

COVID-19 for Fast Track Publication**Characteristics, Symptom Management, and Outcomes of 101 Patients With COVID-19 Referred for Hospital Palliative Care**

Natasha Lovell, MBChB, BSc, MRCP, Matthew Maddocks, BSc, MCSP, PhD, Simon N. Etkind, MB, BChir, BA, MRCP, DTMH, Katie Taylor, BA (Hons)Oxon, MSc, MBBS, MRCP, Irene Carey, MB, BCh, BAO, MSc, FRCP, Vandana Vora, MBBS, FRCP, Lynne Marsh, BM, MSc, MRCP, Irene J. Higginson, BMedSci, BMBS, PhD, FMedSci, FRCP, FFPHM, Wendy Prentice, MBBS, MA, FRCP, Polly Edmonds, MBBS, FRCP, and Katherine E. Sleeman, BSc, MBBS, FRCP, PhD
 King's College Hospital NHS Foundation Trust, London, UK (N.L., M.M., S.N.E., L.M., I.J.H., W.P., P.E., K.E.S.); King's College London (N.L., I.J.H., K.E.S.), Cicely Saunders Institute, London, UK; and Guy's and St Thomas' NHS Foundation Trust, London, UK (S.N.E., K.T., I.C., V.V.)

Abstract

Hospital palliative care is an essential part of the COVID-19 response but data are lacking. We identified symptom burden, management, response to treatment, and outcomes for a case series of 101 inpatients with confirmed COVID-19 referred to hospital palliative care. Patients (64 men, median [interquartile range {IQR}] age 82 [72–89] years, Elixhauser Comorbidity Index 6 [2–10], Australian-modified Karnofsky Performance Status 20 [10–20]) were most frequently referred for end-of-life care or symptom control. Median [IQR] days from hospital admission to referral was 4 [1–12] days. Most prevalent symptoms (n) were breathlessness (67), agitation (43), drowsiness (36), pain (23), and delirium (24). Fifty-eight patients were prescribed a subcutaneous infusion. Frequently used medicines (median [range] dose/24 hours) were opioids (morphine, 10 [5–30] mg; fentanyl, 100 [100–200] mcg; alfentanil, 500 [150–1000] mcg) and midazolam (10 [5–20] mg). Infusions were assessed as at least partially effective for 40/58 patients, while 13 patients died before review. Patients spent a median [IQR] of 2 [1–4] days under the palliative care team, who made 3 [2–5] contacts across patient, family, and clinicians. At March 30, 2020, 75 patients had died; 13 been discharged back to team, home, or hospice; and 13 continued to receive inpatient palliative care. Palliative care is an essential component to the COVID-19 response, and teams must rapidly adapt with new ways of working. Breathlessness and agitation are common but respond well to opioids and benzodiazepines. Availability of subcutaneous infusion pumps is essential. An international minimum data set for palliative care would accelerate finding answers to new questions as the COVID-19 pandemic develops. J Pain Symptom Manage 2020;■:■–■. © 2020 American Academy of Hospice and Palliative Medicine. Published by Elsevier Inc. All rights reserved.

Key Words

COVID-19, coronavirus, palliative care, symptom management, hospice, end of life

Key Message

In this first case series of 101 patients with COVID-19 referred to palliative care, input was brief; most patients died in less than three days. The most common symptoms were breathlessness and agitation, controlled in most cases using relatively small doses of opioid and benzodiazepine, delivered by subcutaneous infusion. To meet the rapidly growing need for

palliative care, services must adapt. Training and guidance for nonspecialists will help ensure symptoms are addressed promptly.

Introduction

People diagnosed with COVID-19 have an estimated mortality of 1%–3%, with those with multimorbidity most at risk of dying.¹ Estimates vary widely, but

Address correspondence to: Katherine E. Sleeman, BSc, MBBS, FRCP, PhD, King's College London, Cicely Saunders Institute, Bessemer Road, London SE5 9PJ, UK. E-mail: Katherine.Sleeman@kcl.ac.uk

Accepted for publication: April 6, 2020.

COVID-19 could directly cause up to 510,000 deaths in the U.K. and 2.2 million in the U.S.² Although the clinical characteristics of COVID-19 patients have been described, the focus has been on risk factors for ICU admission and death.³ Data are lacking on the palliative care needs of people with COVID-19, including symptom burden and response to treatment, to help inform service planning for palliative care and hospice services in the U.K. and elsewhere. Here we describe the symptom burden, management, response to treatment, and outcomes for patients with COVID-19 referred to the palliative care teams in two large NHS hospital trusts in London, U.K.

Method

Design and Setting

This is a case series of 101 inpatients with confirmed COVID-19 infection, referred to the hospital palliative care teams at two large acute NHS Hospital Trusts in London, U.K. The two trusts comprise four hospitals and include a Highly Communicable Infectious Disease Unit. They serve populations who, during March 2020, had among the highest prevalence of COVID-19 in the U.K.

Data Collection and Analysis

Data were extracted from medical and nursing case notes by clinician-researchers (N. L., P. E., K. T., J. B., and S. E.). Variables included the following: baseline demographic and clinical characteristics; referral ward; comorbidities categorized by the Elixhauser Index⁴; clinician-assessed palliative care phase of illness (stable, unstable, deteriorating, and dying or deceased) based on care needs and suitability of the current care plan⁵; and Australia-modified Karnofsky Performance Status.⁶ Symptoms were identified from standardized palliative care notes. Symptom control medicines with doses were extracted from drug charts, and clinical impressions of effectiveness were determined based on documentation at follow-up (e.g., improved breathing, agitation, comfort). Descriptive analyses were performed using SPSS (V.24, Armonk, NY). Comparisons between groups were expressed as medians and interquartile ranges (IQRs) due to the data distribution.

Results

For full demographic and other details, see [Table 1](#). Between March 4 and March 26, 2020, 101 patients with COVID-19 were referred to palliative care, most frequently for end-of-life care or symptom control. Referrals rapidly increased from the first ($n = 2$) to the fourth week ($n = 51$). Sixty-four patients were men; the median age was 82 [72–89]. The Elixhauser

Table 1
Demographic and Clinical Characteristics, Palliative Care Contacts, and Outcomes of 101 Hospital Inpatients With COVID-19 Referred to Palliative Care

| Characteristic | Median [IQR] or n |
|---|---------------------|
| Age, yrs | 82 [72–89] |
| Sex, male:female | 64:37 |
| Elixhauser Comorbidity Index | 6 [2–10] |
| Comorbidities | |
| Hypertension | 54 |
| Diabetes | 36 |
| Dementia | 31 |
| Advanced/metastatic cancer | 25 |
| Chronic pulmonary disease | 22 |
| Renal failure | 21 |
| Congestive heart failure | 18 |
| Stroke/neurological disorder | 12 |
| Peripheral vascular disorder | 4 |
| Liver disease | 2 |
| AKPS | 20 [10–20] |
| Missing | 15 |
| Level of care | |
| Ward-based care | 95 |
| High dependency unit | 5 |
| Intensive care unit | 1 |
| Reason(s) for referral to palliative care | |
| End-of-life care | 70 |
| Symptom control | 41 |
| Care planning | 4 |
| Psychological support | 1 |
| Phase of illness | |
| Dying | 63 |
| Unstable | 24 |
| Deteriorating | 7 |
| Stable | 1 |
| Missing | 6 |
| Days of palliative care involvement | 2 [1–4] |
| Palliative care contacts | 3 [2–5] |
| Contacts by recipient | |
| Patient | 2 [1–3] |
| Family | 1 [0–1] |
| Hospital staff | 2 [1–4] |
| Contacts by type | |
| In person | 3 [1–4] |
| Telephone | 1 [0–1] |
| Outcome | |
| Death | 75 |
| Discharged | 13 |
| Back to team | 10 |
| Home | 2 |
| To hospice | 1 |
| Remains under palliative inpatient care | 13 |

AKPS = Australia-modified Karnofsky Performance Status; IQR = interquartile range.

Data are median [IQR] or n .

Comorbidity Index was 6 [2–10]; the most common comorbidities were hypertension (54), diabetes (36), and dementia (31). Seventy-six patients had been admitted with COVID-19 and 25 were existing inpatients who developed COVID-19; median [IQR] days from admission to referral were 2 [1–6] and 16 [7–30] for these groups, respectively. At the time of referral, most patients ($n = 95$) were receiving ward-based care, with six on high-dependency or intensive care units (ICUs).

Table 2
Symptoms, Drugs Prescribed, and Drug Effectiveness in
101 Hospital Inpatients With COVID-19 Referred to
Specialist Palliative Care

| Symptoms at Time of Referral | N = 101 |
|---|-----------------|
| Breathlessness | 67 |
| Agitation | 43 |
| Drowsiness | 36 |
| Pain | 23 |
| Delirium | 24 |
| Secretions | 11 |
| Fatigue | 9 |
| Fever | 9 |
| Cough | 4 |
| Other symptoms ^a | 12 |
| Symptom relieving drugs given by subcutaneous infusion | 58 |
| Morphine + midazolam | 23 |
| Morphine + midazolam + glycopyrronium | 8 |
| Morphine alone | 4 |
| Morphine + haloperidol | 1 |
| Morphine + midazolam + haloperidol | 1 |
| Fentanyl + midazolam | 9 |
| Fentanyl + midazolam + glycopyrronium | 3 |
| Alfentanil alone | 2 |
| Alfentanil + midazolam | 4 |
| Alfentanil + cyclizine | 1 |
| Alfentanil + midazolam + haloperidol | 1 |
| Midazolam alone | 1 |
| Median (range) dose/24 hours | |
| Morphine (mg) | 10 (5–30) |
| Fentanyl (microgram) | 100 (100–200) |
| Alfentanil (microgram) | 500 (150–1000) |
| Midazolam (mg) | 10 (5–20) |
| Glycopyrronium (microgram) | 1200 (600–2400) |
| Haloperidol (mg) | 2 (1–2) |
| Cyclizine (mg) | 50 |
| Clinical impression of effectiveness ^b | |
| Yes | 40 |
| Unclear (patient died before follow-up) | 13 |
| No | 5 |

^aDiarrhea (3), reduced oral intake (3), anxiety (2), seizures, ascites, incontinence, dysuria (1 each).

^bBased on follow-up documentation, for example, improved breathing, agitation, comfort.

For full details of symptoms, drugs prescribed, and outcomes, see Table 2. The most prevalent symptoms were breathlessness, agitation, drowsiness, and pain. Twenty-four patients had symptoms of delirium. Ninety-six patients were prescribed “as needed” medication for symptom relief, and 58 patients were prescribed a subcutaneous infusion for symptom relief. Of the 37 patients who were prescribed morphine by subcutaneous infusion, the median final dose was 10 mg/24 hours. Fifty infusions contained midazolam, median final dose 10 mg/24 hours. The infusion was assessed as at least partially effective for 40/58 patients, while 13 patients died before effectiveness could be reviewed.

Patients spent a median [IQR] of 2 [1–4] days under the palliative care team and received 3 [2–5] contacts. As of March 30, 2020, patients had died (75), been discharged (13), or continued to receive palliative care input (13).

Discussion

We provide the first report of characteristics, symptom management, and outcomes of patients with COVID-19 referred for hospital palliative care. The main symptom experienced by these patients was breathlessness, similar to that found earlier in the disease trajectory.⁷ In addition, we find patients near the end of life commonly experience agitation, while cough is infrequent. Time spent under the palliative care team was brief (median time 2 days), and symptom control with subcutaneous infusion was achieved in most cases using relatively small doses of opioid and benzodiazepine. Seventy-four percent of patients died.

Many services are currently facing dramatic increases in the number of people severely affected by COVID-19. In this series, the number of patients with COVID-19 referred for palliative care each week increased from 2 to 51 over four weeks. This is likely to necessitate changes in ways of working for palliative care teams such as an increase in remote patient assessment.

A proactive approach to symptom recognition, assessment, management, and escalation for people with COVID-19 is likely to be helpful.⁸ Providing brief and accessible ward-base teaching on managing breathlessness and agitation, with a low threshold for prescribing anticipatory medicines for those with prognostic uncertainty, can ensure symptoms are addressed promptly.⁹ Encouragingly, our data indicate that patients’ symptoms can be managed using opioids and benzodiazepines at low doses. Subcutaneous infusions were frequently used to achieve symptom control. It is essential that adequate stocks of equipment are available to provide symptom control medication for those affected by COVID-19, both in inpatient and community settings.

Agitation was common among our patients. A high level of psychological distress may result from rapid deterioration and be exacerbated by isolation due to visitor restrictions. Ways to mitigate against this include use of technology such as tablet computers to communicate with carers and friends, though this may not be practical for people near the end of life. Chaplaincy, social work, and psychology teams’ support are valuable.⁹

The demographic characteristics of patients in this case series, predominantly older men with comorbidities, reflect global data on COVID-19 mortality risk.³ Hypertension and diabetes, the most frequent comorbidities in our patients, were risk factors for poor outcomes in a study of Chinese patients with COVID-19.¹⁰ A small proportion of patients in our case series were referred to palliative care for reasons other than COVID-19 but subsequently diagnosed as COVID-19 positive. It is important to acknowledge that their

palliative care needs include both COVID-19 and non-COVID-19-related problems. In addition, there are likely to be knock-on impacts on non-COVID-19 patients resulting from the escalation in referrals, many of whom will receive less palliative care input as a result.

We included only patients referred to palliative care, and we have no information about the palliative care needs of other inpatients with COVID-19. We had few referrals from ICUs. Around 50% of patients with COVID-19 who are admitted to ICUs subsequently die and they are likely to have high palliative needs.^{11,12} Information about symptoms was identified from the free-text notes, and we did not collect data on symptom severity. We report only on inpatient hospital patients and did not include community or inpatient palliative care units/hospices. The assessment of response to medication was subjective, and as the length of palliative care involvement was relatively short, there was not always sufficient time to assess effectiveness. Finally, this is an early case series and patterns are likely to change as the pandemic progresses.

Conclusion

Patients severely affected by COVID-19 frequently experience symptoms and distress, and palliative care is an essential part of the response to this pandemic. Urgent research is needed to understand more about symptom prevalence and management, and how best to deliver palliative care to those dying in ICU and community settings. An international minimum data set for COVID-19 patients receiving palliative care would accelerate finding answers to these questions.

Disclosures and Acknowledgments

The authors have no conflicts of interest to declare. All authors are members of the King's Health Partners Palliative Care Clinical Academic Group. The authors are grateful to other members of this group including Shaheen Khan, Teresa Beynon, Nick Gough, Rachel Burman, Sabrina Bajwah, Ruth Ting, and Richard Towers for supporting this work. The authors thank Jennifer Brooke for supporting data collection, and Andrew Wilcock for helpful comments on an early draft. The authors acknowledge the intense efforts of their colleagues at this time, including those within the palliative care teams and the Highly Communicable Infectious Disease Unit at Guy's and St Thomas NHS Foundation Trust.

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-

profit sectors. K. E. S. is funded by a National Institute of Health Research (NIHR) Clinician Scientist Fellowship (CS-2015-15-005), M. M. is funded by an NIHR Career Development Fellowship (CDF-2017-10-009), I. J. H. is an NIHR Senior Investigator Emeritus. I. J. H. and M. M. are supported by the NIHR Applied Research Collaboration South London (NIHR ARC South London) at King's College Hospital NHS Foundation Trust. I. J. H. leads the Palliative and End of Life Care theme of the NIHR ARC South London and co-leads the national theme. S. N. E. and N. L. are previous Cicely Saunders International PhD training fellows. The views expressed are those of the authors and not necessarily those of the NHS, the NIHR, the Department of Health and Social Care, or the funding charities.

Ethical approval: The work was registered as a service evaluation with the King's College London and Guy's and St Thomas' NHS Foundation Trust Clinical Effectiveness Teams (registration numbers: PC043, PC044, and 10774).

References

1. Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72314 cases from the Chinese center for disease control and prevention. *JAMA* 2020;323:1239–1242.
2. Ferguson NM, Laydon D, Nedjati-Gilani G, et al. Impact of non-pharmaceutical interventions (NPIs) to reduce COVID-19 mortality and healthcare demand. Report, Imperial College London. Available at: <https://www.imperial.ac.uk/media/imperial-college/medicine/sph/ide/gida-fellowships/Imperial-College-COVID19-NPI-modelling-16-03-2020.pdf>. Accessed May 1, 2020.
3. Chen N, Zhou M, Dong X, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *Lancet* 2020;395:507–513.
4. van Walraven C, Austin PC, Jennings A, et al. A modification of the Elixhauser comorbidity measures into a point system for hospital death using administrative data. *Med Care* 2009;47:626–633.
5. Eagar K, Green J, Gordon R. An Australian casemix classification for palliative care: technical development and results. *Palliat Med* 2004;18:217–226.
6. Abernethy AP, Shelby-James T, Fazekas BS, et al. The Australia-modified Karnofsky Performance Status (AKPS) scale: a revised scale for contemporary palliative care clinical practice [ISRCTN81117481]. *BMC Palliat Care* 2005;4:7.
7. Yang X, Yu Y, Xu J, et al. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. *Lancet Respir Med* 2020. [https://doi.org/10.1016/s2213-2600\(20\)30079-5](https://doi.org/10.1016/s2213-2600(20)30079-5).
8. Bajwah S, Wilcock A, Towers R, et al. Managing the supportive care needs of those affected by COVID-19. *Eur Respir J* 2020;55:2000815.

9. Etkind SN, Bone AE, Lovell N, et al. The role and response of palliative care and hospice services in epidemics and pandemics: a rapid review to inform practice during the COVID-19 pandemic. *J Pain Symptom Manage* 2020. (In press).

10. Guan WJ, Liang WH, Zhao Y, et al. Comorbidity and its impact on 1590 patients with COVID-19 in China: a nationwide analysis. *Eur Respir J* 2020. <https://doi.org/10.1183/13993003.00547-2020>.

11. Intensive Care National Audit & Research Centre report on COVID-19 in critical care. Report, ICNARC. 2020. Available at: <https://www.icnarc.org/Our-Audit/Audits/Cmp/Reports>. Accessed May 1, 2020.

12. Curtis JR, Kross EK, Stapleton RD. The importance of addressing advance care planning and decisions about do-not-resuscitate orders during novel coronavirus 2019 (COVID-19). *JAMA* 2020. <https://doi.org/10.1001/jama.2020.4894>.