

Relationship between corticosteroid effect on dyspnea, prognosis prediction, and actual survival

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Research Article

Keywords: advanced cancer, dyspnea, corticosteroid, palliative care

Posted Date: February 17th, 2021

DOI: <https://doi.org/10.21203/rs.3.rs-161473/v1>

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Abstract

Background and Aim: The effect of corticosteroids on dyspnea in patients with advanced cancer is expected to be associated with patient prognosis, though details about this are unclear. Thus, we aimed to investigate the relationship between prognostic indicators, actual survival, and the effect of corticosteroid administration on dyspnea in patients with advanced cancer.

Method: We predicted the prognosis using the PaP score (palliative prognostic score) at the time of corticosteroid administration in 56 consecutive patients with cancer who started corticosteroid treatment for dyspnea at a single palliative care unit, and compared it with the actual survival. In addition, we investigated the relationship between the effect of corticosteroids on dyspnea, the prognostic score before administration, the actual survival, and other background factors.

Results: The effect of corticosteroids strongly correlated with the actual survival, but not the prognostic score before corticosteroid administration, although it was correlated with prognostic score and actual survival. In addition, the effect of corticosteroids on dyspnea was less associated with other factors.

Conclusion: The corticosteroid effect strongly associated with actual survival, but not the prognostic score. It was suggested that the effect of corticosteroids in patients could be predicted by using a more accurate prognosis prediction in the future.

Introduction

Corticosteroids are administered to relieve various symptoms that occur in patients with advanced cancer. They are thought to be effective in relieving fatigue, loss of appetite, and pain in patients with advanced cancer [1] [2] and are used in many palliative care settings. They are also effective in alleviating dyspnea in patients with advanced cancer [3] [4]. However, the effects of corticosteroids on dyspnea in patients with cancer are still controversial, warranting the need for further research [5].

Corticosteroid use for dyspnea in patients with advanced cancer is very effective in certain pathological conditions; however, due to its strong adverse effects, it should not be used indiscriminately [6]. Despite this, some specialists use it for such conditions [4], or have studied factors for predicting the effects of corticosteroids [7]. However, it is still difficult to clearly predict the effect of corticosteroids on dyspnea in patients with advanced cancer.

Regarding the effects of corticosteroids and patient prognosis, clinical effects are considered to be limited when the prognosis of patients is poor [8]. This fact suggests that the effect of corticosteroids could be predicted before administration of corticosteroids [7]. However, there are limited reports on the relationship between corticosteroid effect, prognosis prediction, and actual survival in patients with advanced cancer.

In this study, we evaluated the effect of corticosteroids on dyspnea in patients with advanced cancer, and the relationship between it, prognosis prediction and the actual survival.

Methods

We investigated the effects of corticosteroids on dyspnea, the prognosis prediction before corticosteroid administration, and the actual survival after corticosteroid administration in patients with advanced cancer admitted to a palliative care unit.

Among the patients admitted to the single-center palliative care unit, those who did not receive corticosteroids before admission and who received corticosteroids for the first time to relieve dyspnea after admission were included. To facilitate comparison, all corticosteroid doses were converted to betamethasone equivalents (0.2 mg betamethasone were equal to 1 mg methylprednisolone).

We used the PaP score to predict prognosis of patients, thereby stratifying them into Group A (good prognosis), Group B (median prognosis), and Group C (worse prognosis) according to the original method [9]. The presence or absence of symptoms was evaluated by the physician and nurse duty during corticosteroid administration. The clinical prediction of survival was estimated by the physician in charge when the corticosteroid was administered, and the blood test was evaluated for blood sampling within a week before corticosteroid administration.

The effect of corticosteroids was evaluated at 4 degrees: 1 (*unchanged or worse*), 2 (*symptom improvement was limited to a few days*), 3 (*symptom improvement continued for 5 days or more*), and 4 (*symptom improvement for 5 days or more*). If a degree of 3 or more was evaluated, and corticosteroid therapy was effective. To see the effects of corticosteroids, we excluded patients who died within 4 days of corticosteroid administration.

Statistical analysis was conducted using SPSS Statistics version 25.0 (IBM Corp. Armonk, NY, USA). The chi-square test was used to compare each factor and effect of corticosteroid, and the Mann-Whitney U test was used for ranked variables. Differences were considered significant at $p < 0.05$. Multivariate logistic regression analysis was performed with factors identified as significant in the univariate analysis. The relationship between the PaP score and the measured survival was evaluated using the Kaplan-Meier method. This study was conducted in accordance with the Declaration of Helsinki and was approved by the Institutional Review Board of our center.

Results

From 879 patients who were treated between November 2007 and October 2013, we examined 48 cases who met the aforementioned eligibility criteria. In our institute, the median survival of 879 patients during the study period was 24 days (quartile 10, 53), with the most common primary lesion being thoracic cancer (46.4%), followed by gastrointestinal cancer (29.8%), and head and neck cancer (6.8%).

Figure 1 shows the relationship between the corticosteroid effect and actual survival. Comparing the effects of corticosteroids on dyspnea, patients in whom corticosteroids were effective had a better prognosis, and administering corticosteroids earlier was expected to be more effective than administering it immediately before death.

Figure 2 shows whether the actual survival was stratified by the PaP score on patients with dyspnea before the administration of corticosteroids. Although Group A patients were few, Group B and Group C patients were well stratified, and the patient survival after corticosteroid administration could be estimated by using the PaP score before corticosteroid administration (median survival was 53, 28, and 14 days, respectively).

Table 1 shows the relationship between patient background and corticosteroid dose, each factor of PaP score, and delirium, which are important factors in other prognostic predictions [10] [11]. More patients had thoracic lesions compared to findings from other end-of-life patients, because there were many patients with lung cancer in the original patient background, and many patients without lung cancer presented with thoracic lesions. Suggestions from some reports reveal that abdominal lesions and delirium symptoms are associated with improvement of dyspnea. However, the PaP score was not associated with the effect of corticosteroid.

Discussion

Corticosteroids are used to relieve dyspnea in patients with cancer. They could be effective in treating dyspnea in patients with cancer caused by specific pathological conditions such as lymphangitis carcinomatosa, central airway obstruction, and superior vena cava syndrome [6], but the effect has not yet been elucidated [12] [13].

We believe that prognostic predictions might reflect the effects of corticosteroids [7], because healthcare professionals believe that corticosteroids are ineffective in patients with cancer considered to have a short survival [14], and its effects generate a good survival [8]. However, as far as we know, no finding clarifies these facts. Thus, this is the first study to clarify the relationship between the effects of corticosteroids on dyspnea in patients with cancer, prognostic indicators, and actual survival.

From our findings, actual survival was the best predictor of corticosteroid effects compared to other factors. Generally, corticosteroids are drugs administered to relieve symptoms, not with the intention of prolonging patient survival. However, dyspnea in patients with cancer is a factor that affects their survival, and various indicators reveal it as a prognostic factor [9] [10] [15]. A previous report also showed that corticosteroid administration may be associated with patient prognosis [16]. In addition, many central airway obstruction and lymphangitis carcinomatosa are considered to have a strong effect on patients' survival, and relief of such life-threatening conditions may directly lead to prolonged life [17] [18].

If the effect of corticosteroids on dyspnea is related to patient survival, it may be predicted by the prognosis prediction index before its administration. Although various indices are used for prognostic prediction, the PaP score is a universal prognostic index. Although this score is difficult to use in the clinical or palliative medicine because of the need for blood sampling, prognostic indicators including blood tests are more accurate in predicting accurate survival [19]. In this study, the actual survival could be accurately stratified by the PaP score, and it functioned well as a prognostic index. However, the PaP score and corticosteroid effects were not correlated [7], while the actual survival was accurately reflected in corticosteroid effects. This suggests that the PaP score was still insufficient as a prognostic predictive tool, and it may be possible to predict the effect of corticosteroids on dyspnea if a more accurate prognosis can be predicted. We also examined other factors that may predict the effects of corticosteroids. However, the actual survival of the patient was the most predictable of the effect of corticosteroids compared to the factors shown so far. It is possible that this was because previous studies did not investigate actual survival.

This data was less effective for corticosteroids on dyspnea than reported previously [13]. It was considered that the effects of corticosteroids were insufficient because the dose of corticosteroids used was less than usual. However, there is no clear standard for the dose of corticosteroids for dyspnea, and in clinical practice, the dose is often lower than the usual dose, especially when administered to patients with a short-term survival such as a palliative care unit. The dose of corticosteroid used was approximately the same as the dose used in other Japanese palliative care units [14], and the efficacy was similar to the experienced efficacy rate [4]. Furthermore, in this study, there was no correlation between the initial dose of corticosteroids and their effect [20]. In addition, the effect of corticosteroids might be low in patients with short survival, so it was considered that the response rate was low when there were many patients with short survival, as in this case.

There were several limitations to our study. First, this was a retrospective study. Since the effect of corticosteroids on dyspnea was not scored on a subjective scale but from the perspective of the medical staff, there might be an overdiagnosis bias thereby suggesting that corticosteroids are effective. However, the PaP score, which is a subjective evaluation, was evaluated at the time of corticosteroid administration, and the bias was minimized as much as possible. In addition, suggestions reveal the difficulty to evaluate terminal dyspnea symptoms on a subjective scale [21]; therefore, in this study, an objective evaluation was performed by medical professionals.

Although the presence or absence of lung lesions was analyzed, we did not investigate the details associated with these lesions, such as central airway obstruction and lymphangitis carcinomatosa. This was because many investigated cases had lung abnormalities, in addition to cancer, chronic obstructive pulmonary disease, and interstitial pneumonitis, as well as drug-induced pneumonitis and radiation pneumonitis associated with cancer treatment. In this study, as many thoracic lesions were not organized in grades, it was difficult to evaluate each of them, though the presence or absence of lung lesions was evaluated. Similarly, abdominal lesions were evaluated including liver metastasis and peritoneal

dissemination. Moreover, for end-of-life patients with a mixture of various lesions, we could presume such an evaluation as more suitable for actual clinical practice.

In conclusion, patients with long-term survival were more likely to expect the effect of corticosteroids, though difficult to accurately predict it with the prognosis prediction still in use. With the development of a more accurate prognosis prediction method, it may be possible to predict the effect of corticosteroids on dyspnea by using it before administration.

Declarations

Acknowledgement

We would like to thank Editage (www.editage.com) for English language editing.

Funding

The authors did not receive support from any organization for the submitted work.

Conflict of Interest

All authors declare that they have no conflict of interest to the content of this article.

Ethics approval

This study was conducted in accordance with the Declaration of Helsinki and was approved by the Institutional Review Board of Yamaguchi-Ube Medical Center (2020-02).

Consent to participate and Consent to publication

This study was a retrospective observational study of patients who had already been treated, and met the conditions of “observational studies using existing materials” in “Ethical Guidelines for Epidemiological Studies in Japan.” So, we omitted individual informed consent and consent to publication.

Availability of Data

The data that support the findings of this study are available from the corresponding author, Hideki Katayama, upon reasonable request.

Code availability

N/A

Authors' contribution

Conceptualization and Data collection, H. Katayama, M. Tabata; Writing-original draft preparation, H. Katayama, M. Tabata, Y. Mimura; Writing-review and editing, K. Kiura, H. Kamei, J. Matsuoka; Supervision,

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Tables

Table 1

Clinical characteristics of patients and results of univariate analysis.

		total		Corticosteroid effects		OR	p value
		N	(%)	yes	no		
Gender	Male	33	(68.8)	16	17	0.3	0.584
	Female	15	(31.3)	6	9		
Age	Under 75	25	(52.1)	12	13	0.1	0.753
	Over 75	23	(47.9)	10	13		
Primary tumor site	Lung	31	(64.6)	16	15	3.05	0.692
	Gastrointestinal	4	(8.3)	2	2		
	Head and Neck	4	(8.3)	1	3		
	Breast	3	(6.3)	1	2		
	Urinary tracts	2	(4.2)	0	2		
	Others	4	(8.3)	2	2		
	thoracic lesion	With	44	(91.7)	21		
	Without	4	(8.3)	1	3		
Abdominal lesion	With	15	(31.3)	3	12	5.87	0.015
	Without	33	(68.8)	19	14		
Dose of Corticosteroid (adjusted by betamethasone)	Under 2mg	7	(14.6)	3	4	4.97	0.174
	2-4mg	27	(56.3)	15	12		
	4-8mg	11	(22.9)	2	9		
	Over 8mg	3	(6.3)	2	1		
Opioid administration	yes	47	(97.9)	21	26	1.21	0.272
	no	1	(2.1)	1	0		
Palliative prognostic score	Group A (0-5.5)	3	(6.3)	1	2	2.35	0.31
	Group B (5.6-11)	27	(56.3)	15	12		
	Group C (11.1-17.5)	18	(37.5)	6	12		
Edema	yes	6	(12.5)	2	4	0.43	0.511
	no	42	(87.5)	20	22		
Delirium	yes	16	(33.3)	4	12	4.2	0.041
	no	32	(66.7)	18	14		

Table 2

Results of logistic regression analysis of the relationship between corticosteroid effect and various factors.

	OR	p value
Actual survival	1.064	0.005
Abdominal lesion	0.237	0.097
Delirium	1.931	0.428

Figures

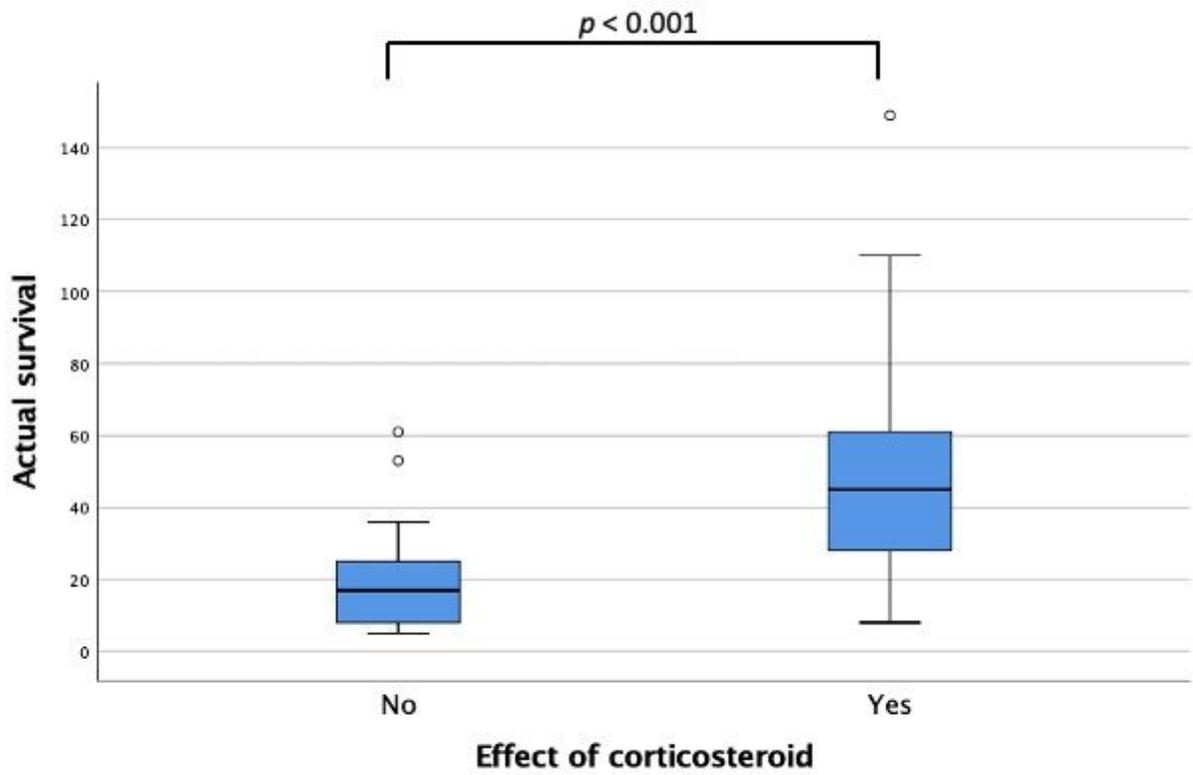


Figure 1

Relationship between corticosteroid effect and actual survival.

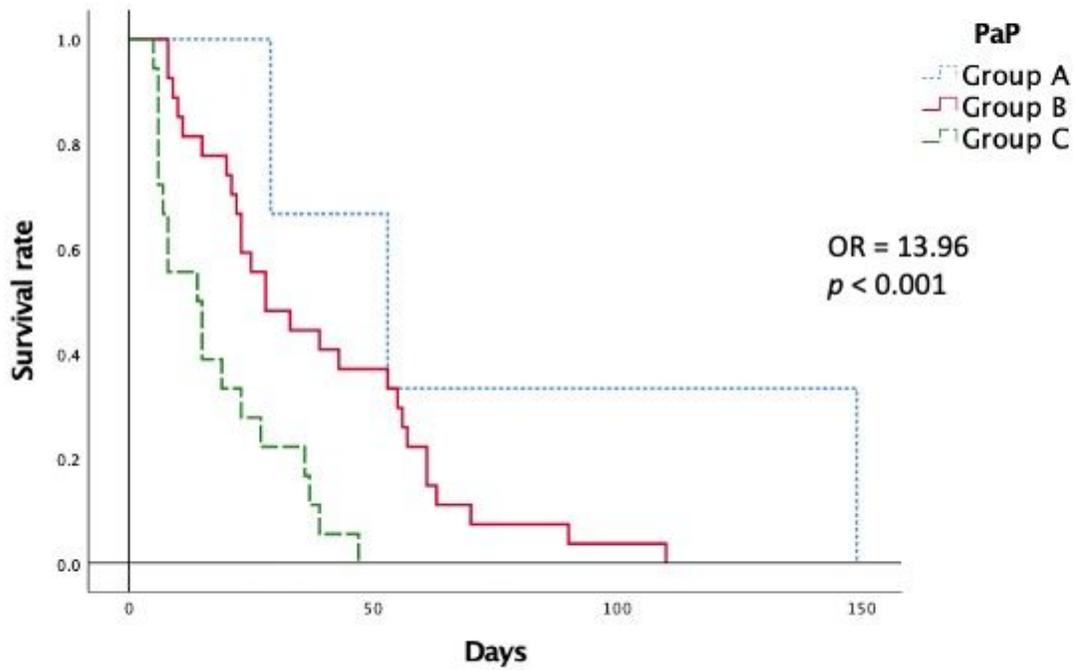


Figure 2

Kaplan-Meier analysis of patient actual survival stratified by PaP score.