*Original article*

# Postoperative patient blood management: transfusion appropriateness in cancer patients

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**Background** - While patient blood management (PBM) principles are not specific to cancer patients, their application contains the pathophysiological premises that could also benefit this patient population. In this study, we assessed the effects of implementing a PBM bundle for cancer patients in the postoperative period.

**Materials and methods** - The Azienda USL-IRCCS of Reggio Emilia implemented a two-step PBM bundle for the postoperative period of cancer patients hospitalised in the semi-intensive post-surgery (SIPO) ward. Step 1 included seminars and lessons specifically targeting SIPO personnel; Step 2 introduced Points of Care (POCs) for the continuous monitoring of haemoglobin (Radical7, Masimo Corp, Irvine, CA, USA). We conducted 3 audits on 600 cancer patients recruited between 2014 and 2017: Audit 1 on 200 patients before the application of our PBM bundle; Audit 2 after Step 1 on 200 patients; Audit 3 after Step 2 on 200 patients monitored with POCs. Red blood cell (RBC) transfusion appropriateness in the postoperative period was evaluated using the Italian Society of Transfusion Medicine and Immunohaematology (SIMTI) recommendations.

**Results** - RBC transfusion appropriateness in the postoperative period of cancer patients rose from 38% to 75% after seminars, and reached 79% after the introduction of POC. The mean number of RBC units each patient received remained unchanged after training sessions (1.8 units/patient) while the introduction of POCs saw a simultaneous decrease in the number of prescribed units (1.3 units/patient).

**Discussion** - Our PBM bundle positively impacted RBC transfusion appropriateness in postsurgical cancer patients, both in terms of quality and quantity. A structured PBM programme specifically dedicated to surgical oncology should cover the entire perioperative period and might further improve transfusion appropriateness in these patients. The publication of guidelines on the management of anaemia in surgical oncology should be a priority.

**Keywords:** *patient blood management, red blood cell transfusion, cancer patients.*

## INTRODUCTION

Patient blood management (PBM) is an evidence-based, multidisciplinary approach aimed at optimising the care of patients who might need blood transfusions. The application of PBM principles is recommended for surgical patients, and might have specific beneficial effects on surgical oncology patients for whom perioperative blood transfusions may

Arrived: 18 February 2020
Revision accepted: 11 May 2020
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negatively affect disease recurrence and overall survival, possibly because of an immunosuppressive effect of transfusions[1,2].

The primary goal of PBM is to improve the patient's management (both medical and surgical) in ways that boost and conserve his/her own blood[3]. This approach usually leads to an improvement in patient outcome and a reduction in transfusion episodes, which in turn leads to a reduction in transfusion-associated reactions.

Anaemia is a common complication in cancer patients and its correct management has been associated with improvement in clinical outcome and favourable response to chemotherapy[4].

As the number of cancer patients is increasing worldwide, improving blood product utilisation, specifically that of RBC, is a challenge that needs to be met. Italian and international indications for PBM have historically focused mainly on orthopaedic surgery in adults[5], and even in the countries were PBM is consolidated[6], its importance in surgical oncology is still under-rated. Greater attention to blood management of cancer patients should include not only the pre- and intraoperative period, but also the postoperative period, since we recently observed that a structured PBM policy could significantly improve transfusion appropriateness during this time[7].

The aim of this study was to assess whether the gradual introduction of our PBM bundle could affect the appropriateness of postoperative transfusion therapy in cancer patients, given that transfusions imply additional risks in this specific population[8,9].

## MATERIALS AND METHODS

The study was carried out at the Azienda USL-IRCCS of Reggio Emilia and approved on 30th September 2015 by the Ethics Committee of Reggio Emilia (protocol n. 2015/0021926). Written informed consent was obtained from all study participants according to the Declaration of Helsinki.

### Study design

The study was conducted on cancer patients admitted to the semi-intensive postoperative (SIPO) ward after major cancer surgery, and was designed as follows (**Figure 1**):

1. a preliminary audit on 200 cancer patients (Audit 1, from January to May 2014) aimed at evaluating RBC transfusion appropriateness after major cancer surgery before PBM implementation;
2. a PBM training programme (seminars and training sessions) was organised to ensure SIPO personnel (both physicians and nurses) followed Italian Society of Transfusion Medicine and Immunohaematology (SIMTI) recommendations. An intermediate audit (Audit 2, from January to July 2015) was conducted on 200 cancer patients after the training programme to verify its impact on RBC transfusion appropriateness;
3. introduction of Points Of Care (POCs) for the continuous non-invasive monitoring of haemoglobin (Hb) levels (Radical-7 Pulse CO-Oximeter device, Masimo Corp., Irvine, CA, USA) in the SIPO ward. POCs were intentionally used in support of and not in place of the routine analyses. A final audit (Audit 3, from May 2016 to October 2017) was conducted on 200 cancer patients monitored with POCs.

Patient recruitment was carried out on consecutive patients admitted to SIPO after major onco-surgery who signed informed consent, in order to reach a total of 200 patients for each of the three Audits. POC monitoring lasted a mean of 72 hours for each patient recruited for Audit 3; this interval is based on the mean duration of admission to SIPO. Nurses applied the POCs on consecutive patients who specifically signed informed consent after surgery.

The physician responsible for ordering RBC was the surgeon caring for that patient, as established by our hospital plan. The transfusion medicine personnel did not interfere with the prescribers' decisions.

### Patient blood management training programme

In our hospital, the SIPO ward is managed by nurses: every day there is also an on call physician of each specialty who can examine SIPO patients. The training programme was attended by most of the SIPO nurses and by at least one physician from each post-surgical ward. Training programmes lasted 3 hours and were organised in two sessions:

1. a transfusion medicine physician talked about the importance of managing anaemia in cancer patients, shared the SIMTI recommendations for appropriate RBC transfusion therapy, and explained how to interpret the Hb trend registered by POCs;
2. a Masimo specialist then described how to use POCs and how to apply POC sensors.

At the end of the training programme, we carried out a survey of participant's satisfaction with the event, the results of which will be published separately.

Radical-7 Masimo POCs can monitor up to 5 parameters ($pO_2$, Hb, heartbeat, perfusion index, pleth variability index), but for this study we focused on Hb trend only.

### Patient population

The Azienda USL-IRCCS of Reggio Emilia currently applies the PBM bundle to the following major cancer surgeries (for which transfused patients are, on average, over 15% of the total): colorectal resection, lung resection, liver resection, radical prostatectomy, nephrectomy, bladder resection.

Consecutive cancer patients ≥18 years old who had undergone any of the above-listed surgeries and who were subsequently admitted to the SIPO ward were recruited. Patients undergoing multiple surgeries during the recruitment period were assessed only on first admittance. To avoid overlaps, patients who underwent multiple surgeries during the study period were included only at their first hospital stay. None of the recruited patients received more than one transfusion during their stay in SIPO. Patients with haematologic diseases and patients who received massive transfusion therapy due to postoperative complications were not included in the study.

Surgical procedures were classified according to the Italian surgery and procedure classification, based on the International Classification of Procedures in Medicine. For each patient, the following data were collected from our electronic database: age, sex, diagnosis (oncologic or non-oncologic), comorbidities, type of surgery (intestinal, pancreatic, stomach, hepatobiliary, lung, bladder and kidney, prostate, other - mainly adrenal, breast, gynaecological, oesophagus), date and time of surgery, date and time of admittance and discharge from SIPO post surgery, Hb level measured with routine laboratory test immediately prior and after transfusion therapy, number of RBC units transfused postoperatively (**Table I**).

### End points and appropriateness of red blood cell transfusion

The primary end point was the appropriateness of RBC transfusions in the postoperative period, which was intended as the duration of patient stay in the SIPO ward (generally three days).

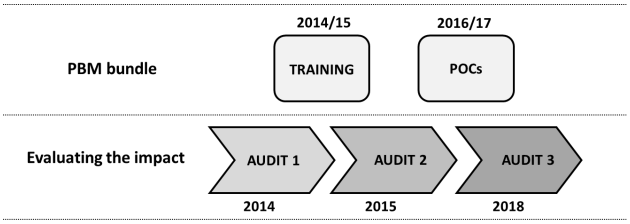


**Figure 1 - Study design. Patient blood management (PBM) bundle implementation (upper row) and evaluation of PBM impact (lower row)**
POCs: Point of Care.

The postoperative transfusion episodes were considered appropriate when in agreement with the SIMTI recommendations[10]:

1. Hb<80 g/L;
2. 80<Hb <90 g/L in the presence of risk factors (i.e. cardiac insufficiency, coronary pathology or cerebrovascular pathology);
3. 90<Hb<100 g/L in the presence of symptoms related to hypoxia (hypotension, ischaemia or lactic acidosis).

Secondary end points were the number of transfused RBC units and the percentage of patients with RBC transfusion.

### Data management and statistical analysis

Data were extracted from the the electronic database and blood bank registry of our hospital.

Continuous data were expressed as mean±standard deviation (SD), and comparisons were made using an independent t-test. Categorical variables were described using frequencies and percentages, and analysed using a $\chi^2$ test. Statistical significance was set at *p≤0.05, **p≤0.001. Analyses and graphs were performed using GraphPad Prism 7.02 (GraphPad Software, San Diego, CA, USA) and OriginPro2018b (OriginLab Corporation, Northampton, Massachusetts, USA) softwares, respectively.

## RESULTS

### Patient population

A total number of 600 cancer patients were included in the analysis (200 patients per audit). The three groups were similar in terms of sex, age, disease, and type of surgery (see **Table I** for details). The three populations were also representative of the cancer patients that are generally admitted to our hospital (*data not shown*).

Of the 600 patients recruited, 90 received RBC units during the postoperative period in the SIPO ward, with similar

*Table I - Demographic data and surgical indications of the recruited patients*

| | Audit 1 | Audit 2 | Audit 3 |
|---|---|---|---|
| Patient population (n) | 200 | 200 | 200 |
| Age (mean years±SD) | 69 ± 12 | 70 ± 12 | 68 ± 12 |
| Males (n) | 135 | 126 | 124 |
| Females (n) | 65 | 74 | 76 |
| Type of surgery (n, % total) | | | |
| Intestinal | 54 (27.0%) | 66 (33.0%) | 72 (36.0%) |
| Pancreatic | 4 (2.0%) | 10 (5.0%) | 10 (5.0%) |
| Stomach | 14 (7.0%) | 22 (11.0%) | 20 (10.0%) |
| Hepatobiliary | 12 (6.0%) | 17 (8.5%) | 14 (7.0%) |
| Lung | 41 (20.5%) | 51 (25.5%) | 38 (19.0%) |
| Bladder and kidney | 34 (17.0%) | 19 (9.5%) | 17 (8.5%) |
| Prostate | 17 (8.5%) | 0 (0.0%) | 4 (2.0%) |
| Other | 24 (12.0%) | 15 (7.5%) | 25 (12.5%) |

n: number; SD: standard deviation.

percentages among the three audits: 14.5% (29/200) in Audit 1, 16.0% (32/200) in Audit 2, and 14.5% (29/200) in Audit 3 (**Table II**).

### Appropriateness of postoperative red blood cell transfusion therapy

Baseline clinical audit (Audit 1) showed that RBC transfusions were appropriate in 38% of patients (11/29 patients), while after the teaching and training activities (Audit 2), appropriateness of transfusions increased to 75% (24/32 patients). We registered 79% appropriateness of RBC transfusion after the introduction of POCs, with 23/29 patients appropriately transfused (**Figure 2**, Audit 3). We observed a decrease in the total number of RBC units transfused in the postoperative period after the introduction of POCs (**Figure 3A**). The mean number of RBC units each patient received decreased from 1.8 (**Figure 3B**, Audits 1 and 2) to 1.3 (**Figure 3B**, Audit 3).

## DISCUSSION

The growing body of data in the literature suggests that transfusions negatively impact cancer patient outcomes by favouring tumour growth and metastases[11]. The European Society of Medical Oncology (ESMO) recently published new Clinical Practice Guidelines on the management of anaemia and iron deficiency in cancer patients that included recommendations on how to safely manage chemotherapy-induced anaemia with RBC transfusions alone or in combination with drugs (i.e. erythropoiesis-stimulating agents and iron preparations)[12]. Anaemia and thrombocytopenia are common side effects of chemotherapy and can lead to the need for RBC and platelet transfusions, significantly influencing mortality, morbidity, and quality of life. Nevertheless, ESMO guidelines do not discuss how to manage cancer patients in surgical settings.

Although clinical evidence of the effects of a structured PBM programme on long-term outcomes in surgical oncology is still lacking[13], we can expect such a programme to lead to improved long-term outcomes[14]. The application of transfusion guidelines specifically for cancer patients, therefore, should be a priority. The few PBM studies on cancer patients published so far have shown that the role of PBM on major prognostic oncologic indicators (such as overall survival) is far from being clear[15-17].

In a recently published single-centre retrospective study, the implementation of a PBM programme in the perioperative period of cancer patients significantly reduced the need for blood transfusions and resulted in an increase in 2-year overall survival[18].

We previously observed that the gradual introduction of a PBM bundle significantly improved RBC transfusion appropriateness in the postoperative period at our institution[7]. With the present study, we verified the impact of our programme on the surgical cancer patients on the SIPO ward.

Before starting the PBM bundle, RBC transfusion appropriateness was 37.9% (Audit 1). After the seminars specifically targeting all the healthcare professionals, we registered a significant improvement in RBC transfusion appropriateness, which reached 75% in a patient population with comparable characteristics. With the introduction of POCs, which provided immediate and continuous information about Hb levels, appropriateness reached 79%. These data are interesting because, instead of the expected lower performance over time after the training period[19], transfusion appropriateness actually increased by further 4%.

Our study lasted approximately three years (2015-2017), during which time our hospital underwent different phases of operational reorganisation. As a consequence, the distribution of surgical patients in the SIPO ward and other postoperative wards slightly changed, as shown in **Table I**. Since 2015, for example, almost all prostate surgery patients have been admitted to the Urology Unit. However, since prostate cancer patients are rarely transfused in the postoperative period in our hospital, this event did not have any impact on our results.

Another observed consequence of the operational reorganisation was a progressive increase in the SIPO ward of the number of patients who had undergone more

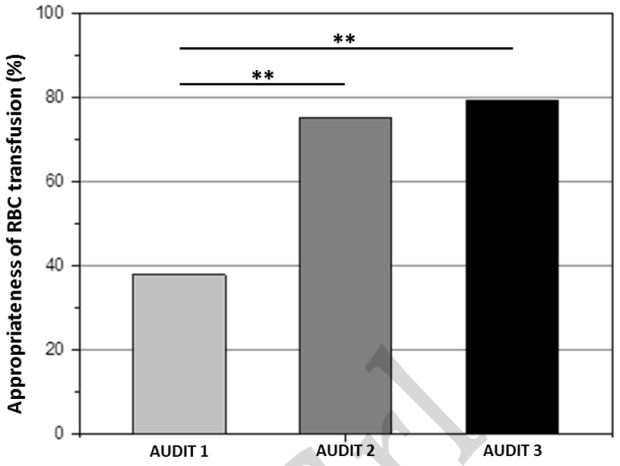


**Figure 2 - Appropriateness of postoperative red blood cell (RBC) transfusion, expressed as % of transfused patients in the postoperative period within the selected ward**
**p≤0.001.

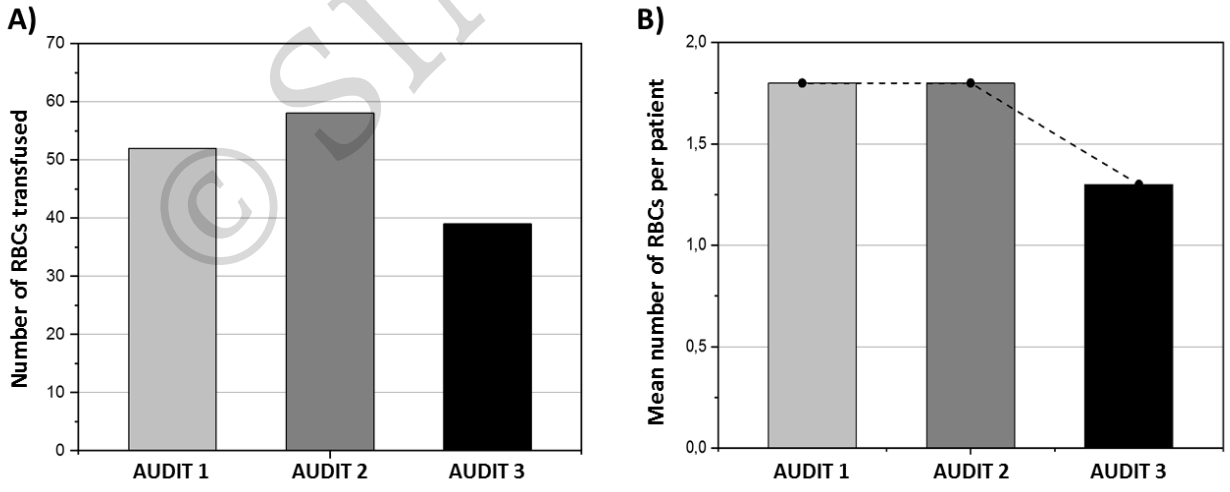


**Figure 3 - Red blood cell (RBC) units transfused in the postoperative period**
(A) Total number of transfused RBC units; (B) mean number of RBC units received by each patient.

complex surgery, for example, intestinal, stomach and pancreatic surgery (**Table I**, Audits 2 and 3).

This higher number of complex patients resulted, at least in part, in the lower mean pre-transfusion Hb levels registered in Audits 2 and 3 (**Table II**).

The significant increase in transfusion appropriateness registered between Audits 1 and 2 (**Figure 2**) is apparently inconsistent with the increased number of transfused RBC units (**Figure 3A**). Our interpretation, however, is that this is due to the progressive increase in the number of complex surgical patients admitted to the SIPO ward during the study period.

It is worth noting that, with the introduction of POCs (Audit 3), the mean number of RBC units each patient received decreased from 1.8 to 1.3 (**Figure 3B**). These approaches, therefore, might have helped the physicians select the most appropriate transfusion therapy, in terms of quality and quantity.

This is a single-cohort study in which patients were not selected according to surgical indication or concomitant disease. We are aware that there are factors that can influence POCs accuracy in monitoring Hb. However, in the postoperative setting under study, where the prevalence of hypovolaemia is relatively low, POCs can help select the best therapeutic approach.

## CONCLUSIONS

In our experience, the results of implementing a postoperative PBM bundle for cancer patient care are encouraging. A structured PBM approach in surgical oncology involving all three pillars is urgently needed. Anaemia in cancer patients is multifactorial and is present,

***Table II** - Demographic data, surgical indications, postoperative hemoglobin (Hb) and number of red blood cells (RBCs) transfused in the postoperative period of the recruited patients*

| | Audit 1 | Audit 2 | Audit 3 |
|---|---|---|---|
| **Transfused patients (n)** | 29/200 (14.5%) | 32/200 (16.0%) | 29/200 (14.5%) |
| **Age (mean years ± SD)** | 72 ± 10 | 75 ± 9 | 72 ± 10 |
| **Males (n)** | 19 | 20 | 20 |
| **Females (n)** | 10 | 12 | 9 |
| **Type of surgery (n transfused/total surgeries)** | | | |
| **Intestinal** | 13/54 | 9/66 | 6/72 |
| **Pancreatic** | 2/4 | 3/10 | 4/10 |
| **Stomach** | 2/14 | 4/22 | 4/20 |
| **Hepatobiliary** | 3/12 | 3/17 | 3/14 |
| **Lung** | 1/41 | 351 | 3/38 |
| **Bladder and kidney** | 5/34 | 8/19 | 9/17 |
| **Prostate** | 0/17 | 0/0 | 0/4 |
| **Other** | 3/24 | 2/15 | 0/25 |
| **Hb pre-transfusion (g/dL)** | 11.4 ± 1.6 | 8.8 ± 1.1 | 9.8 ± 1.7 |
| **N. of RBCs transfused (n)** | 52 | 58 | 39 |
| **RBCs transfused per patient (mean)** | 1.8 | 1.8 | 1.3 |
| **Transfusion appropriateness (n/total)** | 11/29 (37.9%) | 24/32 (75.0%) | 23/29 (79.3%) |

n: number; SD: standard deviation.

in varying degrees, in all tumour types. Its management, therefore, should be accurate and multidisciplinary.
Specific attention should be paid to the recruitment of cancer patients onto PBM programmes, which should be carried forward as early as possible to guarantee the highest efficacy of the therapeutic approach aimed at managing perioperative anaemia and minimising the number of transfusions.

## FUNDING AND RESOURCES

This study was conducted in the Azienda USL-IRCCS di Reggio Emilia, approved by our Local Ethical Committee with protocol n. 2015/0021926 in 30/09/2015, and funded by "Bando Sangue Plasma 2015" of the Centro Regionale Sangue Emilia Romagna.

## AUTHORSHIP CONTRIBUTIONS

LM performed the audits and data analysis. CM contributed to data analysis and wrote the manuscript. EDB recruited patients and performed the audits. MTM organised seminars and training sessions. TAP and RB designed the study and contributed to manuscript preparation. AB designed the study, performed the audits, and contributed to manuscript preparation.

*The authors declare no conflicts of interest.*

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