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# Interprofessional Team-based Care of the Hematopoietic Cell Transplantation Patient With Hepatic Veno-occlusive Disease/Sinusoidal Obstruction Syndrome

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**Summary:** Hepatic veno-occlusive disease/sinusoidal obstruction syndrome (VOD/SOS) is a well-recognized complication of allogeneic and autologous hematopoietic cell transplantation (HCT). The diagnosis and treatment of VOD/SOS require the involvement of multiple specialists covering a wide range of expertise. Interprofessional team-based medical care is standard practice for patients undergoing HCT and has been shown to improve patient and provider satisfaction, enhance efficiency, and improve patient outcomes, particularly for patients in complex medical situations like those with VOD/SOS post-HCT. Interdisciplinary team-based models focus on the synthesis and harmonization of knowledge and methods from different disciplines to create an integrative approach to patient care that both maximizes the expertise of each involved specialist and encourages thought beyond each specialist's discipline. Multidisciplinary team members provide additive support and work collaboratively with the core team to provide knowledge from their field. The composition of the interdisciplinary HCT team should center on the needs of the patient and institutional resources and involve the expertise of additional multidisciplinary team members based on clinical needs. This review focuses on interdisciplinary and multidisciplinary team-based care of patients with VOD/SOS post-HCT and provides an example of a collaborative VOD/SOS team that includes transplant physicians, nurses, pharmacists, nutrition/dietary specialists, and intensive care teams.

**Key Words:** Team-based patient care, interdisciplinary team, multidisciplinary team, hematopoietic cell transplantation, veno-occlusive disease/sinusoidal obstruction syndrome

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Hepatic veno-occlusive disease/sinusoidal obstruction syndrome (VOD/SOS) is a well-recognized complication of allogeneic and autologous hematopoietic cell transplantation (HCT) and is caused by toxic injury to the hepatic sinusoidal cells and hepatocytes.[1] Approximately 10% to 20% of HCT patients are diagnosed with VOD/SOS, although the incidence is far greater in certain high-risk populations.[1–6] A diagnosis of VOD/SOS is based on the classic clinical features of hyperbilirubinemia with jaundice, ascites, fluid retention with weight gain, and tender hepatomegaly developing in the 1 30 days after a transplant. However, the disorder has a range of clinical presentations, including anicteric disease and late-onset VOD/SOS.[3,5,7] Recognition of the nonclassic VOD/SOS presentations and differences in pediatric and adult patients prompted the development of diagnostic criteria that built on the traditional Baltimore and modified Seattle criteria.[1,3,7–9]

VOD/SOS is a multiorgan complication of transplantation that causes substantial morbidity and mortality. Historically, mortality rates of greater than 80% have been reported in patients with untreated severe VOD/SOS.[2] In recent years, mortality has decreased with advances in supportive care and therapies such as defibrotide.[3,10,11] Although survival rates have improved in recent years, morbidity remains high, with 30% to 60% of patients diagnosed with VOD/SOS developing multiorgan dysfunction or failure.[3,11–13] The goal of this manuscript is to highlight how interdisciplinary team management can contribute to enhanced patient and caregiver experiences and improved outcomes for the patient diagnosed with VOD. Although the care described is focused on VOD, the concepts apply to the management of other complex posttransplant complications, including, but not limited to, transplant-associated thrombotic microangiopathy, severe acute graft-versus-host disease, and respiratory failure.

## INTERPROFESSIONAL TEAM-BASED MEDICAL CARE

Interprofessional team-based medical care, regarded as a means to promote quality and safety in the hospital setting,[14,15] can improve patient and provider satisfaction, enhance efficiency, and improve patient outcomes, particularly for patients with critical illness and in complex medical situations.[16–18] A variety of terms are used to describe team-based care: *multidisciplinary*, *interdisciplinary*, *cross-disciplinary*, and *transdisciplinary*. Although sometimes used interchangeably, these terms exist within different frameworks, each suitable to specific medical settings. Cross-disciplinary and transdisciplinary models, because they are most commonly employed in research and intellectual frameworks, are not discussed here. Because of its clinical care focus, this review concentrates on multidisciplinary and interdisciplinary care. In multidisciplinary care, individuals from different disciplines work collaboratively within the clinical limits of their field, described as an additive

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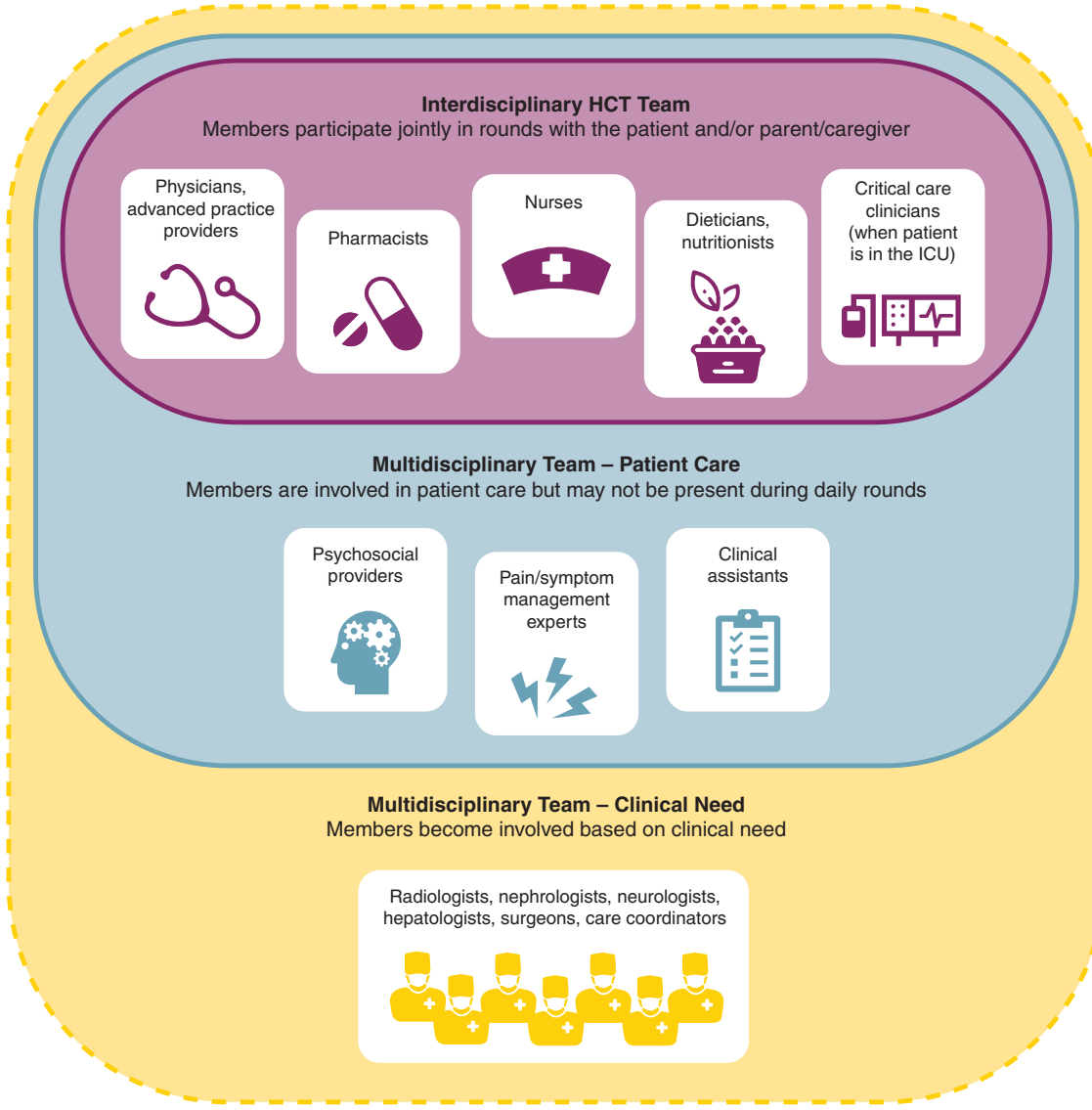


**FIGURE 1.** Team-based model of VOD/SOS care. Providers critical to daily, collaborative, face-to-face care comprise the interdisciplinary core; teams in the multidisciplinary patient care team play crucial daily roles but may not be required during collaborative rounding and can be included outside of that setting; the outer ring of multidisciplinary care is called on to consult and/or provide services on limited (example radiology) or ongoing basis (example: nephrology). HCT, hematopoietic cell transplantation; ICU, intensive care unit; VOD/SOS, veno-occlusive disease/sinusoidal obstruction syndrome.

approach. In interdisciplinary care, the focus is on the synthesis and harmonization of knowledge and methods from different disciplines, described as an integrative approach.[19]

Interprofessional team-based care is standard practice for patients undergoing HCT because of the intensity and multisystem nature of the primary disease, its treatment, and subsequent complications. This is particularly relevant in the care of patients with VOD/SOS, given the complexity of the diagnosis and the involvement of multiple medical providers, psychosocial professionals, care management experts, and others.

In the examples of multidisciplinary and interdisciplinary care listed below, the core HCT team is considered interdisciplinary and composed of physicians, advanced practice practitioners (APPs), nurses, and clinical assistants. The disciplines refer to groups that collaborate in the care of patients with VOD/SOS. In multidisciplinary care, individuals from different disciplines work together while remaining focused on their field. For example, a VOD/SOS model of multidisciplinary care could involve interventional radiology teams placing and co-managing peritoneal drains without their participation in the rest of the patient's care. Interdisciplinary care focuses on the synthesis and integration of the knowledge and expertise of different clinical teams involved in the care of a patient. A VOD/SOS model of interdisciplinary care could involve the HCT and intensive care teams participating in rounds together to care for a critically ill patient.

It is important to acknowledge that although daily, collaborative interdisciplinary care is a goal, time constraints and competing demands make it difficult to achieve this objective. Not meeting collaborative expectations can

**TABLE 1.** Additional Teams Potentially Involved in the Care of the Patient With VOD/SOS

| Team/Service | Collaborative Structure | Roles |
|---|---|---|
| Interventional Radiology | Multidisciplinary | Peritoneal drain and chest tube placement and management |
| Ultrasonography | Multidisciplinary | Diagnostic imaging and monitoring |
| Nephrology | Inter-/Multidisciplinary | Consultative management of hypertension, fluid imbalance, renal replacement |
| Neurology | Multidisciplinary | Consultative guidance in setting of VOD-associated neurological event |
| Pulmonary | Multidisciplinary | Collaborative care in the setting of respiratory compromise |
| Palliative Care | Inter-/Multidisciplinary | Supportive care of patient/family, chaplaincy, symptom management guidance, anticipatory guidance and end of life care |
| Pain Management | Inter-/Multidisciplinary | Consultative management of pain, drug interaction, and clearance expertise |

Specific collaborative frames and roles of teams depend on general hospital, transplant, and specialty practices.

frustrate teams, patients, and caregivers. Communication strategies are helpful when the system is stressed. These can include sending 1 member of the team to joint rounds if all members are unavailable at the designated time, using simple methods of communication (for example, text messages and pages) with time sensitive plan changes, and speaking jointly with patients and care givers when errors or miscommunications occur.

Patient/caregiver and medical team meetings can be valuable in the care of patients with VOD/SOS. These meetings can also stress busy teams who may be caring for multiple medically intense patients and heighten anxiety-worried families. Structured meetings that have agendas and time limits are associated with improved patient family understanding of care and treatment and are recommended.

## COMPOSITION AND PRACTICES OF A COLLABORATIVE VOD/SOS TEAM

The importance of collaborative care has been stressed by various cellular therapy consortia, and the ideal method of care delivery for a patient with VOD/SOS depends, in large part, on the expertise of involved teams and resources available at the transplant center.[5,20] Blended models of interdisciplinary and multidisciplinary care may be the most practical. In these blended models, a core group of providers review data and develop therapeutic and diagnostic plans across specialties, constituting the interdisciplinary component. Other specialists provide recommendations or perform procedures limited to their areas of expertise, constituting the multidisciplinary component. At our centers, the interdisciplinary medical VOD/SOS team is composed of physicians, APPs, nurses, a transplant pharmacist, and a dietician, all of whom attend rounds jointly with the patient and/or parent/caregiver (Fig. 1). When patients are in the intensive care unit (ICU), this team expands to include critical care providers. Psychosocial providers, clinical assistants, and experts in pain and symptom management are essential multidisciplinary team members involved in the care of most patients, and they may or may not be present during daily rounds. Diagnostic and interventional radiologists, nephrologists, neurologists, surgeons, hepatologists, and care coordinators join the multidisciplinary team as clinically needed, and they typically provide recommendations and services limited to their areas of expertise (Fig. 1). This document focuses on common members of the interdisciplinary VOD/SOS team with potential roles of other specialists detailed in Table 1.

The behavior of an effective interdisciplinary VOD/SOS team is grounded in clear communication, respectful collaboration, and shared attention to detail. Standardized daily screening during interdisciplinary rounds can maximize effective communication and focus on details key in the diagnosis of VOD/SOS- weight, electrolytes, fluid balance, pain, and the presence of mental status changes or delirium. These elements, along with transplant pharmacist-supported medication review, are crucial once VOD/SOS is diagnosed. A brief huddle later in the day between physicians, APPs, and nursing to review clinical changes and to define overnight management is helpful. Other straightforward interdisciplinary practices useful in the detection and care of patients with VOD/SOS are outlined in Table 2.

### Transplant Physicians

Transplant physicians are responsible for the oversight and implementation of diagnostic and therapeutic plans, coordination of interdisciplinary and multidisciplinary team members, collaborative leadership in patient/family communication, and education of colleagues in all specialties and levels of training. Early intervention may improve the survival of patients with VOD/SOS, and the physician's role begins before diagnosis.[21] Therefore, it is essential that transplant physicians maintain a high level of suspicion of the diagnosis and have up-to-date knowledge of diagnostics, literature, and practice changes. This is particularly relevant in recent years as diagnostic criteria evolved to recognize the unique characteristics of VOD/SOS in children, including at-risk populations, late-onset illness, and anicteric disease. It is the responsibility of the attending transplant physician to ensure that other members of the team understand these features of pediatric VOD/SOS.

**TABLE 2.** Examples of Interdisciplinary Strategies that can Inexpensively Optimize Care of VOD/SOS Patients Without Significant Investment of Time

| Interdisciplinary Practices |
|---|
| Standardized discussion of critical VOD/SOS elements during rounds |
| Joint rounding of teams involved in the specific care of the patient |
| Designated, consistent rounding times to allow the opportunity for teams to predictably participate |
| Early, brief notification of collaborating teams when rounding or meeting times unexpectedly change |
| Pharmacy review of medications with transplant providers to evaluate for issues of drug clearance and interactions |
| Scheduled brief huddles after rounds to discuss the patient status and plan changes |
| Structured team and caregiver meetings with agendas and time limitations to facilitate focus on key issues without overwhelming patients/caregivers |

Before the development of signs or symptoms of VOD/SOS transplant, physicians perform daily physical examinations of the patient-focused on abdominal examination and the presence of edema. Physicians must carefully monitor trends in fluid balance and weight. This is critical in pediatric patients as small daily changes can indicate progressive fluid overload consistent with VOD/SOS. As signs or symptoms of VOD/SOS develop, transplant physicians guide the diagnostic evaluation, including the timing of imaging and investigation of other potential diagnoses. Once a diagnosis of VOD/SOS is made, transplant physicians direct medical management with defibrotide and other medications, monitor organ function and intervene as needed, determine the necessity for peritoneal drain or chest tubes, communicate with specialty services, and maintain open communication with the patient and their caregivers. The status of patients with VOD/SOS can change rapidly, and physicians should be prepared to make real-time adjustments to the care plan multiple times a day based on the clinical scenario.

## Nurses

Nurses fulfill several essential roles in the diagnosis and treatment of patients with VOD/SOS. The nursing team consists of a dedicated group of bedside nurses assigned to a primary patient, a charge nurse, a nurse practitioner, and a nurse educator.

Bedside nurses provide a continuum of care and develop a rapport with the patient and family. Bedside nurses provide highly skilled, often 1-on-1 nursing care and are knowledgeable about the pathophysiology, risk factors, clinical signs, and management of VOD/SOS, allowing them to closely monitor patients for its occurrence. Their bedside view allows them to quickly notice a change in status, to screen for delirium, and to monitor treatment effectiveness, potential discomfort, or psychosocial concerns.[20,22,23] They are poised to voice any concerns and to advocate for patients. Accurate and timely recognition of VOD/SOS is crucial for the initiation of appropriate treatment, and these nurses use the strength of support assessment for patient assessment and monitoring, the mainstay of effective nursing support.[24] Bedside nurses, along with clinical assistants, acquire and communicate key data for the early detection of VOD/SOS: precise fluid balance, urine output, weight, and abdominal girth. These nurses are experts at administering prescribed treatments and coordinating patient care.

Charge nurses provide additional support to bedside nurses in a variety of ways, including performing some of the bedside nursing tasks and allowing for the bedside nurses' break time. In addition, charge nurses serve as liaisons between bedside nurses and medical staff. They understand patient acuity and staff capability, determine the appropriate level of care for the patient, and coordinate potential transfers of care.

Nurse practitioners are trained in HCT early treatment complications and are able to formulate, in collaboration with the physician team, a treatment plan for VOD/SOS.[25] They ensure that the medical interventions and prescribed evaluations are implemented and effective. On the basis of this information, they can make necessary adjustments to the treatment plan. They frequently reassess the patient and communicate pertinent information to team members and consulting services. They educate patients, families, and staff about the rationale and expected outcomes of prescribed treatments and interventions.

Nurse educators work in collaboration with other nurses, pharmacists, and physicians on the team to develop training tools and educational opportunities for nursing staff regarding VOD/SOS and its treatment. This is an important role as diagnostic tools and therapeutic strategies continue to evolve, and up-to-date knowledge could positively impact the outcome and patient experience.

## Pharmacists

The presence of pharmacists on multidisciplinary teams caring for patients with VOD/SOS is vital. Pharmacists' preexisting knowledge of patients' treatment-related or disease-related risk factors is helpful in predicting the risk of developing VOD/SOS. Once a VOD/SOS diagnosis is suspected or confirmed, early intervention and treatment modalities are crucial. Pharmacists should serve as gatekeepers to prevent medication-related toxicity that may result from declining hepatic and renal function commonly seen with VOD/SOS.

Pharmacists can advise dose adjustments for any medications metabolized or eliminated by the liver and/or kidney. Medications that may require adjustment include, but are not limited to, anti-infectives, antiemetics, and immunosuppressive agents. Pharmacists work with their teams in discussing possibilities for VOD/SOS treatment, such as additional supportive care, heparin, tissue plasminogen activator, or defibrotide. Pharmacists also provide education on proper administration and monitoring parameters for many medications used in this patient population; some examples include defibrotide, enoxaparin, heparin, cyclosporine, and vancomycin.

The main goal in caring for patients with VOD/SOS is to correct fluid overload without compromising renal function.[13,26,27] Pharmacists make recommendations concerning the use of diuretics, colloids, and fluid restriction to help balance fluid and reduce extravascular volume.[28] If renal perfusion is compromised, drug clearance may slow, resulting in elevated levels of medications that could result in toxicity. Dose adjustments are based on an estimate of the patient's current decreased renal function. In some cases, pharmacists recommend not administering certain medications, such as aminoglycosides, whereas recommending dose modifications for others. Many penicillins, carbapenems, and cephalosporins are metabolized and/or excreted through the kidneys.[10,29] Lower doses and/or modified dosing intervals are often necessary until the patient's renal function returns to baseline.

Renal dysfunction can also affect the clearance of opioids prescribed for painful ascites resulting from VOD/SOS or other treatment-related discomfort. Opioids, when administered in renal dysfunction, can cause excess sedation by accumulation of metabolites. Pharmacists can guide their teams as to the safest opiate for a patient, as morphine, oxycodone, and hydromorphone all have active metabolites that accumulate in renal dysfunction; thus, dosing for these medications must be decreased and patients closely monitored. Methadone may be recommended since its renal metabolites are not active. Fentanyl is another option but, given its potency, should be used cautiously.[30]

Depending on the severity of hepatic dysfunction, pharmacists may also recommend decreasing hepatic insults when possible.[26] This includes changing antifungal prophylaxis with fluconazole/voriconazole to echinocandins, such as micafungin, until engraftment. Amphotericin products should be avoided, along with azoles, because they can

 

contribute to the development of VOD/SOS.[13] Pharmacists also recommend close monitoring of medications used for immunosuppression that is metabolized in the liver, such as cyclosporine and tacrolimus. Other recommendations may include the use of lactulose, vitamin K, and other related supportive care to support hepatic function and treat encephalopathy.

In addition to required adjustments in patients with renal dysfunction, many opiates also require adjustments in those with hepatic dysfunction. Most opiate medications and pain relievers, including acetaminophen, must be used cautiously in patients with hepatic impairment and, if used, require close monitoring. Pharmacists may recommend fentanyl, as dose adjustment is usually not necessary, but it should be used with caution. Most pharmacists discourage the use of methadone, which is contraindicated in hepatic dysfunction.[30] In patients who have both renal and hepatic dysfunction, a delicate balance is needed that may require specialized ICU care and sedation for symptom control, with close monitoring for toxicity and response.

Pharmacists should be used as a resource to protect patients from drug toxicities that may occur from and/or may worsen VOD/SOS-associated end-organ dysfunction. Best outcomes require a fully collaborative effort between pharmacists and the rest of the multidisciplinary team.

## Nutrition/dietary Specialists

HCT patients experience changes in protein, energy, and micronutrient metabolism, which place them at risk for malnutrition.[31] In addition to nutritional compromise, patients with VOD/SOS may experience clinically significant electrolyte derangements, protein loss, and fluid shifts with total-body fluid overload with intravascular depletion. Nutritional specialists knowledgeable about and experienced in VOD/SOS provide valuable input in multiple mainstays of supportive care: meticulous fluid management, sufficient caloric intake, and prevention and treatment of electrolyte abnormalities.[32,33] Often, their input includes guidance on the use of parenteral nutrition, which helps modulate fluids, nutrients, and electrolytes, which can be of critical importance in patients with VOD/SOS.[31] The presence of a transplant nutritional expert on interdisciplinary rounds contributes to the development of plans based on the specific fluid and nutritional needs of an individual patient.

## Collaboration With Intensive Care Teams

Patients with severe VOD/SOS may develop multiorgan dysfunction and failure and require care in ICUs. It is common, in this setting, for numerous teams to be involved in the care of a critically ill patient with VOD/SOS.[23] Intensivists are ultimately responsible for the care of these patients, given their expertise in cardiopulmonary and end-organ failure. The intensive treatment is enhanced by the HCT team's knowledge of the patient, underlying disease and comorbidities, medication interactions, and current standards of VOD/SOS management. In this setting, a highly functional interdisciplinary team-based approach benefits patient care, the experience of families and caregivers, and the satisfaction of medical providers.

We recommend a model of structured rounding in the ICU designed to maximize collaboration, information sharing, and the expertise of all team members. This recommendation is based on our experience and studies of interprofessional structured rounds in other settings that have shown superior patient perceptions in openness and inclusivity, patient-centeredness, attending role/shared leadership, teaching, and efficiency.[16,34,35] In this model, individuals from multiple disciplines, along with the caregiver and/or patient, are present, at a consistent time each day, outside the patient's room during the data presentation and shared development of the care plan. An advantage of this model is the predictability of rounding time, which encourages the presence of collaborating teams and provides consistency for the patient and family.[34] Essential members of the rounding team include critical care and transplant physicians, advanced practice providers, nurses, pharmacists, and dieticians/nutritionists. Ideally, transplant nurses and pharmacists are present, in addition to their critical care counterparts, although this is not always possible. Key collaborating specialists, including nephrologists, respiratory therapists, and others, should participate depending on the clinical scenario.

## Administrative and Data Requirements

Pediatric HCT programs operate under multiple regulations and guidelines, including those from the United States Food and Drug Administration (FDA) and the Foundation for the Accreditation of Cellular Therapy. In addition, programs have data reporting obligations to local and study teams along with the Center for International Blood and Marrow Transplant Research. The cumulative burden of regulation and data reporting can weigh heavily on center faculty and staff. This may be particularly challenging when patients experience complications like VOD/SOS as the hospital course may be prolonged, involving multiple services and therapies. The complexity of regulation and reporting needs can be eased when data professionals and administrative professionals are incorporated into the interprofessional team. This can be accomplished by encouraging these professionals to attend clinical meetings when complex patients are discussed, having dedicated education sessions for data and administrative teams, and designating specific medical professionals to serve as clinical mentors for the team.

# SUMMARY

The diagnosis and treatment of VOD/SOS require the involvement of multiple specialists covering a wide range of expertise. Structured interprofessional team-based care models can create synergistic environments that both maximize the expertise of each involved specialist and encourage thought beyond each specialist's discipline. The core interdisciplinary HCT team's composition should center on the needs of the patient and institutional resources and involve the expertise of additional multidisciplinary team members based on clinical need. Prospective, patient-centered and outcomes research in this area may help decrease morbidity and mortality and may improve patient and provider satisfaction.

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