

GUIDELINE

Guideline summary: Intensive care admission, treatment and discharge of critically ill haemato-oncological patients

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Abstract

Haemato-oncological patients are often treated in the intensive care unit (ICU) because of severity of disease and treatment-related side effects. This guideline aims to provide advice for the admission and treatment of haemato-oncological patients in the ICU, in order to improve the quality of care. It is important not to postpone ICU treatment and once admitted a multidisciplinary evaluation of the clinical condition should take place after the first couple of days of ICU support. Furthermore, to facilitate information handover it is recommended to use a checklist at admission. Timing of endotracheal intubation is discussed, using a decision model. Optimal care includes a daily multidisciplinary meeting, specific criteria for transfusion, antibiotic prophylaxis and treatment and use of selective digestive decontamination or selective oral decontamination. A bronchoalveolar lavage does not result in a significantly higher intubation rate, but frequently provides a new diagnosis. It is also advised to use a checklist at ICU discharge and to provide an option for early consultation of the ICU or an ICU liaison nurse, in order to prevent complications after discharge.

Background

Lymphoid cancer and leukaemia are the fifth most frequently occurring types of cancer in the Netherlands and about 8000 patients are newly diagnosed each year. Five- and ten-year survival rates have been slowly increasing in the last decades. The first goal of treatment is remission-induction chemotherapy, usually followed by post-remission treatment. Depending on the patient's risk profile and response to treatment this may be followed by autologous or allogeneic stem cell transplantation (SCT). The intensive treatment modalities as well as the disease itself cause an increased risk for infections and side effects,

based on immune system dysfunction and immunosuppressive medication. Frequently these complications result in severe illness needing ICU support. Given the fact that the survival of haemato-oncological patients as well as ICU patients in general is increasing, the potential benefit of ICU admission for these patients has also increased. Nevertheless, ICU physicians are sometimes reluctant to admit these patients to the ICU and significant local differences exist with regard to admission criteria and treatment guidelines for this specific patient group. The goal of this multidisciplinary national guideline is to improve the quality and results of intensive care treatment for haemato-oncological patients by standardising care before, during and after ICU treatment.

Methods

The guideline was written between 2013-2016 by a multidisciplinary working group consisting of intensivists and haematologists and supported by the Dutch Intensive Care Society, as well as the Haemato Oncology Foundation for Adults in the Netherlands. The guideline is accessible in its full form on the website of the Dutch Intensive Care Society (www.nvic.nl). Multiple questions were formulated and studied through extensive PubMed literature searches by a paired intensivist and haematologist. Specific search strategies were applied, which can be found in the full version of the guidelines, and searches were further refined with the support of a librarian. Included studies were published between 2004-2015 and reviewed for study quality by the working group. The guideline is applicable to all critically ill haemato-oncological patients of 18 years or above. In this article we aimed to summarise the guideline, highlighting the most important topics and recommendations. A division was made into a pre-ICU period, an ICU period and a post-ICU period.

Summary of the recommendations

1. Recommendations for treatment before admission to the ICU

1.1 Identification of the critically ill haemato-oncological patient

Delay of ICU treatment in haemato-oncological patients is an independent predictor of mortality.^[1] Multiple studies describe the importance of early warning scores, early involvement of ICU outreach teams and medical emergency teams.^[2,3] Early activation of a medical emergency team is associated with improved outcome.^[3,4] A timeframe of less than 24 hours between first symptoms and ICU admission is associated with better survival.^[5] Vital parameters should be monitored with the (modified) early warning scores and ICU treatment should not be withheld based on haematological malignancy alone. Furthermore, early admission is of utmost importance and ICU admission should not be delayed in these patients, as it improves outcome.^[5-7]

1.2 Contraindications for ICU treatment

Multiple studies have investigated possible predictors of adverse outcome for haemato-oncological patients in ICU. No conclusive evidence has been found that could be utilised to specifically predict mortality in critically ill haemato-oncological patients. Predictors for mortality in the general ICU population apply to haemato-oncological patients as well. Examples are more than two failing organ systems, high APACHE score and high SOFA score, which are associated with higher mortality.^[8-13] ICU treatment should be withheld from patients with an unfavourable short-term haemato-oncological prognosis, or from those with severe non haemato-oncological illness. In other patients, a trial of ICU support should be strongly considered. The working group advises a standard and

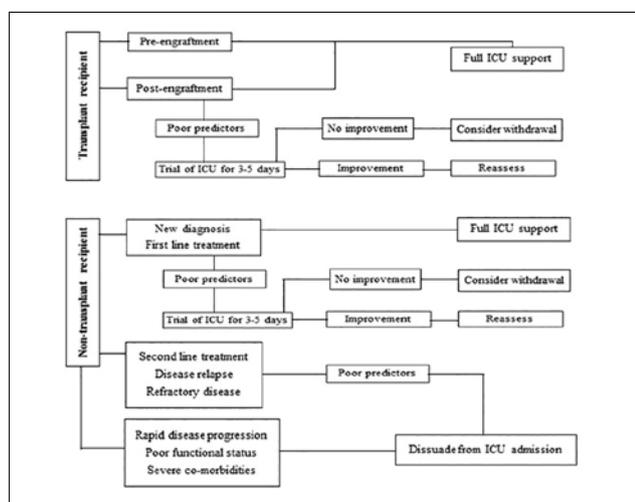


Figure 1. Treatment decision model for initiating intensive care treatment in haemato-oncological patients

Poor predictors: relapsed disease or non-responding to treatment, failing of >2 organs. Adapted from Bird et al.^[9]

structured multidisciplinary evaluation of clinical improvement during an initial ICU trial in the first three to five days after ICU admission. If clinical improvement is not observed, the team should consider withdrawal of ICU support. A decision model is suggested, which may be used to decide whether patients should be admitted to the ICU (*figure 1*). With regard to the transfer of clinical information to ICU physicians at admission, we advise to use a checklist when transferring a patient to the ICU. This checklist is included in the full version of the guideline. Finally, at admission there should be clear agreements on the treatment goals and limitations of treatment.

2 Recommendations during admission in the ICU

2.1 Timing of endotracheal intubation

Specific criteria and optimal timing, as well as the optimal modality of respiratory support, have not been clearly defined in the ICU population and the same applies to the haemato-oncological subgroup. One multicentre study showed that 60% of patients initially treated with non-invasive ventilation (NIV) had to be intubated at a later time.^[14] In this group, mortality was 80%. The odds ratio for death was 5.74 for NIV failure and 3.13 for intubation at admission. A recent meta-analysis showed that NIV is associated with a relatively low mortality rate, but that mortality is clearly increased in those patients who fail to improve with NIV.^[15] Risk factors for NIV failure are severity of illness and the presence of pneumonia or the adult respiratory distress syndrome (ARDS).^[12,16-18] A decision model may be used to provide a guideline for choosing the initial ventilation strategy and is included in *figure 2*.^[19] The working group advises to use

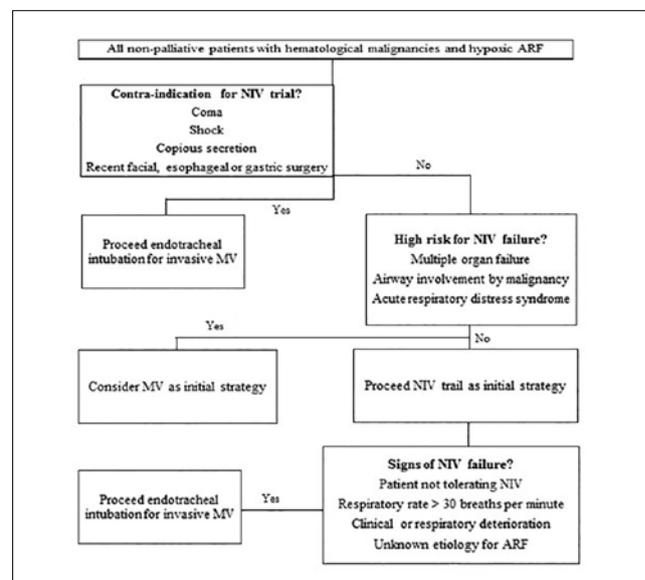


Figure 2: Decision model for initial ventilation strategy in haemato-oncological patient with acute respiratory failure (ARF)

ARF = acute respiratory failure; NIV = non-invasive ventilation; MV = mechanical ventilation. Adapted from Soares et al.^[19]

this model to define the best modality of respiratory support at admission.

2.2 Prognostic factors in the ICU treatment

Several risk classification scores have been identified that may be used to predict mortality of haemato-oncological patients in the ICU. A summary of these risk classification systems is found in *table 1*.^[5,20-24] The intensivist and haematologist should discuss ICU prognosis and timing of re-evaluation and are encouraged to include these risk stratifying scores in their discussion. Evaluation after a period of three to five days is suggested in the literature.

Table 1. Summary of prognostic factors in haemato-oncological patients treated in the intensive care unit (ICU)

Haematological factors	Intensive care factors
High mortality	
ECOG >2 at ICU discharge	Bad performance status
HCT-CI >2 for patients post-allogeneic BMT	High Charlson co-morbidity index (≥5)
Haematological disease: relapse or active disease	High APACHE IV score
Discontinuation of planned haematological treatment	High and/or increasing SOFA score
	Haemodynamic instability
	Invasive pulmonary Aspergillosis
	Invasive mechanical ventilation
Low mortality	
ICU treatment during conditioning treatment pre allogeneic SCT	Time between hospital admission and ICU admission >24 hours
Using 'reduced intensity conditioning regimens'	ICU treatment > 5days

APACHE IV score = Acute Physiology and Chronic Health Evaluation (average ± standard deviation); ECOG = Eastern Cooperative Oncology Group score; BMT = bone marrow transplant; HCT-CI = Hematopoietic Cell Transplantation-Specific Comorbidity Index; SCT = stem cell transplantation; SOFA = Sequential Organ Failure Assessment

2.3 Multidisciplinary care

Optimal ICU care includes a daily multidisciplinary meeting. The working group recommends a daily evaluation of the patient by the intensivist and the haematologist. We strongly advise to invite a pharmacist to the meetings since drug interactions are a common problem in this patient population.

2.4 Antimicrobial treatment

Infections are an important complication in ICU treatment, especially in immune compromised patients such as the haemato-oncological patients. Prophylaxis and treatment should also target opportunistic pathogens in this group. For every haemato-oncological patient admitted to the ICU, decisions about antimicrobial prophylaxis and treatment should be made in close collaboration with the haematologist and infectiologist. It is advised to apply selective digestive decontamination (SDD) or selective oral decontamination (SOD) in haemato-oncological patients. SDD

consists of an oral paste, a suspension of non-resorbable antibiotics for gastrointestinal use and systemic antibiotics, usually a third-generation cephalosporin, for the first four days of ICU admission. Furthermore, it is advised to use systemic antimicrobial prophylaxis (preferably fluoroquinolones) in patients with an expected long duration of neutropenia, although treatment with quinolones in the first few days of the SDD protocol (when a cephalosporin is administered) is superfluous.^[25,26] In high-risk patients (e.g. patients receiving treatment associated with severe oral and gastrointestinal mucositis, such as myeloablative conditioning and chemotherapy used in acute myeloid leukaemia) it is also advised to use systemic prophylaxis against disseminated *Candidiasis*.^[26,27] In selected patients it is also advised to use prophylaxis for *Aspergillus*, *Herpes simplex virus*, *Varicella zoster virus* and *Pneumocystis jiroveci*. Systemic monitoring of cytomegalovirus (CMV) and Epstein-Barr virus (EBV) reactivation should be provided in high-risk patients, such as post-SCT and patients using alemtuzumab. Prophylactic or pre-emptive treatment may be considered to prevent CMV- and EBV-related illness. In the full version of the guideline an extensive protocol is included, which may be used to make treatment decisions with regard to prophylaxis and treatment of infections in this patient group.

2.5 Bronchoalveolar lavage

Bronchoalveolar lavage (BAL) is advised in a worsening or not improving immune compromised patient with respiratory failure, pulmonary infiltrates and uncertainty about the diagnosis. BAL will establish a diagnosis in 42-80% of the cases.^[28-33] In 27% of the cases BAL results lead to changes in treatment strategy.^[32,33] Performance of BAL does not improve mortality per se.^[28,29] The percentage of endotracheal intubations directly after performing BAL is between 4 and 26%.^[31,33,34] When compared with patients not undergoing BAL, the necessity for intubation during ICU admission is 35% for both groups.^[28] It is therefore unlikely that performing BAL will lead to a significantly higher intubation rate. Given the fact that BAL increases the likelihood to acquire a diagnosis, the working group advises that BAL should be performed with a very low threshold in haemato-oncological patients with respiratory insufficiency and an uncertain diagnosis.

2.6 Transfusion of blood products

For haemato-oncological patients in the ICU we advise the same restrictive transfusion guidelines (haemoglobin >4.2 mmol/l and platelet count >10 × 10⁹/l in non-bleeding and non-anticoagulated patients) as used for the overall ICU population. One may take into account, however, that blood counts may decline faster in haemato-oncological patients because of limited bone marrow function. Therefore, a more pro-active transfusion policy should be considered. It is important to implement a clinical practice to quantify the corrected count increment when administering thrombocytes. Specific

instances where irradiated blood products should be given are mentioned in the full version of the guideline.

3 Recommendations in the post-ICU period

At the time of discharge, we advise to make clear decisions regarding the treatment code, limitations and re-admission policy and document these unequivocally. We advise to use a checklist on discharge as well, to facilitate the transfer of knowledge to the haematology ward (checklist can be found in the full version of the guideline). In post-ICU care there is an important role for the ICU liaison nurse in preventing complications after discharge.^[35] A reduction of ICU re-admission was found after introducing an ICU liaison nurse.^[36] Early consultation is important. Finally, we advise to start multidisciplinary revalidation as soon as possible after ICU discharge.

Conclusion

In conclusion, standardisation of care for haemato-oncological patients admitted to the ICU may result in better outcomes for these patients in the ICU. Implementation of the recommendations in this guideline may lead to a more uniform treatment of critically ill haemato-oncological patients in the Netherlands. Interested readers are encouraged to read the full version of the guideline and to use the guideline to implement changes in the chain of care of haemato-oncological patients in their hospitals. A close collaboration with the haematologists and other specialists involved in the chain of care while implementing these changes is essential, and the working group strongly recommends setting up multidisciplinary steering groups for this purpose in all hospitals involved.

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