Nursing role in the assessment and care of hepatic sinusoidal obstruction syndrome patients: a consensus paper by the “Gruppo Italiano Trapianto di Midollo Osseo”

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Abstract

Purpose Sinusoidal obstruction syndrome (SOS) is one of the most serious complications post haematopoietic stem cell transplantation (HSCT). The diagnosis of SOS is clinical, but nurses should be involved in the pre-transplant risk assessment period and play a crucial role in the early detection of signs and symptoms during and after hospitalization. The aim of this work is to achieve a consensus on nurses’ behaviour in caring for SOS.

Methods On behalf of the Italian Group for Bone and Marrow Transplantation (GITMO), a promoter committee was established to put in place a consensus conference approach. A multidisciplinary group of GITMO together with four nurses, three haematology physicians and one patient representative acted as jury, who reviewed the reports and wrote recommendations and suggestions. Recommendations gaining 100% of consensus were considered ‘Golden Points of Care’; if a consensus was achieved by ≥ 75% of the jury’s members, those recommendations were defined as ‘Good Practices’.

Results Eighteen papers written by nurses as first authors have been identified. Golden Points of Care and Good Practices were worked out for the following topics: nurses’ role in general, nurses’ role in pre-transplant assessment, pre-transplant risk assessment and risk stratification, baseline monitoring, suspected mild or moderate SOS, suspected severe or very severe SOS and late-onset cases.

Conclusion SOS is relatively rare; therefore, a holistic approach to the patients’ needs considering nursing role as essential may result in better care outcomes.

Keywords Sinusoidal obstruction syndrome · Veno-occlusive disease · Endothelial complications · Multi-organ failure · Stem cell transplantation · Nurse management

Introduction

Haematopoietic stem cell transplantation (HSCT) is a standard therapy used to treat various onco-haematological malignancies. One of the most serious complications related to endothelial damage due to conditioning regimens is hepatic sinusoidal obstruction syndrome (SOS), also known as veno-occlusive disease (VOD) [1]. It is a complex disease due to toxic metabolites producing endothelial activation with changes in the sinusoids’ permeability, inflammation and haemostatic activation leading to sinusoids’ obstruction. SOS may affect both autologous and allogeneic HSCT patients and it could result in a hepatorenal syndrome, hepatocellular fibrosis and necrosis, and hepatic failure, as well as multi-organ disease and death. Literature shows that mild and moderate SOS forms are often self-limiting or responsive to supportive therapies, whilst severe forms are associated with a high mortality rate, exceeding 80% [2]. This has a significant impact on patient outcomes [3] and costs [4–7]. On a clinical basis, SOS is characterized by increased liver volume,
associated with right upper quadrant pain, jaundice, fluid retention and ascites [8, 9]. It may rapidly evolve towards life-threatening conditions such as multi-organ failure (MOF) [2, 10]. SOS incidence in HSCT population is about 14%, but it can vary depending on a number of risk factors (RFs) and clinical criteria used [11, 12]. The diagnosis of SOS is clinical [13, 14] because of a lack of imaging techniques or biochemical markers, which would be able to provide a disease definition [15]. Furthermore, there is a real difficulty for HSCT patients that undergo liver biopsies, especially during the early post-transplant period.

The diagnostic clinical criteria commonly used in practice, as well as in many clinical trials (Seattle [16], Seattle modified [3] and Baltimore criteria [17]), provide various disease definitions and different data on SOS incidence (Seattle 17.3%, Baltimore 9.6%) [2]. Recent changes in HSCT led to the need for new tools for prognosis in SOS. Furthermore, the lack of criteria for “late-onset forms” diagnosis, which represent about 15–20% of cases [18–20], and the need to optimize treatment-related behaviours and costs [13] required a new definition of the disease. Addressing these issues, Mohty et al. (2016) and Corbacioglu et al. (2017) presented the European Society for Blood and Marrow Transplantation (EBMT) criteria for adult [13] and paediatric [21] patients. In addition to the definitions of the “classical” forms of SOS, a specific tool for the “Late Onset Cases” diagnosis and two tools (paediatrics and adults) for the grading of suspected SOS were added.

Early recognition, diagnosis and treatment are crucial aspects to limit SOS’ severity increasing chances of success [22–25]. Some authors state that nurses should be involved in a pre-transplant risk assessment to optimize risk factor detection and that they have a crucial role in the early detection of signs and symptoms during and after hospitalization [26–33]. Many clinical issues have been investigated; nursing issues have been studied as well, but there is a lack of specific topics such as assessment, monitoring techniques and care standards.

Materials and methods

The consensus conference

A consensus conference (CC) approach has been put in place, focusing on caring for adult and paediatric patients undergoing HSCT who are at risk of developing SOS. The aim of a CC is to obtain useful recommendations for health care professionals to deal with critical situations. Recommendations are gained by an expert group which analyses available literature, searches for critical appraisal and synthesizes the literature on a topic with huge clinical, organizational and practical assistance differences.

The involved professionals and their roles

On behalf of the Italian Group for Bone and Marrow Transplantation (GITMO), a promoter committee (PC) composed of a methodologist, a research nurse and two head HSCT nurses was established. An expert panel (EP) composed of 19 members (17 nurses and 2 physicians), coming from different Italian transplant centres, was identified and worked under the supervision of a research coordinator, analysing the available literature, investigating the research questions and defining the structure of the work. The PC led and supervised the whole process, establishing subgroups of the EP in relation to the topics; their leaders were selected on the basis of their specific competencies. A multidisciplinary group of GITMO (four nurses and three physicians working in adult and paediatric transplant settings) and two experts in research methodology together with one independent haematology physician and one patient representative acted as jury.

Organization of the consensus conference

The PC identified the research questions and conducted literature research on the main databases (PubMed, Cinahl, Embase, Scopus, Cochrane Library) searching for papers written primarily by nurses. Some research, such as the nurse’s role in SOS management, pre-transplant risk assessment and stratification, risk-related baseline monitoring, assessment and monitoring of patients with suspected SOS and assessment and monitoring of “late-onset forms”, were defined previously by the PC. The selected literature was tabulated by title, year, type of question, design, population, objectives, outcomes, relevance and suggestions/recommendations and sent to the EP.

Three EP scheduled meetings were assessed between March and August 2017 and some teleconference meetings were performed. The jury reviewed the reports and wrote recommendations and suggestions, which were first managed by the CC through voting. Recommendations gaining 100% consensus were considered Golden Points of Care. If a consensus was achieved by ≥75% of the jury’s members, those recommendations were defined as Good Practices. A public committee of non-specialists (students, managers, health care professionals, citizens) was also invited to assist the meetings as observers.

Results

Eighteen papers written by nurses as first authors have been identified. Five articles were preliminarily excluded by the PC
due to full-text unavailability or because of being comments or letters on other articles without adding useful input. The remaining full-text articles (Table 1) were selected for the EP work which approached them, using a critical appraisal system.

**General nurses’ role**

Golden Point of Care: “Nurses play a fundamental role in SOS management and should use a proactive approach managing patients”.

**Good Practices:**

- “Nurses who work in BMT units should have advanced knowledge and documented skills about SOS diagnosis and management”
- “Nurses should promote patient’s education regarding SOS”
- “Nurses are responsible for the quality of data collected during patient assessment and monitoring, their documentation and evaluation of non-conformities”

Management of SOS/VOD patients is complex due to its unpredictable features [34]. It is a shared opinion in the literature that nurses play a decisive role in SOS management [13, 30] especially during assessment and monitoring activities [27, 32, 35, 36]. The group discussed some typical relationship aspects between patients and nurses such as time of care, confidence and closeness that have been considered as facilitating factors of recognizing SOS signs. Given that a careful recognition of signs and symptoms is fundamental for early diagnosis [10, 37], it was agreed by the group that SOS management requires specifically trained nurses. BMT nursing staff should approach patients using a proactive model of care [27, 31, 32].

The group agreed that nurses are directly responsible for the quality and documentation of collected data, as well as early and effective communication with physicians about non-conformities.

**Nurses’ role—pre-transplant assessment**

Golden Point of Care: “Nurses should be involved during the pre-HSCT risk assessment path and share the results before patient admission in the HSCT unit”.

**Good Practice:**

- “Nurses should refer to specific assessment protocols during the pre-transplant assessment”

A good assessment should include other than vital signs and biochemical tests, patients’ personal data and lifestyle, clinical history and therapeutic program, performance status and nutritional conditions as well as abdominal evaluation and hepatic disorder signs (jaundice, bleeding). Monitoring of weight variations will be fundamental during patient’s hospital stay, a baseline measure should be registered before admission and a threshold of 5% increase should be determined.

**Pre-transplant risk assessment and risk stratification**

Golden Point of Care: “Pre-transplant risk level attribution for SOS development should be put in place taking into account the results of a careful and thorough assessment performed by the multi-professional team”.

**Good Practice:**

- “Bioethics Committees could give useful support in making transplantation decisions for very complex cases”

Objectives of pre-treatment assessment are the detection of RFs for SOS/VOD development and whenever possible the reduction of their impact before treatment [13].

Haematology physicians are responsible for therapeutic strategies that may be offered to patients; however, the assessment approach should involve different professionals such as nurses and other specialists [30]. The assessment for patients undergoing HSCT includes specific nursing responsibilities [27], and a multi-professional approach during the whole peri-transplant period. The main RFs for SOS development are summarized in Table 2. Assessment interventions cannot always be performed simultaneously by doctors and nurses but the sharing of results amongst health care professionals seems very important [31]. The EP agreed that it is fundamental for nurses to participate at the pre-transplant risk assessment process and to know the results and decisions taken in order to reduce transplantation risks before patient admission into the BMT unit.

Discussion within the EP was largely focused on SOS risk stratification. In 1993, Bearman and colleagues [38] developed an outcome-based predictive model for severe SOS. However, this model seems to be useful only in a very particular setting; therefore, it was not taken into consideration by the EP.

Some authors [37, 39] considered the odds ratio (OR) as a useful element for risk stratification, although doubts remain about its reliability and its significance when patients present multiple RFs. For this reason, a proposal based on OR was considered inadequate by the EP. The EP proposed to stratify patients as:

- Patients at high risk (HR) of SOS who present one or more RFs reported by Mohty et al. (2016) and Corbacioglu et al. (2018)
- All HSCT patients without RFs were considered at standard risk (SR) of SOS

Taking into account these considerations, a pre-transplant assessment protocol was made and synthesized in Table 3.
| Authors | Citation | Year | Publication type | Contents/suggestions | Notes |
|---------|----------|------|-----------------|---------------------|-------|
| Ford R, McClain K, Cunningham BA. | Nurs Clin North Am 18:563–568. | 1983 | Review* | Nursing role: nurses should maintain knowledge of the most recent advances putting them into practice. Care: nursing assessment is of paramount importance in detecting onset and minimizing complication effects. | Overview on SOS management. Paper dates back to a time period when BMT** was still an experimental cure. |
| Buchsel PC, Kelleher J. | Nurs Clin North Am 24:907–938. | 1989 | Review* | Nursing role: expert nursing care is required. Care: daily weight, in/output monitoring, postural hypotension monitoring, mental and neurologic status changes assessment. | Paper focused on general management of BMT patients. Paper dates back to a time period when BMT was still an experimental cure. |
| Grandt NC. | Oncol Nurs Forum 16:813–817 | 1989 | Review | Nursing role: nurses should have knowledge on SOS clinical manifestations and risk factors. Care: early detection, education. | Paper focused on general management of BMT patients. Paper dates back to a time period when BMT was still an experimental cure. |
| Freedman S, Shivnan J, Tilles J, Klemm P. | Crit Care Nurs Q 13:51–62 | 1990 | Review | Nursing role: highly skilled nursing care is necessary. Care: accurate and continuous assessment of fluid balance and intake and output; weight measurement twice a week; abdominal girth measurement; monitoring of serum bilirubin level, liver function tests and serum urea nitrogen levels; monitor patient for toxic effects of medication because of impaired hepatic function. | Paper focused on general management of BMT patients. Paper dates back to a time period when BMT was still an experimental cure. |
| Poliquin CM. | Yale J Biol Med 63:495–502 | 1990 | Review | Nursing role: Effectively managing these treatment-related toxicities requires interdisciplinary efforts of many specialties. Physicians, nurses, dental and psychiatric services, infectious disease, nutritional support, physical/occupational therapies and social service work collaborate to provide the comprehensive care required. Care: fluid and sodium restrictions, diuretic administration, electrolyte replacement, transfusions, analgesic administration, and support to the patient and family, careful assessment for signs and symptoms, maintaining fluid balance and electrolyte status, monitoring vital signs, daily weights, and abdominal girths, monitoring liver enzymes and haematology counts, blood product administration; analgesic administration, assessment for changes in neurological status. | Paper focused on general management of BMT patients. Paper dates back to a time period when BMT was still an experimental cure. |
| Wikle T, Coyle K, Shapiro D. | Am J Nurs 90:48–56 | 1990 | Comparative study | Nursing role: extensive and complex nursing care is required. Care: it is essential for nurses to recognize signs of hepatic deterioration early. Continuous monitoring and recording of intake and output, abdominal girth, weight and postural blood pressure are essential. | Paper focused on general management of BMT patients. Paper dates back to a time period when BMT was still an experimental cure. |
| Shaffer S, Wilson J | Crit Care Nurs Clin North Am 5:531–550 | 1993 | Review | No full text available. | Not included in the Consensus proceeding. |
| Shivnan J, Shelton BK, Omerus BK. | AACN Clin Issues 7:95–108 | 1996 | Case report | No full text available. | Not included in the Consensus proceeding. |
| Johns A. | J Intraven Nurs 21:356–60 | 1998 | Review | Nursing role: focus on managing side effects, preventing complications and patient and family support. Care: frequent monitoring of vital signs, side-effect management, monitoring of fluid balance and administration of blood and intravenous medications. | Paper focused on general management of HSCT patients. |
| Saria MG, Gosselin-Acomb TK | Clin J Oncol Nurs 11:53–63 | 2007 | Review | Nursing role: can positively impact outcomes and decrease ICU admissions. Transplant nurses and critical care nurses working with transplant recipients must continue on collaborative efforts. Care: signs and symptoms early recognition. | Paper focused on general management of HSCT patients. |
| Authors            | Citation                        | Year  | Publication type | Contents/suggestions                                                                                       | Notes                                                                 |
|--------------------|---------------------------------|-------|------------------|----------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------|
| Eisenberg S.       | *Oncol Nurs Forum* 35:385–397   | 2008  | Comprehensive review | Nursing role: Nursing care is extremely complex and challenging and requires a thorough understanding of pathophysiology and symptoms management. Care: the paper provides a nursing care plan focused on support of the affected organs. | The care plan is not focused on clinical severity and is not defined the timing of interventions. Not included in the Consensus proceeding. |
| Krimmel T,         | *Oncol Nurs Forum* 35:37–39     | 2008  | Case report      | No full text available.                                                                                  | Not included in the Consensus proceeding.                              |
| Williams LA.       |                                 |       | Review           |                                                                                                          |                                                                      |
| Oestreicher P.     | *ONS Connect* 23:22–23          | 2008  | Editorial/letter | Recap article.                                                                                           | Not included in the Consensus proceeding.                              |
| Becze E.           | *ONS Connect* 27:16–17          | 2012  | Editorial/letter | Recap article.                                                                                           |                                                                      |
| Sosa EC.           | *Clin J Oncol Nurs* 16:507–513  | 2012  | Review           | Nursing role: nurses play a crucial role in assessing, monitoring and supporting transplantation recipients and their family. Nurses working with HSCT patients should receive education about SOS so that proper assessment and monitoring can be performed. Care: liver enzymes, serum bilirubin, and serum creatinine. Closely monitoring of high-risk patients. Assessment of abdominal girth, weight, in/outputs, pain, oedemas, bleedings. Providing palliative care, psychological and emotional support. Multi-professional involvement. | Chapter on nursing implication.                                      |
| Botti S et al.     | *Ecancermedicalscience* 8:661   | 2016  | Consensus paper  | Nursing role: nurses play a fundamental role and should develop distinctive skills and competences. Care: the paper provides a dynamic assessment/monitoring protocol based on risk assessment results, transplant phase and suspect of SOS. | Results from a nationwide survey on nursing management of SOS included in the paper. Useful pathway flow chart is provided. The monitoring protocol is not based on the actual criteria for SOS diagnosis (EBMT). Chapter on nursing role in SOS assessment and management. Focus on multi-professional approach. |
| Wallhult E et al.  | *Eur J Haematol* 98:322–329     | 2017  | Review           | Nursing role: multidisciplinary teamwork is essential, and nurses should receive specific education on SOS in order to understand the importance of their role in the team, in relation to early detection and intervention. Nurses have an essential role to play, from pre-transplant assessment to medical management and overall care of the patient. So, there is a need for nurse education in this area, especially for junior haematology nurses. Care: the paper provides an assessment/monitoring protocol based on clinical status regarding SOS (risk, suspected, confirmed). | Chapter on nursing role in SOS assessment and management. Focus on multi-professional approach. |
| Ni Chonghaile M,   | *Clin J Oncol Nurs* 22:E7-E17   | 2018  | Review           | Nurses role: Nurses have a frontline role in recognizing the signs and symptoms of SOS, providing supportive care, and communicating compassionately with patients and families. Care: the paper provides an actionable list for monitoring of possible SOS and general recommendations for supportive care. | Suggestions to improve communication with patients and family. Implications for practice are reported. |
| Wolownik K         |                                 |       | Case report      |                                                                                                          |                                                                      |

*Research support, US Gov’t, P.H.S  
**BMT, bone marrow transplantation
Table 2  Risk factors for SOS development in HSCT patients

| Patient or clinical condition related | Treatment related |
|--------------------------------------|------------------|
| · Older age                          | · Unrelated donor |
| · Infants                            | · HLA-mismatched donor |
| · Karnofsky score < 90%              | · Non-T cell–depleted transplant |
| · Metabolic syndrome                 | · Myeloablative-conditioning regimen |
| · Advanced disease (beyond second CR or relapse/refractory) | · Oral or high-dose busulfan-based regimen |
| · Thalassemia                        | · High-dose TBI-based regimen |
| · Osteoporosis                       | · Second HCT |
| · Congenital macrophage activation syndromes | · Previous use of gemtuzumab ozogamicin or inotuzumab ozogamicin |
| · Neuroblastoma                      | · Hepatotoxic drugs |
| · Sickle cell disease                | · Abdominal or hepatic irradiation |
| · Genetic factors (GSTM1 polymorphism, C282Y allele, MTHFR 677CC/1298CC haplotype) | · Female receiving norethisterone |
| · Transaminases 42.5 ULN             |                   |
| · Serum bilirubin 41.5 ULN           |                   |
| · Cirrhosis                          |                   |
| · Active viral hepatitis             |                   |
| · Iron overload                      |                   |

Table 3  Pre-HSCT nursing assessment protocol

| Items                          | Parameters—observations                                                                 |
|--------------------------------|--------------------------------------------------------------------------------------------|
| Personal and clinical data     | Age, gender, diagnosis, actual state and course of the disease, type of transplant, conditioning regimen |
| Performance status             |                                                                                           |
| Nutritional status             | Baseline screening                                                                         |
| Vital signs                    | Blood pressure (BP), HR, SpO₂                                                                 |
| Weight                         | BP orthostatic and clinostat                                                                |
| Abdomen evaluation             | Objective exam: form, volume, skin pigmentation, liver size, abdominal circumference (AC), abdominal pain (spontaneous), induced pain (palpation: guarding, rigidity, rebound), dullness (percussion), evaluation of the hepatic consistency, collateral circles/spiders, bleeding signs |
| Skin evaluation                | Erythema, lesions, haemorrhages, jaundice, other discolorations                            |
| Sclera evaluation              | Micro-haemorrhages, jaundice                                                               |
| Biochemical tests              | Bilirubin (fractioned), transaminases, LDH, creatinine, electrolytes, coagulation profile, platelet count, ferritin, glomerular filtration, oxygen saturation, hepatitis markers |
| Clinical history               | Previous antineoplastic treatments, hepatotoxic treatments (e.g. vancomycin, antiviral, parenteral nutrition, etc...), febrile episodes, liver diseases, traumas, metabolic syndromes |
| Lifestyle                      | Habits that could affect liver function: diet, alcohol, tobacco, drugs, stress             |

*Mor V et al. 1984*  
**Lansky SB. 1987*  
***Body mass index. WHO. 1995*  
****Malnutrition Universal Screening Tool. BAPEN, Must report. 2003  
* Nutritional Risk Screening 2002. ESPEN working group. 2003  
† Screening Tool Assessment Malnutrition Paediatrics. McCarthy H et al. 2012  
CDC, NHANES III survey. 1988–94  
* Blood pressure, heart rate, respiratory rate, blood oxygen level
Baseline monitoring

Golden Point: “Early recognition of signs and symptoms is of paramount importance to provide an early diagnosis of SOS and for the outcome”.

Good Practices:

• “Nurses should refer to SOS specific monitoring protocols during patients’ hospitalization”
• “Intensity of monitoring should be adapted to the patients’ SOS risk level”

Patients undergoing HSCT follow normally strict monitoring protocols before, during and after the hospital admission. These protocols are not focused on endothelial injuries. However, it seems fundamental that nurses know how to carry out a pre-transplant assessment and how to adapt the monitoring baseline intensity to the patient’s risk level proactively [31].

Nursing interventions regarding SOS patients monitoring were listed by Eisenberg in 2008 [32] but they were not assigned to different transplantation steps or to the severity of clinical presentations. From a general perspective, nurses’ abilities could differ significantly due to many factors such as competencies, the ward routine, experience and others. Furthermore, the acquisition of advanced competencies and skills could be useful during the SOS monitoring process [40, 41]. Many papers included in our review belonged to grey literature (narrative reviews, expert opinion papers, letters). However, each one reported the need to provide an early diagnosis of SOS and two of them made a thorough description of nursing skills during patient baseline monitoring also using a similar approach [30, 31]. Our group established two different monitoring baseline protocols for patients at high risk and at standard risk, as shown in Table 4.

Suspected mild or moderate SOS

Golden Point of Care: “Nurses and other HCPs should be trained to early recognition of disease evolution”.

Good Practice:

• “Intensified monitoring protocols should be applied according to clinical severity (EBMT criteria for severity grading parameters), early starting of supportive therapies, fluids and sodium restriction and adequate fluids and electrolytes balance should be considered as crucial”

Mild and moderate VOD are often self-limiting or responsive to support therapies [2] but they may also rapidly evolve towards severe forms [15, 39]. Disease dynamicity requires a “proactive” attitude of health care professionals aimed at anticipating events. The early recognition of new onset signs and symptoms and the monitoring of the evolution of the parameters should be considered as good care practices. Patients who satisfy diagnostic criteria should start differential diagnosis pathways. At the same time, patients should start supportive therapies and consequently be monitored more strictly than at baseline, in order to start the disease-specific treatment (Defibrotide). In addition, it is necessary to monitor renal, pulmonary and central nervous system function to detect early alterations towards MOF. Early implementation of supportive therapies to sustain renal and respiratory functions represents a standard of care in mild or moderate SOS patients. Responsible use of diuretics maintaining a good fluid and electrolytes balance could be useful to prevent ascites. Transfusions of blood products such as albumin and plasma expanders could be considered [13, 15, 32]. Nurses should be well informed about analgesia and/or oxygen therapies, drug review (including medications which reduce the volume of fluids and avoiding hepatotoxic therapies), prevention of infections and psychological support. The EP developed a specific

Table 4 Baseline monitoring protocol

| Parameter | Standard risk Frequency per day | High risk Frequency per day |
|-----------|---------------------------------|-----------------------------|
| Vital signs: BP, HR, RR, SpO2, temperature | 2 | At least 2 |
| Weight | 2 | At least 2 |
| Fluid balance | 1 | At least 2 |
| Abdominal circumference | 1 | At least 2 |
| RUQ pain | At least 1 | At least 2 |
| Sclera: haemorrhages, jaundice | 1 | At least 2 |
| Skin: haemorrhages, jaundice, lesions | 1 | At least 2 |
| Abdomen objective examination | 1 | At least 2 |
| Blood tests: bilirubin (fractioned), transaminases, LDH, creatinine, electrolytes, coagulation profile, platelets count*, ferritin, glomerular filtration | At least 2 times per week and in case of alterations | From 3 times per week to daily in relation to alterations |

Each evaluation must be registered on clinical documentation
Each variation must be promptly shared with physicians
Patients and care givers (CGs) should be educated to promptly report each subjective sign/symptom

*Efficacy of platelet transfusions should be evaluated
**Table 5** EBMT criteria adapted monitoring protocol for mild/moderate and severe/very severe SOS (adults and paediatrics)

| Measures/observations | Timing mild/moderate SOS (per day) | Timing severe/very severe SOS (per day) | Note |
|------------------------|----------------------------------|----------------------------------------|------|
| EBMT criteria          |                                  |                                        |      |
| Weight                 | At least 1                        | At least 2                              |      |
| Bilirubin (total and fractioned) | At least 2                        | At least 4                              |      |
| Transaminase           |                                  |                                        |      |
| Creatinina/GFR*        |                                  |                                        |      |
| Platelets              |                                  |                                        |      |
| Clinical monitoring    |                                  |                                        |      |
| Abdominal girth        | At least 1                        | At least 2                              |      |
| Fluids and electrolytes balance | At least 2                        | At least 4                              |      |
| Abdominal exam: form, volume, skin pigmentation, liver size, pain (spontaneous or induced), dullness (percussion), hepatic consistency, bleeding signs, collateral circles/spiders | At least 4 | At least 2 |          |
| Urine evaluation: colour, smell, volume, frequency, composition (rapid tests) | At least 1 | At least 2 |          |
| Respiratory            |                                  |                                        |      |
| Dyspnoea and respiratory dynamic evaluation | At least 1 | At least 3 |      |
| RR, SpO2****           |                                  |                                        |      |
| BGA****                |                                  |                                        |      |
| Haemorrhages: epistaxis, haemoptoe | At each episode | Continuous |    |
| Cardio-circulatory     |                                  |                                        |      |
| Vital signs: BP, HR****, Temperature | At least 3 | Continuous |    |
| Haemorrhages, pigmentation (jaundice), lesions, puritus | At least 2 | At least 2 |    |
| Oedemmas monitoring    |                                  | At least 1                              |      |
| Central Nervous System |                                  |                                        |      |
| Performance status     |                                  |                                        |      |
| Consciouenss state     |                                  |                                        |      |
| Gastro-intestinal      |                                  |                                        |      |
| Stool evaluation: colour, consistency, smell, quantity, frequency (haemorrhagic signs: haemoptysis, melena, rectorrhagia) | At each | At each |    |
| Bloodoemmas count, platelets count, coagulative profile, electrolytes and other prescribed tests | At least 1 | Up to 2 |    |
| Biological             |                                  |                                        |      |
| Weight                 | At least 3                        | At least 4                              |      |
| Bilirubin (total and fractioned) | At least 3                        | At least 4                              |      |
| Transaminase           |                                  |                                        |      |
| Creatinina/GFR*        |                                  |                                        |      |
| Platelets              |                                  |                                        |      |

*Sclera* Glomerular Filtration Rate; **Right Upper Quadrant; ***Respiratory Rate, Blood Oxygen level; ****Blood Gas Analysis; *****Blood Pressure, Hearth Rate; Computed Tomography, Magnetic Resonance Imaging; Non-Invasive Ventilation; Intensive Care Unit; Modified Early Warning Score for adults, Pediatric Early Warning Score for pediatrics.

Suggestions without having a relation to EBMT diagnosis criteria and severity grading as well as the timing of monitoring are included in the table as results of the EP discussion.

Monitoring protocol for suspected mild/moderate SOS (Table 5).

**Suspected severe or very severe SOS**

Golden Point of Care: “Multi-professional approach to vital functions support and pain management should be put in place”. Good Practices:

- “Specific Intensive Care Unit (ICU) care pathways should be present”
- “Nurses should have documented skills and competencies for the care of critical patients”
Severe and very severe forms of SOS include multi-organ disease or multi-organ failure conditions and could be considered life-threatening illnesses that require intensive care [2, 42]. For this reason, pathways disclosing relationships between transplant programs and ICU wards should be warranted [30, 32, 43]. Frequent development of multi-organ forms requires multi-professional involvement and careful monitoring, especially of renal and respiratory conditions due to patient frailty and rapid disease evolution [31]. An important role is played also by the coagulation [44] and a non-invasive ultrasound technique such as FibroScan, which is a combination of ultrasound morphologic imaging and elastography, can be applied to adults as well as children [45]. In new paediatric severity grading criteria [21], lung functionality and oxygen need are closely considered, by specifying a threshold limit: 2-l oxygen in mild cases and non-invasive or mechanical ventilation in severe forms.

A number of drugs were studied for SOS treatment frequently with scarce results or increased adverse events. Defibrotide was approved in Europe for treatment of post-HSCT severe forms [46] and its use was strongly recommended by EBMT and BCSH/BSBMT guidelines [15, 47]. Due to this recommendation, the subgroup dealing with severe or very severe SOS states that a starter provision of defibrotide should be available in every BMT centre in case of immediate need.

**Late-onset cases**

Golden Point of Care: “An appropriate follow up should be performed for outpatients considered at risk of late-onset SOS”.

Golden Point: “Outpatients considered at risk of late-onset SOS and their caregivers should be properly trained on self-assessment and there should be timely communication of signs and symptoms”.

Good Practices:

- Patients should undergo a re-assessment at discharge taking into account pre-HSCT risks of SOS and what happened to them during hospitalization
- Assessment and monitoring standards may be the same for late-onset SOS and classical forms
- Self-assessment tools should be implemented for outpatients at risk

About 30% of SOS developed in post-transplant outpatients after the first three weeks [46], especially at paediatric age [21]. However, this problem has been largely underestimated by scientific literature before the EBMT criteria and represents one of the main reasons for the development of new diagnostic criteria [13].

The working group agreed that there is no need for a different monitoring protocol than the classical forms; however,
Conclusions

As displayed above, the aim of this work was to achieve a consensus in nurses’ behaviour in the field of SOS care [31]. The methodology used in the work did not allow for generating new evidence, but it was aimed to create a common basis to orientate future research, especially on those “grey areas” considered significant for patients or health care professionals. The literature does not provide evidence regarding nursing care of patients affected by SOS, and the little available knowledge in this field is provided by expert opinion-based papers that frequently gave anecdotal information modulated from caring for liver insufficiency patients or ICU patients.

SOS is relatively rare, but it is considered one of the most important complications that could affect post-transplant patients due to its clinical consequences [48] and costs [5]. Recently the EBMT criteria for severity grading of suspected SOS [13, 21] added a prognostic value at its diagnostic pathway in both paediatric and adult settings; it will probably reduce the importance of differential diagnosis and preferring the early treatment of the condition. From the nurse’s point of view, it seems of paramount importance to have specific protocols regarding assessment and monitoring based on the criteria for SOS diagnosis and grading. However, a holistic nursing approach needs to take into account also a sequence of factors not strictly related to the patient’s liver conditions, which may result in better care outcomes. SOS capability can quickly evolve towards MOD/MOF conditions and imply that nurses are able to recognize related signs and symptoms but also how to manage life-threatening events [46]. Specific training courses could be useful to ensure and maintain nurse’s knowledge of SOS management.

In this work, a progressive intensity model based on risk level and disease severity was used. The interventions were adapted to the patients’ conditions at each level in a proactive way by nurses. Due to the lack of evidence, all recommendations given in this paper are the result of the discussion within an expert group using literature suggestions, as well as a collegial discussion of protocols supported by experts in the field. However, EP considers that a wide application of common protocols could represent a good platform for future nursing research in this area.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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