

Introduction: To calculate the number of days patients with terminal non-small cell lung cancer (NSCLC) spent at home in the last 3 months of life, and to identify factors that predict a lower proportion of days at home.

Material and methods: Retrospective study of 434 deceased patients with NSCLC. The number of days spent in a hospital or nursing home was identified from electronic health records.

Results: Most patients received primary chemotherapy. Only 45% received palliative care provided by a dedicated palliative care team (PCT). In the last 3 months of life, only 39 patients (9%) were not hospitalized. The median number of days spent in hospital was 17, range 0–61. Hospital death occurred in 48%. Admission to a nursing home was recorded in 45%. Overall, the patients spent a median of 64 days at home. Both, older patients and females spent fewer days at home. Family network and aspects of palliative care, possibly reflecting the symptom duration or burden, also impacted days at home.

Conclusions: Long-lasting need for PCT support (not just the final 3 months) and earlier necessity for opioid analgesics were predictive for a reduced number of days at home. However, modifiable factors such as sex were identified too.

Key words: non-small cell lung cancer, palliative therapy, end-of-life care, hospital death, quality indicator.

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Days at home in the last three months of life: patterns-of-care analysis in patients with non-small cell lung cancer

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Compared to previous decades, the introduction of several new treatment approaches has markedly improved the survival outcomes of patients with non-small cell lung cancer (NSCLC). The main drivers are immune checkpoint inhibitors (ICI), targeted agents, and stereotactic radiotherapy [1–3]. Nevertheless, death from uncontrolled NSCLC remains common and is typically preceded by a longer phase of palliative care, which might overlap with active oncological treatment [4–6]. Depending on the prevailing pattern of disease progression, thoracic, brain-metastases-related, bone-metastases-related, other, and mixed symptom trajectories might occur. Common symptoms include pain, cachexia, tiredness, anxiety, and depression [7, 8]. Furthermore, infections, anaemia, and gastrointestinal complications might occur, either as a result of cancer progression or due to treatment with anticancer drugs such as cytotoxic chemotherapy [9, 10]. Many patients with NSCLC are elderly, and their level of social support and ability to function at home is highly variable. Planned and unplanned hospitalizations and hospice or nursing home care are often necessary. Such admissions may or may not be desirable from the patients' perspective, depending on their performance status, symptom burden, and socioeconomic context. Days at home in the last months of life has become a topic of interest, and previous research has suggested this measure might be applied at a system level to evaluate potential barriers to achieving a long period at home [11–13]. Due to the unique characteristics of the publicly funded Norwegian healthcare system, which aims at equal access and avoidance of barriers, a study evaluating this measure and comparing the results to those reported from other countries is of great relevance [14]. Our group previously established a regional quality-of-care database covering all patients with NSCLC managed by the multidisciplinary lung cancer team (MDT) at Nordland Hospital Bodø, the only lung cancer MDT in the county of Nordland, a rural region in northern Norway [15, 16]. This database also includes information about all hospitalizations and institutional care in the last 3 months of life. It was therefore decided to select NSCLC care as the initial measure, acknowledging that previous studies did include different cancer types and the last 6 months of life [11, 12], and that our approach will provide preliminary hypotheses only, which may stimulate future large-scale analyses.

Material and methods

The study included deceased patients with NSCLC (death between 2006 and 2020), who were identified from a pre-existing quality-of-care database.

Patients who did not survive for at least 3 months from diagnosis were excluded ($n = 79$). All patients were managed in a real-life setting after the MDT at Nordland Hospital Bodø had provided the treatment strategy, which was always based on national Norwegian guidelines. All initial stages of NSCLC and all management approaches were included (best supportive care, all types of systemic treatment, radiotherapy, surgery). Due to the absence of other oncology care providers in our rural, sparsely populated healthcare region and the availability of electronic health records (also capturing care at the smaller local hospitals outside of Bodø), all aspects of longitudinal NSCLC care were captured, and the study resembled a cancer registry study, albeit with a limited number of patients. The electronic health records showed whether a patient was admitted from home or a primary healthcare institution. The same information was available from discharge notes. Previous studies with identical preconditions have already elaborated on the completeness of sociodemographic and management data and other advantages of the quality-of-care surveillance in our geographic region [15–17]. All patients were covered by the national public healthcare system. Therefore, no financial barriers prevented access to hospital or nursing home care, supportive measures, radiotherapy, drugs, etc. Dedicated hospice care was not available. If indicated, the primary healthcare sector also provided home care (mobile nurses etc.), typically in close collaboration with the nearest hospital and the hospitals' multidisciplinary palliative care team (MPCT). For example, a hospitalized patient might have been discharged to a public temporary care facility before moving back to home. We were unable to capture visits at primary care physician offices or community-based emergency care offices. Multidisciplinary palliative care team referral was individualized and not based on clear rules for expected survival or other baseline parameters. Pathways for routine early palliative care were not implemented. The multidisciplinary palliative care team at Nordland Hospital Bodø and the smaller local hospitals provide in- and outpatient consultations and advance care planning, and collaborate closely with each other, the oncologists and hospital wards, and the home care providers. They also play a coordinating role and often supervise transition between different institutions and departments. Typical problems managed by MPCTs include pain, nutrition, dyspnoea, and psychological support, to name a few. The primary healthcare sector's mobile nurses, physicians, and nursing home staff can all reach out to the closest MPCT and ask for specialist advice. One of the aims is to prevent unnecessary hospitalization. Busy primary care or family physicians are not necessarily able to provide all types of support at all points in time (public holidays, summer vacation, sick leave, etc.). Eventually, their involvement is greatly person dependent.

Statistical analysis and ethics

Baseline data at the time of NSCLC diagnosis and patterns of care were extracted and compared between different subgroups. The number of days not spent at home (hospital in-patient, nursing home) was subtracted from

91 (a uniform proxy for the last 3 months). The IBM SPSS 27 software package (IBM SPSS Statistics, Somers, NY, USA) was employed for all statistical analyses. For comparison of dichotomous variables, the chi-square test, and Fisher's exact test, where applicable, were employed, and for continuous variables, the Mann-Whitney U test was used. Furthermore, the Pearson correlation coefficient was employed to measure a linear correlation between 2 sets of data. The significance level was set to 5%, and all tests were carried out two-sided. The study was performed as a retrospective analysis in the context of our longitudinal monitoring of NSCLC management. As a quality-of-care analysis, no approval from the Regional Committee for Medical and Health Research Ethics (REK) was necessary.

Results

Study population

The study included 434 deceased patients (females: $n = 177$, 41%) with a median age of 69 years at diagnosis (range 39–89) and a median survival of 11.6 months. Most patients were married or lived with a partner ($n = 290$, 69%; patients with children: $n = 375$, 86%). The majority lived in a community without a hospital ($n = 234$, 54%). Most patients had variable degrees of comorbidities, while 178 (41%) had a diagnosis of NSCLC alone. Active smoking was recorded in 150 patients (35%), and 24 were never smokers (6%). Adenocarcinoma ($n = 210$, 48%) was more common than squamous cell carcinoma ($n = 147$, 34%), others, or mixed types. Initially, 222 patients (51%) had non-metastatic disease (stage I–III). A total of 135 patients (31%) were diagnosed with brain metastases during the disease trajectory.

Treatment and care

As indicated in Table 1, most patients received primary cytotoxic chemotherapy. Only 45% received care that involved the MPCT at some time after diagnosis of NSCLC. Twenty-three per cent received active treatment during the last 4 weeks of life, either with systemic treatment or radiotherapy. Compared to chemotherapy or targeted agents such as gefitinib or erlotinib during the last 4 weeks of life, radiotherapy administration was more common. In particular, palliative short-course regimens for bone or brain metastases were utilized. A minority of patients were treated for life-threatening airway or vena cava superior compression (radiation \pm chemotherapy) and died despite our efforts to prolong their survival. Another small subgroup died from unexpected treatment-induced complications such as neutropaenic sepsis. Overall, from the present retrospective point-of-view, approximately 50% of treatment during the last 4 weeks of life may be categorized as overtreatment and the other half as proper palliative treatment attempts.

Analgesic opioid treatment was common (73%). It was initiated earlier than in the last 3 months in 17%, between 3 months and 1 month in 39%, and in the last month in 17%. Continuous administration of analgesics *via* pump was utilized in 44%, largely (35%) in the last month of life. Also, steroids were commonly administered (73%).

Treatment was initiated earlier than in the last 3 months in 12%, between 3 months and 1 months in 38%, and in the last month in 23%.

In the last 3 months of life, only 39 patients (9%) were not hospitalized. The median number of days spent in hospital was 17, range 0–61. Home death was uncommon (12%). Hospital death occurred in 48%. Admission to a nursing home was recorded in 45% of patients. Four per cent spent the complete last 3 months in a nursing home. Sixty-nine patients (16%) were admitted for 14 days or less.

The patients spent a median of 64 days at home, corresponding to 70% of the last 3 months. Only 21 patients (5%) spent all 91 days at home. Thirty-seven patients (9%) spent at least 90% of their time in hospitals and/or nursing homes.

Predictive factors

Several factors were not significantly associated with the number of days at home. These included year of death, length of overall survival, living in a community with a hospital, having any comorbidity, NSCLC stage and histology, presence of brain metastases, having received thoracic radiotherapy, having received any systemic treatment, having received any ICI, and having received any targeted agents in the presence of an actionable mutation. Table 2 shows the significant predictors, e.g. age and sex. Both, older patients and females spent fewer days at home. The age-related difference was driven by nursing home utilization, while hospitalization was comparable in patients stratified by median age. The mean number of days in nursing homes was 11 in patients younger than 69 years (17 in patients ≥ 69 years; median 0 in both groups; $p = 0.01$). Further correlations included the type of near family network and several aspects of palliative care.

Discussion

According to data from the Norwegian cancer registry, lung cancer is more common in males [18] – a finding also reflected in the present study. Regarding the study population (mainly patients in their sixties and older), relevant findings included that most patients had a family caregiver network. In general, treatment was in accordance with national guidelines and discussed in weekly MDT conferences. The proportion of patients who received some type of active anti-cancer treatment in the last 4 weeks of life was relatively high (23%), and the referral rate to a MPCT at some time after cancer diagnosis was lower (45%) than one might intend to achieve in light of the reported benefit [6]. As recently summarized by Temel *et al.*, early involvement of specialty-trained palliative care clinicians improves patient-reported outcomes, such as quality of life, and health care delivery, including hospice utilization [19]. Support might also include management of side effects caused by anticancer therapy, coping with uncertainty regarding prognosis, and advance care planning.

In the last 3 months of life, only 9% of the patients in the present study were not hospitalized. Hospital death occurred in 48%, while home death was uncommon. These findings remain unchanged from our previous analysis [16].

Table 1. Baseline and treatment characteristics, $N = 434$

| Parameter | n | % |
|---|-----|----|
| Gender | | |
| Female sex | 177 | 41 |
| Male sex | 257 | 59 |
| Family | | |
| Married or partnered | 290 | 67 |
| Not married or partnered | 144 | 33 |
| Children | 375 | 86 |
| Charlson comorbidity index | | |
| No comorbidity | 178 | 41 |
| Any comorbidity | 256 | 59 |
| Lung cancer type | | |
| Adenocarcinoma | 210 | 48 |
| Squamous cell carcinoma | 147 | 34 |
| Other, mixed, or unspecified | 77 | 18 |
| Treatment aspects | | |
| Best supportive care | 33 | 8 |
| Initial surgical resection | 77 | 18 |
| Initial curative intended (chemo) radiotherapy | 40 | 9 |
| Any immune checkpoint inhibitor (any line) | 53 | 12 |
| Targeted agent in NSCLC with actionable mutation | 8 | 2 |
| No care by multidisciplinary palliative care team | 239 | 55 |
| Never received thoracic radiotherapy | 150 | 35 |
| Never received systemic treatment | 133 | 31 |
| Only one line of systemic treatment | 163 | 38 |
| More than one line of systemic treatment | 138 | 32 |
| Active oncology treatment in the last 4 weeks of life | 99 | 23 |
| Invasive procedure for pleural effusion in the last 3 months of life, e.g. pleurodesis | 48 | 11 |
| Invasive procedure for bronchial obstruction in the last 3 months of life, e.g. stent insertion | 6 | 1 |

NSCLC – non-small cell lung cancer

A hospital utilization rate of 91% is higher than expected from the literature [20], and may indicate regional problems with providing a sufficient non-hospital-care infrastructure in our rural county, where small communities struggle to recruit primary care physicians and other necessary human resources. Admission to a nursing home was recorded in 45% of patients. Dedicated hospice care is still lacking in our region, but larger communities have started to dedicate a certain amount of nursing home capacity, e.g. one floor, to palliative end-of-life care. Even these facilities struggle with recruitment of specialty-trained staff, and for the smaller communities the staffing of regular nursing home services is already challenging. The study patients spent a median of 64 days at home, corresponding to 70% of the last 3 months. Individual variation was large. Longer-term in-

Table 2. Predictive factors

| Parameter | Number of days at home, median | Significance level, <i>p</i> -value* | Comments |
|--|--------------------------------|--------------------------------------|--|
| Female sex | 62 | 0.005 | |
| Male sex | 66 | | |
| Married or partner, having children | 67 | < 0.0001 | First category vs. any other: <i>p</i> < 0.0001 |
| Married or partner, no children | 59 | | |
| Unmarried (no partner either), but children | 59 | | |
| Neither spouse/partner/children | 56.5 | | |
| Palliative care team not involved | 69 | 0.001 | Not vs. any: 0.012 |
| Palliative care team involved at least 3 months before death | 49 | | |
| Palliative care team involved late (< 3 months before death) | 63 | | |
| Opioid analgesics not prescribed | 71 | 0.001 | Not vs. any: <i>p</i> = 0.002 |
| Opioid analgesics early (at least 3 months before death) | 58 | | |
| Opioid analgesics late (< 3 months before death) | 63 | | |
| Continuous analgesics <i>via</i> pump not utilized | 68 | < 0.0001 | First 2 categories vs. others: <i>p</i> = 0.002 |
| Continuous analgesics <i>via</i> pump in the last 2 weeks | 68 | | |
| Continuous analgesics <i>via</i> pump in the last 3–4 weeks | 50 | | |
| Continuous analgesics <i>via</i> pump > last 4 weeks | 41 | | |
| Steroids not prescribed | 67 | 0.003 | Not vs. any: <i>p</i> = 0.12 Not or late vs. early: <i>p</i> = 0.03 |
| Steroids early (at least 3 months before death) | 58 | | |
| Steroids late (< 3 months before death) | 66 | | |
| Age (continuous variable) | n.a. | 0.009 | Pearson correlation |
| Multivariate analysis (significant factors only) | | | |
| Married (or partner) and children | | 0.006 | vs. 3 other categories |
| Palliative care team not involved | | 0.001 | vs. 2 other categories |
| Continuous analgesics <i>via</i> pump not utilized or in the last 2 weeks only | | 0.027 | vs. 2 other categories |

volvement of a MPCT and necessity for steroids and/or opioid analgesics before the last 3 months, i.e. possible indicators for long-lasting symptoms, were predictive for a reduced number of days at home. The same was true for longer duration of pump administration of continuous analgesics, and in addition not having a spouse or partner and children, i.e. patients living alone. Additional factors such as sex and age were identified too. The existence of confounding factors explaining some of the observed statistical associations cannot be ruled out in a retrospective study such as this one. It appears possible that patients doing well at home were not referred to a MPCT, while those needing hospitalization in the absence of already established MPCT involvement were referred before discharge.

It seems understandable that complete home care may be difficult in patients who need the support of a hospital's MPCT, although implementation of larger or cross-sectoral teams or home hospice may ameliorate the rates of hospitalization (the main reason for being away from home in this study). Nevertheless, acute situations such as severe infections or pulmonary embolism will always necessitate a certain frequency of hospitalization in patients with incurable NSCLC. The individual willingness to han-

dle difficult situations at home, prepare for home death, and accept considerable distress is also variable, both for patients themselves and for family caregivers [21–23]. It is therefore not desirable to declare a certain number of days at home as the gold standard or to propose a one-size-fits-all approach in terminal care. Some patients have strong preferences for hospice or nursing home care, and early institution of such care may be the best option [24, 25]. It must also be acknowledged that occasional patients already live in a nursing home, due to age and comorbidity, when a diagnosis of NSCLC is made. In the present study, the mean number of days in nursing homes was 11 in patients younger than 69 years and 17 in patients \geq 69 years old. As stated previously, the measure of days at home might be applied at a system level to evaluate potential barriers to achieving a long period at home [12].

In a SEER-Medicare database study, decedents diagnosed with lung cancer at age \geq 66 years between January 2007 and December 2013, who survived \geq 6 months from diagnosis were included [26]. Between 6 months and one month before death, full-month hospice and inpatient/skilled nursing increased. Cancer-directed treatment decreased 31.9–18.5%. Associations between sociodemo-

graphic characteristics and care setting suggest differences in care preferences or access barriers. In a UK study, no association was found between aggressive end-of-life care (greater than or equal to one of the following indicators occurring during the last 3 months of life: greater than or equal to 2 emergency department visits, ≥ 30 days in hospital, and death in hospital) and patients' age, gender, and marital, financial, or health status [27].

A population-based study using health administrative data from Ontario, Canada was reported by Andersen *et al.* [12]. It included almost 73,000 patients who died from cancer (not limited to NSCLC) and evaluated the last 180 days of life. The median age at diagnosis was 67 years. These patients spent a median of 164 days at home (91% of 6 months). If one makes the assumption that the Norwegian patients would have been at home for another 90 days in the preceding three months, which seems unrealistic, the observed figure of 64 days at home plus the hypothetical 90 days sums up to 154 days in a 6-month time period, which is less than in Ontario. The strongest predictors for less time at home in the Canadian study were female sex (also reported here) and no receipt of palliative care before the last 6 months of life (not available in our database). Greater comorbidity predicted fewer days at home (not significant in our study). Interestingly, patients with lung cancer spent the most time at home.

Lam *et al.* studied more than 290,000 Medicare beneficiaries aged 66 years or older with a cancer diagnosis, who died in the years 2014 to 2017 [13]. These authors calculated a measure termed 'healthy days at home' for the 180 days before death by subtracting the following components from 180 days: the total number of days spent in inpatient and outpatient emergency departments, including observation days, skilled nursing facilities, inpatient psychiatry, inpatient rehabilitation, long-term hospital settings, and inpatient hospices. The mean number of healthy days at home was 154. Due to different methodology, including but not limited to exclusion of patients younger than 66 years, comparison to the present study's results is difficult. Inpatient days and skilled nursing facility days contributed to the largest reductions in healthy days at home (10.7 and 9.7, respectively), followed by hospice hospital days (2.4). Older beneficiaries experienced more skilled nursing facility days and fewer inpatient days, compared with their younger counterparts. Just like in the Canadian study [12], lung cancer patients had the highest number of (healthy) days at home (mean 156). Overall, younger patients had more healthy days at home. The same was true for female patients. The latter finding illustrates that the results from different countries with different healthcare systems and/or studied populations were heterogeneous. Nevertheless, measures such as days at home or healthy days at home are useful to understand, quantify, and improve cancer care at the end of life.

The limitations of the present study, which focused on NSCLC rather than all types of cancer, must be considered when trying to put its results into context. Due to higher statistical power, larger studies might reveal significant correlations where our study did not. In addition, disparities may become less likely if a national healthcare system

with universal coverage and easy access to care aims at providing equal access. Emergency room visits not leading to hospitalization were not captured in our electronic database. The same is true for primary-healthcare-sector contributions, which may influence time spent at home. Also, previous research included a period of 6 months [12, 13] while we limited the study period to the last 3 months. Finally, we were unable to determine the extent to which hospitalizations were clinically appropriate and/or in line with the patient's goals of care at that time. In other words, it remains unknown how many days at home each individual patient wanted to experience and whether or not this was endorsed by the family caregivers and made possible by optimal, seamless collaboration of family physician/mobile nurses and hospital-based MPCT (if involved at all).

Conclusions

Long-lasting need for MPCT support (not just the final 3 months) and earlier necessity for opioid analgesics were associated with a reduced number of days at home. However, there is no reason to believe that avoiding or delaying necessary palliative measures provides any benefit. Rather, availability of support (including hospice care), and its timing and intensity should be optimized, together with seamless collaboration between different healthcare sectors, to improve the deficits demonstrated in the present and previous studies.

The authors declare no conflict of interest.

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