

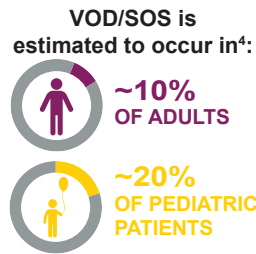
VOD/SOS Diagnostic Criteria OVERVIEW

Diagnostic criteria for veno-occlusive disease/sinusoidal obstruction syndrome (VOD/SOS) are continuously revised to allow for earlier detection to improve patient outcomes.

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

VOD/SOS is a potentially life-threatening complication following HCT

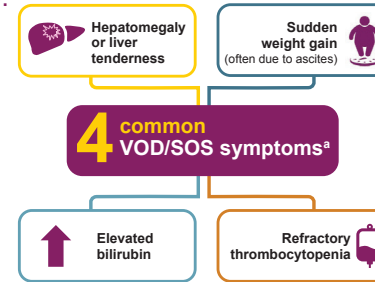
- A **>80% mortality rate** is associated with the most severe forms of the disease¹⁻³
- Incidence varies by age, primary disease, conditioning regimen, type of transplant, underlying disease, and diagnostic criteria used^{3,4}



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

Clinical presentation of VOD/SOS may include⁴⁻⁸:

- Hepatomegaly
- Edema and ascites
- Weight gain
- Unexplained consumptive and transfusion-refractory thrombocytopenia
- Jaundice
- Abdominal discomfort and pain
- Elevated bilirubin
- Portal hypertension
- Decrease in velocity or reversal of flow via Doppler ultrasound (late clinical manifestation)



Limitations of classical VOD/SOS diagnostic criteria may exclude some VOD/SOS patients

Classical criteria⁸⁻¹⁰:

- Only recognize VOD/SOS up to Day 21 post-HCT
- Require the presence of hyperbilirubinemia (Baltimore criteria only)⁹

Late-onset VOD/SOS (beyond Day 21 post-HCT) has been reported to occur in:



Classical criteria for VOD/SOS diagnosis include the Baltimore and Modified Seattle criteria

Baltimore criteria (1987)⁹

Liver dysfunction developing by Day 21 with hyperbilirubinemia (≥ 2 mg/dL), *plus* at least 2 of the following:

- Ascites
- Hepatomegaly (usually painful)
- Weight gain $\geq 5\%$ over baseline

Modified Seattle criteria (1993)¹⁰

Incidence of ≥ 2 events within 20 days of HCT:

- Hyperbilirubinemia (> 2 mg/dL)
- Hepatomegaly or right upper quadrant pain of hepatic origin
- Sudden weight gain due to fluid accumulation ($> 2\%$ weight gain)

Diagnostic criteria for VOD/SOS are continuously revised to allow for earlier detection to improve patient outcomes

	Baltimore ⁹ 1987	Modified Seattle ¹⁰ 1993	EBMT criteria ¹³ 2023	EBMT ⁴ 2018	Mahadeo ⁷ 2019	Cairo/Cooke criteria ⁸ 2020
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 ^c			✓	✓	✓	✓
Includes Doppler ultrasound imaging ^d			✓ (probable VOD/SOS)		Not recommended	✓
Hepatic wedge pressure			✓		Not recommended	✓ ^e
Biopsy			✓		Not recommended	✓ ^e

Abbreviations: EBMT, European Society for Blood and Marrow Transplantation; HCT, hematopoietic cell transplantation; VOD/SOS, veno-occlusive disease/sinusoidal obstruction syndrome.

Footnotes: ^aThese features may not always be present. ^bThis was addressed, in part, by the Modified Seattle criteria. ^cHepatomegaly and/or ascites. ^dReversal of portal venous flow.

^eWhile not recommended, if conducted, this can be diagnostic independent of any other findings.

References: 1. Mohty M, et al. *Bone Marrow Transplant*. 2020;55(3):485-495. 2. Mohty M, et al. *Bone Marrow Transplant*. 2015;50(6):781-789. 3. Coppell JA, et al. *Biol Blood Marrow Transplant*. 2010;16(2):157-168. 4. Corbacioglu S, et al. *Bone Marrow Transplant*. 2018;53(2):138-145. 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. Jones RJ, et al. *Transplant*. 1987;44(6):778-783. 10. McDonald GB, et al. *Ann Intern Med*. 1993;118(4):255-267. 11. Kernan NA, et al. *Br J Haematol*. 2018;181(6):816-827. 12. Corbacioglu S, et al. *Biol Blood Marrow Transplant*. 2020;26(7):1342-1349. 13. Mohty M, et al. *Bone Marrow Transplant*. 2023;58(7):749-754.