

Red cell transfusions in patients with cancer in palliative care: a multicentric study

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Abstract

Background: Anemia is frequent in palliative care, and transfusions are often used to correct it. Research indicates that transfusions are sometimes based solely on hemoglobin levels rather than patients' symptoms and administered in those with very short survival.

Objective: To survey the transfusion practice of Portuguese palliative teams.

Methods: This is a multicentric and retrospective study involving patients who received red blood cell transfusions in 2021, followed by palliative care teams.

Results: Five palliative care teams participated and included 86 patients who underwent 122 transfusion episodes; 49 (57%) were male, and the median age was 76 years (43–100). The median hemoglobin level before transfusion was 7.4 g/dL (3.7–11.5). Symptomatic improvement was observed in 30 (25%) episodes; in 19 (16%), there was no improvement; and the outcome was not recorded in 73 (60%). Fatigue (38%) and low hemoglobin level (37%) were the most common reasons for transfusion. Decisions to transfuse, recorded primarily by one palliative care team, were often made by nonpalliative care doctors concurrently treating these patients, mostly in the emergency department. Those patients had more complications and significantly shorter survival compared with those whose transfusions were decided by palliative care physicians.

Conclusion: The decisions made by palliative care physicians regarding red blood cell transfusion deviated from the recommendations as seen in other similar studies.

Keywords: transfusions, red blood cells, palliative care, anemia in advanced cancer

Introduction

Anemia is widespread in patients with advanced cancer. Studies show a frequency of 30%–90%, depending on cancer type and disease stage.¹ Most cases are due to chronic inflammation.² However, other conditions can cause or contribute to anemia, such as a deficit of vitamin B12 and folate, blood loss including occult blood, renal insufficiency, hypothyroidism, and hemolysis.³ However, in palliative care, the causes of anemia are rarely investigated.⁴ In palliative care, the response to anemia is more often transfusion.

Like other interventions, correcting anemia in palliative care aims primarily to enhance well-being. Fatigue and dyspnea are the symptoms that most frequently prompt transfusions.⁵ Nevertheless, palliative care at present increasingly acts alongside specific treatments, such as antineoplastic treatments in the case of cancer. In this context, transfusions can aim not only to improve well-being but also to prolong life.

Untoward effects of red cell transfusions, such as transfusion-transmitted diseases or hemolytic reactions, are rare in developed

countries.⁶ However, transfusion-associated circulatory overload (TACO) can happen, especially in old and frail patients and those with heart failure.⁷ Moreover, blood is a limited and expensive resource that depends on the goodwill of benevolent donors. These factors advise the use of blood transfusions judiciously.

Established guidelines exist for judicious use of red blood cells.^{8,9} Those guidelines recommend restrictive criteria for transfusions with defined hemoglobin levels. However, there are no defined hemoglobin levels for patients exclusively in palliative care. Transfusions should be decided based on symptoms that might improve, although it remains uncertain whether they will be effective. The effectiveness of the transfusion can only be observed after a trial. The expected survival should also be considered, as transfusions are frequently given to patients who live for less than 2 weeks.⁴

Research on red cell transfusions in palliative care indicates that they are often misused, based only on hemoglobin levels, and sometimes given at levels higher than those recommended for

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other medical situations.⁴ To the best of our knowledge, only 1 study on the use of transfusions in palliative care was conducted in Portugal by one of the authors of this article.¹⁰ That study was limited to a single palliative care department. The current study aims to extend the scope of practice and survey it in more Portuguese palliative care centers.

Methods

This multicentric and retrospective study examined the practice of Portuguese palliative care teams regarding red cell transfusions and their impact on symptoms, particularly dyspnea and fatigue. An invitation to participate in this study was sent through the Portuguese Association for Palliative Care and directly to Portuguese public and private palliative care teams whose contact information was known. Five teams agreed to participate in the study.

The inclusion criteria for the study were as follows:

- Patients who were followed by the palliative care team and received a red cell transfusion in 2021 after being admitted to palliative care.
- Patients with primary cancer diagnosis.
- Patients who were not receiving antineoplastic treatment, except short courses of radiotherapy for symptom control.
- Patients who were aged at least 18 years.

Patients who underwent red cell transfusions in the past 4 weeks before the start of the study were excluded.

The data included demographic information collected before each transfusion episode, along with symptoms, hemoglobin level, Eastern Cooperative Oncology Group performance status, consciousness level, weight, creatinine level, and observation of patients before, after, and on the following day. Survival after the last transfusion was also recorded. The consciousness level was assessed using the Consciousness Scale for Palliative Care.¹¹

Data were statistically analyzed to identify coding errors and inconsistencies, and corrections were made when needed. An exploratory analysis was performed to describe the sample. Survival was calculated using Cox regression. Wilcoxon-Mann-Whitney test was used to compare samples that did not have a normal distribution. The level of significance was deemed to be 0.05. The analysis was conducted using version 29.0 of IBM SPSS statistical software.

Results

This study involved 5 palliative care teams. Three teams included patients followed by palliative care units/departments only and 2 combined patients followed by palliative care units/departments and patients followed by palliative care and other departments. There were no transfusions at home.

This study included 86 patients; 49 (57%) were male. The median age was 76 years (range: 43–100). The most frequent cancer type was gastrointestinal, followed by urologic cancer (Table 1).

The 86 patients underwent 122 episodes of transfusion: 61 (71%) underwent 1 episode of red blood cell transfusion, 18 (21%) two, 3 (3%) three, and 4 (5%) four. The transfusion episodes occurred as inpatients in a palliative care setting in 83 (68%) cases and other hospital departments followed by a hospital palliative care team in 39 (32%) cases. The decision to transfuse was made by the palliative care team in 96 (79%) cases and by other doctors in 26 (21%), 19 (73%) of whom were in the emergency department; 25 of these cases were attributed to a single team.

Table 1

Demographic data

Primary cancer	N	%
Gastrointestinal	34	40
Urologic other	15	17
Prostate	7	8
Head and neck	7	8
Gynecologic	6	7
Hematologic	6	7
Lung	4	5
Breast	3	3
Other	4	5
Total	86	100

The median hemoglobin level before transfusion was 7.4 g/dL (3.7–11.5). There were no significant differences in the hemoglobin level based on whether the transfusion was decided by the PC team or others ($P = .549$). The most common reasons for transfusion were fatigue in 46 (38%) episodes and low hemoglobin alone in 45 (37%) (Table 2).

A clinical assessment was performed on 117 (96%) patients before the transfusion. In 111 (91%) cases, the patient's weight was unknown before transfusion, and the creatinine was also unknown in 32 (30%) cases. Informed consent was written in 73 (60%) cases, but it was not in 3 (3%), and in 46 (38%) cases, the information was not documented.

Only 45 (37%) patients had hemoglobin levels assessed after the transfusion. Three (3%) patients had volume overload: 2 had only 1 episode of transfusion, each receiving 1 unit, while 1 patient underwent 4 episodes of transfusion. During the first episode, when the complication occurred, the patient received 2 units, and in subsequent episodes, only 1 unit was administered without problems. No other complications were recorded. All complications occurred in transfusions decided by physicians other than the palliative care team.

Patients were evaluated in 121 (99%) cases after the transfusion. However, assessments were conducted the next day in only 58 (48%) episodes. Symptomatic improvement occurred in 30 (25%) transfusion episodes; in 19 (16%), there was no improvement. The outcome was not recorded in 73 (60%) episodes (Table 3). The most frequently improved symptoms were dyspnea and fatigue alone or combined.

The median survival after the last transfusion was 15.5 days (1–1186). The median survival of patients whose transfusion was decided by palliative care doctors was 16 days, whereas the

Table 2

Reasons for transfusion

	N	%
Low hemoglobin level alone	45	37
Dyspnea	5	4
Fatigue	21	17
Active bleeding	25	20
Dizziness	1	1
Dyspnea and fatigue	7	6
Fatigue and dizziness	2	2
Dyspnea, fatigue, and dizziness	1	1
Bleeding and fatigue	12	10
Bleeding, dyspnea, and fatigue	2	2
Bleeding, fatigue, and dizziness	1	1
Total	122	100

Table 3
Symptoms improved after the transfusion

	n	%	Total
Fatigue	18	15	30 (25%)
Dyspnea	6	5	
Dyspnea and fatigue	4	3	
Dyspnea, fatigue, and dizziness	1	1	
Fatigue and dizziness	1	1	
No improvement	19	16	92 (75%)
Not recorded	73	60	

median survival of patients when others took the decision was 7 days ($P = .032$); hazard ratio 1.95 (95% IC: 1.06–3.60).

Discussion

Currently, the recommended standard for blood cell transfusions is restrictive. This means that the usual threshold for prescribing transfusions should be a hemoglobin level of 7.0 g/dL unless the patient is bleeding, has an ischemic cardiac disease, or is undergoing cardiac or orthopaedic surgery, when the threshold can be raised to 8 g/dL.⁹ In palliative care, there is limited evidence of the benefit of transfusions in guiding decisions.⁴ Although the hemoglobin level is relevant in palliative care, it should not be the only criterion. Instead, symptoms that may be relieved by transfusion, such as dyspnea and fatigue, should be the primary consideration.⁴ However, palliative care also intervenes in patients still receiving antineoplastic treatment. In those situations, the decision to transfuse belongs to the oncologists.

This study's median hemoglobin level was 7.4 g/dL, indicating that most transfusions were administered when the hemoglobin level exceeded the standard threshold. This practice is not unusual in palliative care, as several studies show similar findings.⁴ Moreover, as noted in other studies, over one-third of the transfusions were driven solely by the hemoglobin level rather than the improvement of symptoms. In one audit, the percentage was higher than that observed in this study and was even the most frequent reason for transfusion.⁴

Some recommendations for transfusions in several settings, including palliative care, were not generally followed. First, the investigation for the cause of anemia was only pursued in less than half of the patients. Identifying the cause of anemia is important as it allows for consideration of alternative treatments, which is strongly recommended.¹² Furthermore, weight was not measured in almost all transfusion episodes. Weight is important because transfusing 4 mL/kg increases the hemoglobin level by 1 g/dL,¹³ but that increment should be only applied to patients weighing approximately 70–80 kg; therefore, patients with lower body weights require less than 1 unit of red blood cells. In addition, although a clinical assessment was performed before and after the transfusions, the hemoglobin level after the transfusion was not assessed, as recommended.⁴

TACO occurred during 3 transfusion episodes, even though only 1 unit was transfused in 2 cases. This highlights that transfusions involve risks, and nowadays, in developed countries, volume overload is the most significant risk, as other risks linked with infectious and immunological factors are tightly controlled.⁶ This study found TACO in 3 patients within the 1–5% incidence in the reported range.⁶ The patient received 2 units of red blood cells in one case, while the other 2 received only 1. This underscores the importance of assessing the patient's risk of TACO, namely the volume related to weight. Nevertheless,

volume is not the only factor associated with TACO; infusion rate, patient age, renal function, and underlying cardiac disease should also be considered.⁷ In palliative care, it is recommended to assess the patient's weight before the transfusion, limiting the volume to 4 mL/kg unless the patient is actively bleeding, administering 1 unit slowly in 3 to 4 hours, and considering the concomitant use of a diuretic.⁴

The symptomatic outcomes were not recorded in most cases, making it impossible to draw any conclusions. In 16%, there was no improvement, which is a common occurrence.⁴ The median survival after the last transfusion was approximately 2 weeks, which is also common.⁴

This study has a particularity: the decisions made by doctors who do not work in palliative care. This situation occurred almost exclusively in one hospital where the palliative care team works within the palliative care department and assists many patients in other departments. All complications occurred when nonpalliative care doctors decided to perform transfusions. The median survival of patients in nonpalliative care departments was significantly lower than that of patients whose decisions were made by palliative care doctors. These findings suggest that nonpalliative care doctors may lack the training to identify patients in the last days of life and/or the circumstances of the decisions, such as those performed in the emergency department, where there is a lack of information on the patients' state and prognoses.

This study has several limitations. As a retrospective study, it inherently lacks the recording of several parameters that could provide valuable information. Therefore, the impact of transfusions cannot be known for a significant percentage of patients. Furthermore, the number of teams and patients included was low to characterize the country's practice. One unexpected finding was the number of decisions made by nonpalliative care doctors in patients followed by a palliative care team, primarily in 1 hospital. While this can be seen as a weakness of this study, it reveals that in one case, patients in palliative care still go to the emergency department, where inadequate decisions can be made due to the nonpalliative care physicians' lack of preparedness when managing end-of-life patients and the possible lack of information those doctors had on the patients' prognoses. This team should reflect on its practice because such a high number of critical decisions taken by others may not be desirable.

Conclusions

This study shows that transfusions in palliative care were often used in patients with short survival and hemoglobin levels higher than the usually recommended level. Moreover, many transfusions were motivated only by the hemoglobin level without symptomatic considerations. Although these results are criticized, they are not different from data from other countries.

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