcia C. Gomes¹, Rogéria Pereira¹, Carla Peçanha¹, Tatiana Goldgaber¹

¹Post-Acute Care Services and Palliative Care Program, Hospital Placi, Rio de Janeiro, Brazil; ²Research Laboratory of Intensive Care Medicine, Fundação Oswaldo Cruz, Rio de Janeiro, Brazil

Contributions: (I) Conception and design: LG Soares, AM Japiassu; (II) Administrative support: LG Soares, AM Japiassu, LC Gomes, R Pereira; (III) Provision of study materials or patients: All authors; (IV) Collection and assembly of data: LG Soares, AM Japiassu, LC Gomes; (V) Data analysis and interpretation: LG Soares, AM Japiassu; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

Correspondence to: Luiz Guilherme L. Soares, MD. Post-Acute Care Services and Palliative Care Program, Hospital Placi, Rua Martins Torres 98, 24240705, Niterói, Rio de Janeiro, Brazil. Email: lgsoares@gmail.com.

Background: As death approaches, there may be similarities in terms of physical symptoms among dementia and cancer. This study aimed to estimate the prevalence and intensity of dyspnea, pain, and agitation among people dying with late stage dementia versus those dying with advanced cancer.

Methods: A retrospective analysis, conducted in a post-acute care facility (PACF) in Rio de Janeiro, Brazil. We reviewed the electronic charts for the Edmonton Symptom Assessment System (ESAS) scores, from death backwards in time (3 days).

Results: We included 57 patients who died with dementia and 54 patients who died with cancer. The prevalence of dyspnea (dementia: n=34, 60% vs. cancer: n=39, 72%; P=0.23), and agitation (dementia: n=7, 13% vs. cancer: n=14, 25%; P=0.17) were statically similar between the two groups. Pain was less common in dementia (dementia: n=19, 34% vs. cancer: n=31, 57%; P=0.02). There were no significant differences in the percentage of patients with moderate to severe dyspnea (dementia: n=28, 49% vs. cancer: n=33, 61%; P=0.28), and moderate to severe agitation (dementia: n=4, 7% vs. cancer: n=12, 23%; P=0.09). Dementia patients were less likely to experience moderate to severe pain than cancer patients (dementia: n=14, 25% vs. cancer: n=25, 46%; P=0.03). The diagnosis of cancer was independently associated with pain, severe symptoms, and the co-occurrence of dyspnea, pain, and agitation (odds ratio >1).

Conclusions: People dying with dementia and those dying with cancer experienced similar rates of dyspnea, and agitation. However, pain was significantly more prevalent and intense among people dying with cancer.

Keywords: End of life care; dementia; cancer

Submitted May 02, 2018. Accepted for publication May 04, 2018.

doi: 10.21037/apm.2018.05.06

View this article at: <http://dx.doi.org/10.21037/apm.2018.05.06>

Introduction

Palliative care aims to provide the best care possible for patients facing life-threatening illness and support for their families (1). Although cancer remains the most common condition among patients referred to specialized palliative care programs (2,3), the importance to extend palliative care services to people with non-malignant diseases such as dementia has been widely recognized (4).

In most cases, dementia is a progressive and incurable neurodegenerative disorder, and the average survival time after dementia diagnosis is around 8 years (5). Around the world, several palliative care programs are now serving people with dementia (6). In a recent study we found that advanced cancer and late stage dementia were the two most common underlying diagnosis among people admitted to a palliative care program in Brazil (7). Unfortunately, the organization and quality of palliative care services are usually better for cancer than for dementia (8). In fact, people with dementia are more likely to receive inappropriate end of life care than those who are cognitively intact (9).

Despite the undoubtful benefits of palliative care, the evidence supporting effective strategies for dementia is not as robust as the evidence for cancer. Data from isolated studies suggest that there may be similarities in terms of dyspnea, pain, and agitation among people dying with dementia and people dying with cancer (10–13). However, little is known about how dementia compares with cancer when death approaches. Because transition from cure to palliation often occurs late in the dying process, such comparative analysis would be useful to improve the quality of protocols on the domain of physical comfort, and to guide the provision of palliative care services across different patient populations and care settings. Therefore, the purpose of this study was to estimate the prevalence and intensity of dyspnea, pain, and agitation among people dying with late stage dementia compared with those dying with advanced cancer.

Methods

Study setting and the palliative care program

Located in Rio de Janeiro, Brazil, The Hospital Placi is a private, 30-bed post-acute care facility (PACF). In Brazil, PACFs usually provide multiple services (skilled nursing facility, inpatient functional rehabilitation, and hospice care)

at the same location. A palliative care program has been fully integrated into the main portfolio of post-acute care services. The interdisciplinary palliative care team holds responsibility for documentation of advance care planning, symptom management, psychosocial support, and bereavement interventions.

Symptom assessment

Symptom assessments were performed every day at 10:00 and 20:00, by registered nurses, who were trained to document the Edmonton Symptom Assessment System (ESAS), in a face-to-face visit. The ESAS is a numeric rating scale (NRS) that ranges from 0 (no symptom) to 10 (worst possible), used to quantify nine symptoms (pain, activity, nausea, depression, anxiety, drowsiness, appetite, well-being, dyspnea), and an optional extra symptom (14). Our palliative care team included the symptom “agitation” as the optional extra symptom. The results were systematically documented in the electronic chart. For study purposes, we looked at the last six consecutive ESAS scores of dyspnea, pain, and agitation, from the moment of death backwards in time (3 days). Then, each symptom was categorized as none (ESAS =0), mild (ESAS =1–3), moderate (ESAS =4–7), or severe (ESAS =8–10).

Data collection and criteria

The aim of the study was to estimate the prevalence and intensity of dyspnea, pain, and agitation among dying patients with dementia compared with those dying with cancer. This study used both prospective and retrospective data, which were obtained from electronic health records. We evaluated the hospital database to identify patients with dementia, and patients with cancer, who died from 1 June 2013 to 31 December 2017. Patients were considered eligible for the study if they were at least 18 years old, had a physician’s diagnosis of late stage dementia and a Cognitive Performance Scale of 5 or 6 (15), or advanced cancer (recurrent or metastatic), and had an observation period of at least 3 days before death. If the same patient had dementia, and cancer, the disease was coded as cancer. We also collected general information on admission like age, gender, length of stay (LOS), and baseline Karnofsky Performance Scale (KPS). The ethical committee of the Fluminense Federal University approved the study (No. 64110516.1.0000.5243) and provided waiver of patient consent.

Table 1 Demographic and clinical characteristics

| Patient characteristics | Dementia (N=57) | Cancer (N=54) | P value |
|---------------------------------|-----------------|---------------|---------|
| Mean age, years [range] | 86 [59–102] | 73 [32–92] | <0.001 |
| Female sex, n [%] | 28 [49] | 41 [64] | 0.11 |
| Mean LOS [range] | 102.3 [3–467] | 15.1 [3–104] | <0.001 |
| KPS, mean [range] | 31.1 [20–50] | 36.5 [20–50] | 0.002 |
| Dementia type, n [%] | | | |
| Alzheimer | 26 [45] | | |
| Vascular | 12 [21] | | |
| Lewy bodies/Parkinson's disease | 5 [9] | | |
| Unknown | 9 [16] | | |
| Others | 5 [9] | | |
| Primary cancer site, n [%] | | | |
| Lung | | 12 [22] | |
| Colon/rectum | | 9 [17] | |
| Pancreas | | 6 [11] | |
| Breast | | 5 [9] | |
| Genitourinary | | 5 [9] | |
| Others | | 17 [32] | |

LOS, length of stays in days; KPS, Karnofsky Performance Scale.

Statistical analysis

We calculated an ideal sample size of 108 patients (54 patients with dementia *vs.* 54 patients with cancer) to identify a statistical difference of each symptom (dyspnea, pain, and agitation), with a power of 80%. Standard descriptive statistics were used to summarize demographic characteristics. All numeric variables were expressed as mean values, and categorical variables were expressed as absolute numbers, and percentage.

We estimated the prevalence and intensity for each symptom studied, separately for both groups. Symptom intensity was determined as the percentage of patients with symptoms at moderate to severe level (ESAS >4). We used student *t*-test to compare numeric variables, and Fisher's exact test or chi-square correlations to evaluate categorical variables. The P value lower than 0.05 was considered significant.

A multivariate logistic regression analysis was also performed, to evaluate independent factors associated with dyspnea, pain, agitation, severe symptoms (ESAS >7), and

the co-occurrence of symptoms (at least two symptoms during the last 3 days of life); we performed this analysis with the variables: age, gender, LOS, and the diagnosis of dementia or cancer.

Results

Sample characteristics

Our final study sample comprised 111 deceased patients, 57 patients with dementia, and 54 patients with cancer. Dementia patients were older and had longer LOS compared with cancer patients. We found no differences for gender, and KPS (*Table 1*).

Prevalence of dyspnea, pain, and agitation: dementia *vs.* cancer

Dyspnea was detected in 34 (60%) patients with dementia *vs.* 39 (72%) patients with cancer (P=0.23). Agitation occurred in 7 (13%) patients with dementia *vs.* 14 (25%)

Table 2 Symptom prevalence: dyspnea, pain, and agitation

| Symptoms | Dementia (n=57) | Cancer (n=54) | P value |
|------------------|-----------------|---------------|---------|
| Dyspnea, n [%] | 34 [60] | 39 [72] | 0.23 |
| Pain, n [%] | 19 [34] | 31 [57] | 0.02 |
| Agitation, n [%] | 7 [13] | 14 [25] | 0.17 |

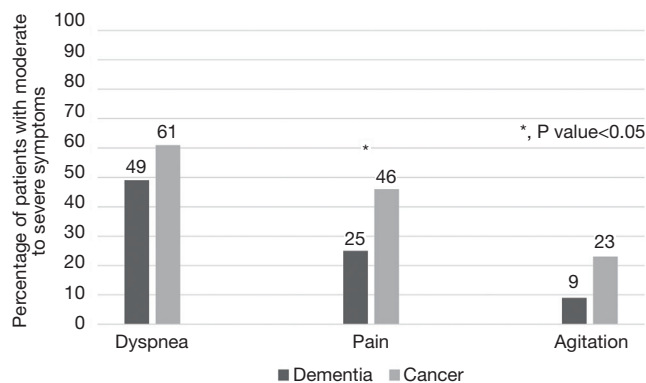


Figure 1 Comparison of symptom intensity. Dyspnea and agitation were similarly severe between the two groups. Pain was statistically more intense in cancer than in dementia.

patients with cancer ($P=0.17$). Pain was identified in 19 (34%) patients with dementia *vs.* 31 (57%) patients with cancer ($P=0.02$). These results are summarized in *Table 2*.

Symptom intensity: dementia vs. cancer

There were no significant differences in the percentage of patients with moderate to severe dyspnea (dementia: $n=28$, 49% *vs.* cancer: $n=33$, 61%; $P=0.28$), and moderate to severe agitation (dementia: $n=4$, 7% *vs.* cancer: $n=12$, 23%; $P=0.09$). Patients with dementia were less likely to experience moderate to severe pain (dementia: $n=14$, 25% *vs.* cancer: $n=25$, 46%; $P=0.03$) than patients with cancer (*Figure 1*).

Factors associated with dyspnea, pain, agitation, severe symptoms, and the co-occurrence of symptoms

In the multivariate analysis, cancer was the only independent factor associated with pain, [odds ratio (OR): 1.13, $P=0.02$], along with more severe symptoms (OR: 1.32, $P=0.001$), and the co-occurrence of symptoms (OR: 1.02, $P=0.01$).

Discussion

To our best knowledge, this is the first study directly comparing typical end of life symptoms such as dyspnea, pain, and agitation among people dying with dementia and people dying with cancer, using the same tool, and during the same time frame. We limited the analysis to the last 3 days of life in order to better address the period of time where symptoms become more intense, and patients require more palliative care interventions. Our study focused on dyspnea, pain, and agitation because these symptoms have been associated to several negative outcomes at the end of life such as multiple care setting transitions (16), inappropriate use of acute care resources (17), caregivers burden (18), and loss of dignity in terminally ill patients (19).

We found that dyspnea was the most prevalent symptom in both groups of patients. Our findings were in line with studies that showed high prevalence rates of dyspnea among terminally ill patients during their last days of life (10,11,20). In the present study, the vast majority of patients with dementia had had a tube feeding and tracheostomy already in place at the time of palliative care referral. In Brazil, people with late stage dementia are often admitted to intensive care units to receive life sustaining treatments (7). In fact, the use of mechanical ventilation in hospitalized people with dementia has increased over the last decades (21). Because Catholicism strongly prevails in Brazil, many family members do not agree with the decision about withholding or withdrawing hydration and artificial nutrition at the end of life, and requests for interventions that prolong the process of dying are quite common. In this study, delayed palliative care transitions could have contributed to a distinct pattern of symptoms, with less dehydration and cachexia, and more respiratory secretions and dyspnea during the last moments of life (10,22).

Our results showed that approximately one third of patients with dementia, and more than a half of patients with cancer had pain. As expected, people with late stage dementia was not able to give any valid self-reports, so that

the level of pain was mainly based on nurse's judgment or caregiver's perception. A previous work found that pain assessment in dementia is a controversial issue, with poor correlation between different instruments (23). The use of tools that rely on the observation of pain related behaviors such as facial expressions, body postures, and vocalizations are not accurate, potentially resulting in inappropriate treatment of pain (24). Indeed, cognitive decline is considered an independent risk factor for poor pain control at the end of life (25), and strategies such as enhancing assessment (26) or providing palliative care services may not necessarily improve pain management (27). At the bedside, if pain was suspected, our palliative care team used a pragmatic approach, which consisted of an empiric analgesic trial with opioids, followed by a careful reappraisal of pain related behaviors in a few minutes. Further prospective studies are necessary to identify better tools to manage pain among people with late stage dementia.

Our study provided preliminary information about the prevalence rates of cancer pain in Brazil. Considering that patients were seen by a specialized palliative care team in a private hospital, these rates were probably underestimated, and did not reflect the "real world" in Brazil, where traditionally the access to opioids is limited. Although advances have been made since the World Health Organization meeting of experts aimed at improving cancer pain in Latin America, more than two decades ago (28), gaps in education, social equality, and public policies remain important barriers for effective cancer pain control in Brazil (29).

In this study the rates of agitation were not as impressive as the rates of dyspnea and pain, and lower than other estimates (10,12,13). The reasons behind these results were not well understood. There is a possibility that in the dementia group, the symptom agitation had been overlooked by our palliative care team, and patients erroneously classified as having pain. It is well known that agitation is a multifactorial and complex symptom, often associated with pain in dementia (30). Another plausible explanation is that an intermittent pattern of agitation (sometimes with resolution) can occur among dying patients with dementia (12). In addition, some advanced cancer patients become less agitated, and more somnolent at the end of life (11). Furthermore, opioids, benzodiazepines, and neuroleptics were frequently used in both groups, which could have decreased the overall rates of agitation.

This study has important limitations. First, data on symptom assessment were not collected specifically for

research purposes, and the retrospective nature of this study was itself a limitation. Second, we arbitrarily narrowed the list of symptoms to look at dyspnea, pain, and agitation. Other sources of suffering for patients and families were not captured in this study and should be addressed in future research. Third, because of the lack of detailed information on these patients, we could not draw any conclusion about the appropriateness of end of life care delivered. Fourth, we used the ESAS, which is a simple and practical tool, but it has not been validated for dementia. Finally, as the trajectory of functional decline in dementia is usually less abrupt when compared to cancer, people with dementia had longer average LOS than people with cancer. This fact could have resulted in distinct approaches by the palliative care team, between the two groups of patients.

In summary, people dying with late stage dementia experienced rates of dyspnea, and agitation that were similar to people dying with advanced cancer. However, pain was significantly more prevalent and intense among people dying with cancer. Cancer patients were at increased risk for pain, more severe symptoms, and the co-occurrence of dyspnea, pain, and agitation. Given the elevated rates of distressing physical symptoms found in this study, our preliminary findings suggest that there is a wide room for improvement in terms of existing protocols for dyspnea, pain and agitation among people dying with dementia and those dying with cancer in Brazil.

Acknowledgements

None.

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

Ethical Statement: The ethical committee of the Fluminense Federal University approved the study (No. 64110516.1.0000.5243) and provided waiver of patient consent.

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Cite this article as: Soares LG, Japiassu AM, Gomes LC, Pereira R, Peçanha C, Goldgaber T. Prevalence and intensity of dyspnea, pain, and agitation among people dying with late stage dementia compared with people dying with advanced cancer: a single-center preliminary study in Brazil. *Ann Palliat Med* 2018;7(4):437-443. doi: 10.21037/apm.2018.05.06