

Original Article

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Timing of palliative care access and outcomes of advanced cancer patients referred to an inpatient palliative care consultation team in Brazil

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Abstract

Objective. Little is known about the outcomes of cancer patients referred to palliative care (PC) teams in developing countries. Our aim was to examine the timing of PC access and outcomes of patients with advanced cancer referred to an inpatient PC consultation team in Brazil.

Method. Retrospective study of consecutive patients with advanced cancer admitted to a tertiary care general hospital (April 2015–December 2016) and referred for the first time to an inpatient PC consultation team. Patients' demographics, clinical features, time from first consult to death or discharge, and outcomes on medication use, clinical interventions, and end-of-life preferences were retrieved. An analysis was performed before and after PC.

Result. One hundred eleven patients were included. Median age was 68; 72% had an Eastern Cooperative Oncology Group performance status ≥ 3 . The median timing of PC access was 9 days (first interquartile = 3, third interquartile = 19). The use of analgesics (from 75% to 85%, $p = 0.001$) and opioids (from 50% to 73%, $p < .001$) increased. A lower proportion was receiving antibiotics (68% vs 48%, $p < 0.001$), thromboprophylaxis (44% vs 26%, $p < 0.001$), antihypertensives (28% vs 15%, $p = 0.001$), and antiemetic agents (64% vs 54%, $p = 0.027$). Chemotherapy use was lower (39–25%, $p < 0.001$). More patients had an end-of-life preference (39% to 25%, $p < 0.001$) and were not willing to receive intubation (32% vs 60%, $p < 0.001$), intensive care treatment (30% vs 55%, $p < 0.001$), cardiopulmonary resuscitation (35% vs 62%, $p < 0.001$), and artificial nutrition (22% vs 34%, $p < 0.001$).

Significance of results. Although PC referrals occurred exceedingly late during the cancer disease trajectory, positive changes were observed in medication profiles, clinical interventions use, and end-of-life preferences of patients with advanced cancer referred to a specialized inpatient PC consultation team in Brazil. Further efforts are needed to improve early palliative cancer care in developing countries.

Introduction

The World Health Organization (WHO) defines palliative care (PC) “as an approach that improves the quality of life of patients and their families facing the problem associated with a life-threatening illness, through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other problems, physical, psychosocial and spiritual” (World Health Organization, 2017).

Palliative care is beneficial for patients with advanced cancer in both the outpatient and inpatient settings (Dalal & Bruera, 2017). Previous studies have demonstrated that PC improves cancer patients' quality of life, mood, satisfaction with care (Bakitas et al., 2009; Temel et al., 2010; Zimmermann et al., 2014), healthcare-related outcomes such as costs of care, and end-of-life (EOL) quality care indicators such as number of emergency department visits, hospitalizations, hospital deaths, and intensive care unit admissions (Greer et al., 2016; Higginson & Evans, 2010; Hui et al., 2014).

Based on this evidence, current guidelines and position statements from the American Society of Clinical Oncology, European Society for Medical Oncology, and other influential organizations recommend that PC should be integrated early in the disease trajectory of patients with advanced cancer, concurrently with cancer-directed therapies (Ferrell et al., 2017; Jordan et al., 2018; Sepúlveda et al., 2002).

Despite this recommendation and the well-recognized growing need for PC because of the aging of the world population and the increase in cancer prevalence, PC is underdeveloped in most parts of the world, and most patients have late or no access to PC (Connor & Bermedo, 2014). In the last Worldwide Palliative Care Alliance/WHO report that mapped the level of PC

development among 234 nations, only 8.5% (most of which were in high-income countries from North America and Europe) have achieved an advanced stage of PC integration into the national healthcare systems (Lynch et al., 2013b). Furthermore, little is known about the outcomes of cancer patients referred to specialized inpatient PC teams in developing countries (Hannon et al., 2016).

In a recently published systematic review examining several patient-reported and healthcare-related outcomes of patients with advanced cancer referred to an inpatient PC team, there were no studies including patients from developing nations (Yang et al., 2016). Hence, there is a great need to examine the outcomes of cancer patients referred to specialized PC teams in the developing regions of the world.

In Brazil, the largest country of Latin America and world's ninth-largest economy (World Development Indicators, 2016), the National Cancer Institute estimates that 600,000 new cancer cases will occur each year for the 2018–2019 biennium (Instituto Nacional de Câncer, 2018). Similar to other low- and middle-income nations, although the number of cancer patients needing PC is growing rapidly, the availability of specialized PC services is generally low (Connor & Bernedo, 2014). The aim of our study was to examine the timing of PC access and outcomes of patients with advanced cancer admitted to a tertiary care general hospital in Brazil and referred for the first time to an inpatient PC team.

Methods

At our institution, a 657-bed private practice tertiary care general hospital, a consultation team of three physicians and a nurse provide specialized PC to the inpatient population. PC consultations include a thorough assessment and management of patients' physical and emotional symptoms, illness understanding and goals of care, psychosocial and spiritual needs, and EOL issues. Discussions regarding the risk and benefit of all clinical interventions, procedures, and medications, as well as advanced care planning discussions, are frequently held with patients, families, and the primary referring team to develop a personalized plan of care based on the patient's individual needs, goals, values, and prognosis. If necessary, members of other disciplines, such as psychologists, physical therapists, nutritionists, and social workers, are available upon demand. All patients are followed on a daily basis by the PC team.

The eligibility criteria for this retrospective study included (1) diagnosis of advanced cancer, defined as locally advanced, recurrent, or metastatic for solid tumors, and relapse or refractory for hematologic malignancies; (2) age 18 years or older; and (3) patients with advanced cancer referred for the first time to the inpatient PC team during admission.

We retrospectively reviewed the institutional database to identify all consecutive patients with advanced cancer referred for the first time to the inpatient PC team between April 2015 and December 2016. From the 124 patients with advanced cancer identified, 13 were excluded because they were seen for a comprehensive geriatric assessment before starting cancer therapy instead of for a PC consultation by one of the PC team members, who is also a geriatrician. The medical records of the remaining 111 inpatients consulted were assessed to collect data on patient's demographics (age, gender, and religion), clinical characteristics (cancer type, Eastern Cooperative Oncology Group performance status, Charlson Comorbidity Index, and reason for admission),

primary referring team, final disposition (death or discharge), length of hospital stay, and settings of PC consult and inpatient death (i.e., ward, step-down unit, or intensive care unit). Also, we retrieved information regarding the use and types of scheduled medications, including the use of any analgesics, opioids, coanalgesics, antibiotics, antipsychotics, statins, antiemetics, thromboprophylaxis, and antihypertensive agents; and documentation of EOL preferences as registered by the PC team in the patient assessment note. The latter includes the willingness to receive orotracheal intubation, intensive care treatment, cardiopulmonary resuscitation, and artificial nutrition (enteral or parenteral) at the day of PC referral and at the last day of admission.

Information on clinical interventions, including the use of artificial nutrition (enteral or parenteral), dialysis, vasopressors, mechanical ventilation, chemotherapy, and radiation therapy, was collected at the day of PC referral and reviewed for any changes occurring during the admission period. A comparative analysis of before-and-after PC consultation was performed. In addition, we assessed the institutional PC forms to capture the core domains addressed by the PC team during admission. Finally, to study the timing of PC access, we calculated the interval between hospital admission and first PC consultation as well as the time from PC consultation to death or discharged.

This study received approval from the Institutional Review Board of Hospital Israelita Albert Einstein (project number CAAE: 69522417.1.0000.0071). Because of retrospective data collection, the need for informed consent was waived.

Statistical analysis

The categorical variables were summarized by absolute frequencies and proportions and the numerical variables by medians, quartiles, and minimum and maximum values (Altman, 1990). The McNemar tests for paired proportions were used to compare medication use, clinical interventions, and EOL preferences before and after the PC consultation. Statistical tests were performed with SPSS software at a 0.05 significance level (IBM Corp., 2016).

Results

One hundred eleven patients were included. Median age was 68, and 53% of patients were female. Main reasons for admission were infection (16.2%), pain (13.5%), and disease progression (13.5%). Most had an Eastern Cooperative Oncology Group performance status ≥ 3 (72%) and were consulted on the regular wards (74%). Median age-adjusted Charlson Comorbidity Index was 8 (first interquartile = 7; third interquartile = 10). Fifty-seven patients died during admission, most of them in a regular ward (61.4%). Other patient characteristics are described in Table 1.

The median length of stay was 17 days (first interquartile = 9; third interquartile = 40). The median time between hospital admission and initial PC consultation was 5 days (first interquartile = 2; third interquartile = 17), whereas the median interval from first PC consultation to death or discharge was 9 days (first interquartile = 3; third interquartile = 19).

After PC consultation, the use of analgesics (from 75% before to 85% after, $p = .001$) and opioids (from 50% to 73%, $p < .001$) increased, and fewer patients were receiving antibiotics (68% before vs 48% after, $p < .001$), thromboprophylaxis (44% vs 26%, $p < .001$), antihypertensives (28% vs 15%, $p = .001$), and antiemetic agents (64% vs 54%, $p = .027$) (Table 2). Chemotherapy use decreased from 39% to 25% ($p < .001$) (Table 3). Also, after

Table 1. Patient demographics and clinical characteristics (*n* = 111)

Characteristics	<i>n</i>
Age, y	
Median (range)	68 (32–91)
Sex	
Male (%)	52 (46.8)
Female (%)	59 (53.2)
Religion	
Catholic (%)	71 (64.0)
Jewish (%)	16 (14.4)
Other (%)	15 (13.5)
No religion (%)	9 (8.1)
Primary referring team	
Oncology (%)	74 (66.7)
Hematology (%)	37 (33.3)
Reason for admission*	
Infection (%)	18 (16.2)
Pain (%)	15 (13.5)
Disease progression (%)	15 (13.5)
Antineoplastic treatment (%)	13 (11.7)
Dyspnea (%)	10 (9.0)
Delirium (%)	6 (5.4)
Bleeding (%)	6 (5.4)
Treatment toxicity (%)	6 (5.4)
Malignant bowel obstruction (%)	5 (4.5)
Other (%)	17 (15.3)
Cancer type*	
Hematologic (%)	38 (34.2)
Gastrointestinal (%)	19 (17.1)
Lung (%)	16 (14.4)
Genitourinary (%)	16 (14.4)
Breast (%)	10 (9.0)
Other (%)	12 (10.8)
ECOG	
0–2 (%)	31 (27.9)
3–4 (%)	80 (72.1)
Age-adjusted Charlson Comorbidity Index	
Median (Q1; Q3)	8 (7; 10)
Minimum–maximum	2–15
Setting of first consult	
Ward (%)	82 (73.9)
Step-down unit (%)	13 (11.7)
Intensive care unit (%)	16 (14.4)
Setting of inpatient death (<i>n</i> = 57)	
Ward (%)	35 (61.4)

(Continued)

Table 1. (Continued.)

Characteristics	<i>n</i>
Step-down unit (%)	7 (12.3)
Intensive care unit (%)	15 (26.3)

ECOG, Eastern Cooperative Oncology Group; Q1, first quartile; Q3, third quartile.
*Sum does not add up 100% because of rounding.

PC consultation more patients had an EOL preference documented (36% vs 65%, $p < .001$) and more were not willing to receive intubation (32% vs 60%, $p < .001$), intensive care treatment (30% vs 55%, $p < .001$), cardiopulmonary resuscitation (35% vs 62%, $p < .001$), and artificial nutrition (22% vs 34%, $p < .001$) (Table 4). No other significant differences in patients' medication use, clinical interventions, or EOL preferences were found (Tables 2–4).

The domains most frequently assessed and managed by the PC team were family distress (74%), emotional distress (67%), EOL care/issues (64%), and symptom management (41%) (Appendix 1).

Discussion

To our knowledge, this is the first study to examine the timing of PC access and outcomes of patients with advanced cancer admitted and referred to an inpatient PC consultation team at a private practice tertiary care general hospital in Brazil. We found that, although PC referrals occurred late in the disease trajectory, there were an increase in the use of analgesics; decrease in the prescription of antibiotics, antihypertensives, antiemetics, and thromboprophylactic agents; a reduction in the use of chemotherapy; and an improvement in patients' preferences toward less aggressive EOL care.

In our study, patients were referred exceedingly late to PC during the course of their illness: Most had a poor performance status at referral, and the time from initial consultation to death or discharge was only a few days (median = 9). Limited PC exposure periods, within the range of days, have been found in other studies conducted in countries from the same WHO PC development group as Brazil (group 3a) (Lynch et al., 2013a), where the provision of PC is isolated and the level of integration between PC services and the mainstream health system is low (Baek et al., 2011; Al-Saleh et al., 2017). For example, in a retrospective review of patients receiving palliative cancer care referred to the first independent PC center in Kuwait, a developing country in the Eastern Mediterranean area, Al-Saleh et al. (2017) found that the median time from PC referral to death was 41 days, with a majority of patients (58%) being seen within 30 days from death. Similarly, in a study conducted by Baek et al. (2011) in a cohort of patients with advanced cancer registered in 34 inpatient PC services in Korea, the median survival after the first PC encounter was <30 days (median = 18).

On the other hand, in countries where the level of PC development and integration is much more advanced (WHO group 4) (Lynch et al., 2013a), longer intervals from referral to death have been found (Cheng et al., 2005; Nitecki et al., 2018). In two North American cohorts of patients treated at tertiary care medical centers with access to subspecialty PC services, one including patients with ovarian cancer and the other including patients with advanced cancer of different primary sites, the median time from PC referral to death was 3.36 months

Table 2. Medication use before and after PC

Medication	Before, n (%)	After, n (%)	p
Analgesics			
Yes	83 (74.8)	94 (84.7)	0.001
No	28 (25.2)	17 (15.3)	
Opioids			
Yes	56 (50.5)	81 (73.0)	<0.001
No	55 (49.5)	30 (27.0)	
Coanalgesics*			
Yes	28 (25.7)	29 (26.6)	>0.999
No	81 (74.3)	80 (73.4)	
Antibiotics			
Yes	76 (68.5)	53 (47.7)	<0.001
No	35 (31.5)	58 (52.3)	
Antiemetics			
Yes	71 (64.0)	60 (54.1)	0.027
No	40 (36.0)	51 (45.9)	
Thromboprophylactics			
Yes	49 (44.1)	29 (26.1)	<0.001
No	62 (55.9)	82 (73.9)	
Antihypertensives			
Yes	31 (27.9)	17 (15.3)	0.001
No	80 (72.1)	94 (84.7)	
Statins			
Yes	7 (6.3)	4 (3.6)	0.375
No	104 (93.7)	107 (96.4)	
Antipsychotics			
Yes	44 (39.6)	39 (35.1)	0.405
No	67 (60.4)	72 (64.9)	

PC, palliative care.

*Two patients were excluded from this analysis because of missing data.

(Nitecki et al., 2018) and 1.9 months (Cheng et al., 2005), respectively. Therefore, the very limited time between an initial PC consult to death in our study possibly reflects the low level of PC development and integration at our institution and in Brazil as a whole, placing patients at risk of not being able to receive the well-known benefits of a timely PC referral (Bauman & Temel, 2014; Davis et al., 2015).

Barriers to early PC referrals may include the absence of PC education and training among oncology health care providers, leading to misconceptions that PC is synonymous with EOL and hospice care (Hui et al., 2015b); lack of financial resources to implement structures that permit early referrals, such as outpatient PC clinics (Hui et al., 2010); and the absence of standardized referral criteria that are tailored to patient needs and local resources (Hui & Bruera, 2016). Future research is needed to develop and test strategies that can overcome these barriers, ultimately optimizing referrals and enhancing the integration of PC into oncology care at our institution and in the healthcare systems of developing countries.

Table 3. Clinical interventions before and after PC

Clinical interventions	Before, n (%)	After, n (%)	p
Enteral nutrition			
Yes	24 (21.6)	20 (18.0)	0.454
No	87 (78.4)	91 (82.0)	
Parenteral nutrition			
Yes	13 (11.7)	8 (7.2)	0.180
No	98 (88.3)	103 (92.8)	
Dialysis			
Yes	6 (5.4)	5 (4.5)	>0.999
No	105 (94.6)	106 (95.5)	
Vasopressors			
Yes	7 (6.3)	4 (3.6)	0.453
No	104 (93.7)	107 (96.4)	
Mechanical ventilation			
Yes	12 (10.8)	13 (11.7)	>0.999
No	99 (89.2)	98 (88.3)	
Chemotherapy*			
Yes	43 (39.1)	28 (25.5)	<0.001
No	67 (60.9)	82 (74.5)	
Radiation therapy*			
Yes	5 (4.5)	6 (5.5)	>0.999
No	105 (95.5)	104 (94.5)	

PC, palliative care.

*One patient was excluded because of missing data.

After the specialized PC team was involved in patients' care, we found significant changes in their medication profiles. A higher proportion of patients were receiving pain control medications, such as opioids. Fewer were taking drugs for comorbid conditions, such as antihypertensives and thromboprophylactic agents; in addition, a lower proportion was receiving antibiotics and antiemetics. Except for the less frequent use of antiemetics (which could be related to the significant reduction in the use of chemotherapy that we also found), this overall pattern of change suggests that by regularly assessing pain and other symptoms and the risks and benefits of all medications, the PC team was able to direct patients' medication profile toward the use of drugs for symptom control. They also could reduce the prescription of agents with an unfavorable risk/benefit ratio for EOL use.

Previous studies had similar results (Hui et al., 2015a; Masman et al., 2015). For instance, among a cohort of PC patients, mainly with a cancer diagnosis (89%), and admitted to a PC center with a multidisciplinary team in place, Masman et al. (2015) found that the use of analgesics increased from 56.7% to 94.6%, with the prescription of opioids increasing from 42% to 92%. Also, in a retrospective study analyzing the chronological changes in the medication profiles of patients with advanced cancer referred to an inpatient PC consultation team and later admitted to an acute PC unit, Hui et al. (2015a) observed a pattern very similar to ours, characterized by an increase in the use of symptom-directed drugs, such as corticosteroids, laxatives, neuroleptics, and antiulcer agents; a decrease in the proportion of patients

Table 4. End-of-life preferences before and after PC

Any documented preference	Before, n (%)	After, n (%)	p
Yes	40 (36.0)	72 (64.9)	<0.001
No	71 (64.0)	39 (35.1)	
Orotracheal intubation			
Yes	75 (67.6)	45 (40.5)	<0.001
No	36 (32.4)	66 (59.5)	
Intensive care treatment			
Yes	78 (70.3)	50 (45.0)	<0.001
No	33 (29.7)	61 (55.0)	
Cardiopulmonary resuscitation			
Yes	72 (64.9)	42 (37.8)	<0.001
No	39 (35.1)	69 (62.2)	
Artificial nutrition			
Yes	86 (77.5)	73 (65.8)	<0.001
No	25 (22.5)	38 (34.2)	

PC, palliative care.

receiving antilipemics and antihypertensives; and a trend toward less EOL use of anti-infectives.

With regard to the frequency of clinical interventions, use of chemotherapy decreased significantly, denoting that this population of frail patients with advanced cancer received a better quality of EOL care after the involvement of the specialized PC team. Previous data have shown that chemotherapy for patients with terminal cancer is associated with worse quality of life and is not associated with prolonged survival (Prigerson et al., 2015; Wright et al., 2014). Hence, both American Society of Clinical Oncology and the National Quality Forum have endorsed chemotherapy use near death to be a poor indicator of the quality of EOL care (American Society of Clinical Oncology, 2018; National Quality Forum, 2012). Nevertheless, although a 15% reduction in chemotherapy use is a noteworthy result of our study, we believe that this effect could have been even higher if PC referrals did not occur too late in the disease course. As has been previously demonstrated, the timing of PC access directly influences EOL quality care indicators, with a more prominent improvement in the aggressiveness of EOL care when the PC initial encounter occurs earlier, months before death, and when patients are being seen in the outpatient setting (Hui et al., 2014; Triplett et al., 2017). Currently, our institution is implementing a novel outpatient PC clinic embedded in the oncology center to promote early integrated palliative cancer care. Further research is warranted to evaluate the outcomes of this measure on chemotherapy use and other EOL quality care indicators at our hospital and other private practice institutions in Brazil.

The overall documentation of EOL preferences improved after the delivery of concurrent palliative cancer care was initiated, with more patients preferring not to receive life-sustaining measures. This implies that despite the limited time from PC consult to death or discharge, the integration of the specialized PC team in patients care was able to enhance patients' accurate understanding

of their disease. This hypothesis is supported by the fact that one of the most frequent domains assessed and managed by the inpatient PC team in the current cohort was the EOL care/issues domain (Dahlin, 2009), of which assessing and documenting patients' EOL preferences are integral parts. Furthermore, recent studies have shown that patients with terminal cancer who accurately understand their disease are more likely to prefer comfort-directed care instead of life-prolonging measures (Mack et al., 2010; Tang et al., 2014), and that inpatient PC teams are capable of improving prognostic awareness in this population (Loke et al., 2011; Lu et al., 2016). On the other hand, at least one-third of the patients were still willing to receive at least one aggressive EOL measure, pointing again to the need of promoting earlier PC integration, now as a means of improving patients' understanding of their illness (Bauman & Temel, 2014).

This study has several limitations. First, it was conducted in a single, academic, private practice general hospital, which limits the generalizability of our findings to other settings and advanced cancer patient populations. Second, the sample size of our cohort and the lack of a control group prevent us from drawing conclusions based on our results. Third, we did not capture data after admission on discharged patients, which might have affected our findings as part of them are amenable to changes over time (i.e., EOL preferences). Fourth, because EOL preferences were retrieved as registered by the PC team in the patient assessment note, this could have biased the accuracy of these variables.

In conclusion, PC referrals occurred exceedingly late in the cancer disease trajectory. Nevertheless, positive changes were observed in the medication profiles, use of clinical interventions, and EOL preferences of patients with advanced cancer referred to a specialized inpatient PC team at a tertiary care private practice general hospital in Brazil. Further efforts are needed to improve early palliative cancer care in developing countries.

Supplementary material. The supplementary material for this article can be found at <https://doi.org/10.1017/S1478951518000597>.

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Conflicts of interest statement. The authors declare that there are no conflicts of interest.

References

- Al-Saleh K, Al-Awadi A, Soliman N.A, et al. (2017) Timing and outcome of referral to the first stand-alone palliative care center in the Eastern Mediterranean region, the Palliative Care Center of Kuwait. *American Journal of Hospice & Palliative Care* 34(4), 325–329.
- Altman DG (1990) *Practical statistics for medical research*. London: Chapman and Hall/CRC.
- American Society of Clinical Oncology (2018) *ASCO Institute for Quality*. Available from <https://www.asco.org/practice-guidelines/quality-guidelines>.
- Baek YJ, Shin DW, Choi JY, et al. (2011) Late referral to palliative care services in Korea. *Journal of Pain and Symptom Management* 41(4), 692–699.
- Bakitas M, Lyons KD, Hegel MT, et al. (2009) Effects of a palliative care intervention on clinical outcomes in patients with advanced cancer: The Project ENABLE II randomized controlled trial. *Journal of the American Medical Association Oncology* 302(7), 741–749.
- Bauman JRand Temel JS (2014) The integration of early palliative care with oncology care: the time has come for a new tradition. *Journal of the National Comprehensive Cancer Network* 12(12), 1763–1771.
- Cheng WW, Willey J, Palmer JL, et al. (2005) Interval between palliative care referral and death among patients treated at a comprehensive cancer center. *Journal of Palliative Medicine* 8(5), 1025–1032.

- Connor SR and Bermedo MCS** (2014) *The global atlas of palliative care at the end of life*. Geneva, CH/London: Worldwide Hospice Palliative Care Alliance, World Health Organization.
- Dahlin C** (2009) The 2009 National Consensus Project for Quality Palliative Care (NCP) Guidelines (400). *Journal of Pain and Symptom Management* 37(3), 485–486.
- Dalal S and Bruera E** (2017) End-of-life care matters: Palliative cancer care results in better care and lower costs. *Oncologist* 22(4), 361–368.
- Davis MP, Temel JS, Balboni T, et al.** (2015) A review of the trials which examine early integration of outpatient and home palliative care for patients with serious illnesses. *Annals of Palliative Medicine* 4(3), 99–121.
- Ferrell BR, Temel JS, Temin S, et al.** (2017) Integration of palliative care into standard oncology care: American Society of Clinical Oncology Clinical Practice Guideline Update. *Journal of Clinical Oncology* 35, 96–112.
- Greer JA, Tramontano AC, McMahon M, et al.** (2016) Cost analysis of a randomized trial of early palliative care in patients with metastatic non-small-cell lung cancer. *Journal of Palliative Medicine* 19(8), 842–848.
- Hannon B, Zimmermann C, Knaut FM, et al.** (2016) Provision of palliative care in low- and middle-income countries: Overcoming obstacles for effective treatment delivery. *Journal of Clinical Oncology* 34(1), 62–68.
- Higginson IJ and Evans CJ** (2010) What is the evidence that palliative care teams improve outcomes for cancer patients and their families? *Cancer Journal* 16(5), 423–435.
- Hui D and Bruera E** (2016). Integrating palliative care into the trajectory of cancer care. *Nature Reviews Clinical Oncology* 13(3), 159–171.
- Hui D, Elsayem A, De La Cruz M, et al.** (2010) Availability and integration of palliative care at US cancer centers. *Journal of the American Medical Association Oncology*, 303(11), 1054–1061.
- Hui D, Kim SH, Roquemore J, et al.** (2014) Impact of timing and setting of palliative care referral on quality of end-of-life care in cancer patients. *Cancer* 120(11), 1743–1749.
- Hui D, Li Z, Chisholm GB, et al.** (2015a) Changes in medication profile among patients with advanced cancer admitted to an acute palliative care unit. *Supportive Care in Cancer* 23(2), 42–432.
- Hui D, Park M, Liu D, et al.** (2015b) Attitudes and beliefs toward supportive and palliative care referral among hematologic and solid tumor oncology specialists. *Oncologist* 20(11), 1326–1332.
- IBM Corp** (2016). IBM SPSS Statistics for Windows. Armonk, NY.
- Instituto Nacional de Câncer** (2018) *Estimativa 2018*. Available from <http://www1.inca.gov.br/estimativa/2018>.
- Jordan K, Aapro M, Kaasa S, et al.** (2018) European Society for Medical Oncology (ESMO) position paper on supportive and palliative care. *Annals of Oncology* 29(1), 36–43.
- Loke S-S, Rau K-M and Huang C-F** (2011) Impact of combined hospice care on terminal cancer patients. *Journal of Palliative Medicine* 14(6), 683–687.
- Lu C-Y, Shen W-C, Kao C-Y, et al.** (2016) Impact of palliative care consultation service on terminally ill cancer patients: A 9-year observational cohort study in Taiwan. *Medicine* 95(10), e2981.
- Lynch T, Connor S and Clark D** (2013a) Mapping levels of palliative care development: A global update. *Journal of Pain and Symptom Management* 45(6), 1094–1106.
- Lynch T, Connor S and Clark D** (2013b) Mapping levels of palliative care development: A global update. *Journal of Pain and Symptom Management* 45, 1094–1106.
- Mack JW, Weeks JC, Wright AA, et al.** (2010) End-of-life discussions, goal attainment, and distress at the end of life: Predictors and outcomes of receipt of care consistent with preferences. *Journal of Clinical Oncology* 28(7), 1203–1208.
- Masman AD, van Dijk M, Tibboel D, et al.** (2015) Medication use during end-of-life care in a palliative care centre. *International Journal of Clinical Pharmacy* 37(5), 767–775.
- National Quality Forum** (2012) Cancer Endorsement Maintenance 2011. Available from: http://www.qualityforum.org/Projects/Cancer_Endorsement_Maintenance_2011.aspx.
- Nitecki R, Diver EJ, Kamdar MM, et al.** (2018) Patterns of palliative care referral in ovarian cancer: A single institution 5-year retrospective analysis. *Gynecology Oncology* 148(3), 521–526.
- Prigerson HG, Bao Y, Shah MA, et al.** (2015). Chemotherapy use, performance status, and quality of life at the end of life. *Journal of the American Medical Association Oncology* 1(6), 778–784.
- Sepúlveda C, Marlin A, Yoshida T, et al.** (2002) Palliative Care: The World Health Organization's Global Perspective. *Journal of Pain and Symptom Management* 24(2), 91–96.
- Tang ST, Liu TW, Chow JM, et al.** (2014) Associations between accurate prognostic understanding and end-of-life care preferences and its correlates among Taiwanese terminally ill cancer patients surveyed in 2011–2012. *Psychooncology* 23(7), 780–787.
- Temel JS, Greer JA, Muzikansky A, et al.** (2010) Early palliative care for patients with metastatic non-small-cell lung cancer. *The New England Journal of Medicine* 363(8), 733–742.
- Triplett DP, LeBrett WG, Bryant AK, et al.** (2017) Effect of palliative care on aggressiveness of end-of-life care among patients with advanced cancer. *Journal of Oncology Practice* 13(9), e760–e769.
- World Development Indicators** (2016) The World Bank. Available from <https://datacatalog.worldbank.org/dataset/gdp-ranking>.
- World Health Organization** (2017) *WHO Definition of Palliative Care*. Geneva: WHO. Available from <http://www.who.int/cancer/palliative/definition/en/>. Last accessed February 24, 2018.
- Wright AA, Zhang B, Keating NL, et al.** (2014) Associations between palliative chemotherapy and adult cancer patients end of life care and place of death: prospective cohort study. *BMJ: British Medical Journal*, 348, G1219.
- Yang GM, Neo SH, Lim SZ, et al.** (2016) Effectiveness of hospital palliative care teams for cancer inpatients: A systematic review. *Journal of Palliative Medicine* 19(11), 1156–1165.
- Zimmermann C, Swami N, Krzyzanowska M, et al.** (2014) Early palliative care for patients with advanced cancer: a cluster-randomised controlled trial. *Lancet* 383(9930), 1721–1730.