VOD/SOS OVERVIEW

Veno-occlusive disease/sinusoidal obstruction syndrome (VOD/SOS) is a potentially life-threatening complication following hematopoietic cell transplantation.

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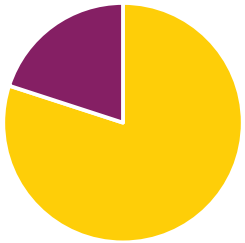
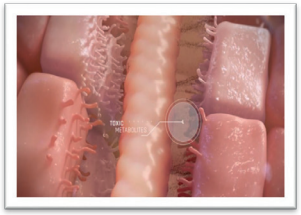
Veno-Occlusive Disease/Sinusoidal Obstruction Syndrome (VOD/SOS)

High mortality rates are seen in VOD/SOS with renal or pulmonary dysfunction



A >80% mortality rate is associated with the most advanced forms of VOD/SOS[1,2] highlighting the importance of early diagnosis

VOD/SOS is caused by endothelial cell (EC) activation and injury after HCT or chemotherapy[4]



Accumulation of toxic metabolites triggers EC activation and injury

Activated ECs:
- ⬆Procoagulant factors
- ⬆Inflammatory mediators
- ⬆Metalloproteinases

Damaged ECs:
- ⬆Heparanase
- ⬇Cytoskeletal structure
- ⬆Gaps in the endothelium

Deterioration of the endothelium leads to sinusoidal narrowing and blockage by embolized ECs

Incidence varies based on risk factors (eg, age, primary disease, and HCT conditioning regimen)

VOD/SOS is estimated to occur in[2]:

Adults (~10%)

Pediatric patients (~20%)

Risk factors for VOD/SOS can include[3]:

Pretransplant factors
- Younger age
- Pre-existing hepatic conditions
- Underlying diagnosis
- Prior treatment with GO or InO
- Prior abdominal radiation
- Genetic predisposition
- Karnofsky index <90%
- Impaired pulmonary function

Transplant-related factors
- Allogeneic HCT
- Unrelated/HLA mismatch
- Previous HCT
- High-intensity conditioning regimens
- Total body irradiation
- GvHD prophylaxis

Obstruction of hepatic sinusoidal flow results in sinusoidal hypertension and VOD/SOS symptoms

Four common VOD/SOS symptoms[2,5-8,a]


Hepatomegaly or liver tenderness


Sudden weight gain (often due to ascites)


Elevated bilirubin


Refractory thrombocytopenia

VOD/SOS without hyperbilirubinemia has been reported in:

15% of adult patients[9]

~30% of pediatric patients[6,9,10]

Signs of VOD/SOS often peak within the first weeks after HCT, but onset of VOD/SOS beyond Day 21 (late-onset) has been reported

In a large prospective study, late-onset VOD/SOS was observed in[11]:

17% (95/570) of pediatric patients

39% (169/430) of adults

Diagnostic criteria for VOD/SOS have evolved to allow for earlier detection to improve outcomes

	Baltimore[12]	Modified Seattle[13]	EBMT[14]	EBMT[2]	Mahadeo[7]	Cairo/Cooke[8]
Patient population	Age agnostic	Age agnostic	Adult	Pediatric	Pediatric	Age agnostic
No time constraint to diagnose VOD/SOS (>21 days)			✓	✓	✓	✓
Recognizes anicteric VOD/SOS		✓	✓	✓	✓	✓
Includes refractory thrombocytopenia				✓	✓	✓
Includes abdominal ultrasound[b]			✓	✓	✓	✓
Includes Doppler ultrasound imaging[c]			✓ (probable VOD/SOS)		Not recommended	✓
Hepatic wedge pressure			✓		Not recommended	✓[d]
Biopsy			✓		Not recommended	✓[d]

Abbreviations: EBMT, European Society for Blood and Marrow Transplantation; EC, endothelial cells; GO, gemtuzumab ozogamicin; GvHD, graft versus host disease; HCT, hematopoietic cell transplantation; HLA, human leukocyte antigen; InO, inotuzumab ozogamicin; VOD/SOS, veno-occlusive disease/sinusoidal obstruction syndrome.

Footnotes: [a]These features may not always be present. [b]Hepatomegaly and/or ascites. [c]Reversal of portal venous flow. [d]While not recommended, if conducted, this can be diagnostic independent of any other findings.

References: 1. Coppell JA, et al. *Biol Blood Marrow Transplant*. 2010;16(2):157-168. **2.** Corbacioglu S, et al. *Bone Marrow Transplant*. 2018;53(2):138-145. **3.** Corbacioglu S, et al. *Biol Bone Marrow Transplant*. 2019;25(7):1271-1280. **4.** Hildebrandt GC, Chao N. *Br J Haematol*. 2020;190(4):508-519. **5.** Carreras E. *Br J Haematol*. 2015;168(4):481-491. **6.** Myers KC, et al. *Biol Blood Marrow Transplant*. 2015;21(2):379-381. **7.** Mahadeo KM, et al. *Lancet Haematol*. 2020;7(1):e61-e72. **8.** Cairo MS, et al. *Br J Haematol*. 2020;190(6):822-836. **9.** Corbacioglu S, et al. *Biol Blood Marrow Transplant*. 2020;26(7):1342-1349. **10.** Naples JC, et al. *Bone Marrow Transplant*. 2016;51(1):135-137. **11.** Kernan NA, et al. *Br J Haematol*. 2018;181(6):816-827. **12.** Jones RJ, et al. *Transplantation*. 1987;44(6):778-783. **13.** McDonald GB, et al. *Ann Intern Med*. 1993;118(4):255-267. **14.** Mohty M, et al. *Bone Marrow Transplant*. 2023;58(7):749-754.

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