

SEE THE SIGNS BEFORE VOD ERUPTS

Vigilant monitoring is important regardless of risk factors, as VOD can occur in any patient following HSCT

FIRST 21 DAYS ARE CRITICAL TO VOD DETECTION¹⁻³



ALTHOUGH VOD GENERALLY EMERGES WITHIN THE FIRST 21 DAYS POST HSCT, IT **CAN** OCCUR LATER^{2,4,5}

Historically, the Baltimore and modified Seattle criteria have been used for diagnosis of VOD, but newer criteria have been published to address historical limitations^{2,4,7,8}

CAIRO/COOKE REVISED CRITERIA

Diagnostic criteria for VOD in children and adults

ANY 2 OF THE FOLLOWING AFTER HSCT^{9,b}:

OR

ANY 1 OF THE FOLLOWING AFTER HSCT^{9,b}:

- Elevated bilirubin (≥ 2 mg/dL) or greater than upper institutional limits^c
- Unexpected weight gain ($\geq 5\%$ compared to baseline weight pre-HSCT)
- Excessive platelet transfusions consistent with refractory thrombocytopenia post HSCT
- Hepatomegaly for age or increased size over pre-HSCT
- Right upper quadrant pain
- Ascites confirmed by physical exam and/or imaging studies
- Reversal of portal venous flow (hepatofugal flow) by Doppler ultrasound

- Hepatic biopsy consistent with VOD
- Unexplained elevated portal venous wedge pressure

Though it is not recommended, a liver biopsy or direct portal wedge pressure measurements can be used when making a diagnosis of VOD, if necessary⁹

These proposed criteria have not been prospectively validated in clinical trials

With an **84%** overall mortality in VOD with multi-organ dysfunction, diagnosis can't wait^{6,a}
IF YOU SEE THE SIGNS OF VOD, DON'T DELAY AN EVALUATION

^aBased on 19 studies from a meta-analysis of 135 studies.

^bProbably or definitely secondary to VOD/SOS and not other etiologies.⁹

^cIn patients with an already elevated bilirubin prior to HSCT conditioning, this criterion should not be utilized in the diagnostic criteria.⁹

HSCT=hematopoietic stem-cell transplantation; VOD=veno-occlusive disease (also known as sinusoidal obstruction syndrome, or SOS).

EBMT CRITERIA FOR CHILDREN

EBMT diagnostic criteria for VOD in children, with implementation guidance

NO LIMITATION FOR TIME OF VOD ONSET

The presence of 2 or more of the following is required^{5,a}:

- Unexplained consumptive and transfusion-refractory thrombocytopenia^{b,c}
 - Otherwise unexplained weight gain on 3 consecutive days, despite the use of diuretics, or weight gain >5% above baseline value
 - Hepatomegaly above baseline value (best if confirmed by imaging)^{b,d}
 - Ascites above baseline value (best if confirmed by imaging)^{b,d}
 - Rising bilirubin from a baseline value on 3 consecutive days or bilirubin ≥ 2 mg/dL within 72 hours
- Mahadeo et al recommend use of a structured radiologic reporting template when there is clinical concern for VOD¹⁰

Mahadeo et al endorse pediatric and AYA criteria for VOD as proposed by EBMT and provide implementation guidance for standardization across centers¹⁰

EBMT CRITERIA FOR ADULTS

EBMT diagnostic criteria for VOD in adults

VOD THAT OCCURS ≤ 21 DAYS POST HSCT⁴

Baltimore criteria^e:

Presentation of bilirubin ≥ 2 mg/dL and at least 2 of the following:

- Painful hepatomegaly
- Weight gain (>5%)
- Ascites

LATE-ONSET VOD >21 DAYS POST HSCT⁴

Baltimore criteria^e beyond Day 21

OR histologically proven VOD

OR 2 or more of the following criteria must be present:

- Bilirubin ≥ 2 mg/dL (or $34 \mu\text{mol/L}$)
- Painful hepatomegaly
- Weight gain (>5%)
- Ascites

AND hemodynamic or/and ultrasound evidence of VOD (hepatomegaly, ascites, and decrease in velocity or reversal of portal flow)

These proposed criteria have not been prospectively validated in clinical trials

^aWith the exclusion of other potential differential diagnoses.

^bAdditional implementation guidance from Mahadeo et al is available for thrombocytopenia, hepatomegaly, and ascites.¹⁰

^c ≥ 1 weight-adjusted platelet substitution/day to maintain institutional transfusion guidelines.

^dSuggested: imaging (US, CT, or MRI) immediately before HSCT to determine baseline value for both hepatomegaly and ascites.

^eDefined as classical VOD in EBMT criteria.

AYA=adolescent and young adult; CT=computed tomography; EBMT=European Society for Blood and Marrow Transplantation; MRI=magnetic resonance imaging; US=ultrasonography.

To learn more about identifying and diagnosing VOD visit [KNOWVODPRO.COM](https://www.knowvodpro.com)

TO LEARN MORE ABOUT IDENTIFYING AND DIAGNOSING VOD VISIT [KNOWVODPRO.COM](https://www.knowvodpro.com)



Scan here to request your VOD Identification
and Diagnosis Checklist



References: **1.** Carreras E, Díaz-Beyá M, Rosiñol L, et al. The incidence of veno-occlusive disease following allogeneic hematopoietic stem cell transplantation has diminished and the outcome improved over the last decade. *Biol Blood Marrow Transplant.* 2011;17(11):1713-1720. **2.** Carreras E. Early complications after HSCT. In: Apperley J, Carreras E, Gluckman E, et al, eds. *The EBMT Handbook.* 6th ed. Paris, France: European School of Haematology; 2012:176-195. **3.** Tsigotis PD, Resnick IB, Avni B, et al. Incidence and risk factors for moderate-to-severe veno-occlusive disease of the liver after allogeneic stem cell transplantation using a reduced intensity conditioning regimen. *Bone Marrow Transplant.* 2014;49(11):1389-1392. **4.** Mohty M, Malard F, Abecassis M, et al. Revised diagnosis and severity criteria for sinusoidal obstruction syndrome/veno-occlusive disease in adult patients: a new classification from the European Society for Blood and Marrow Transplantation. *Bone Marrow Transplant.* 2016;51(7):906-912. **5.** Corbacioglu S, Carreras E, Ansari M, et al. Diagnosis and severity criteria for sinusoidal obstruction syndrome/veno-occlusive disease in pediatric patients: a new classification from the European Society for Blood and Marrow Transplantation. *Bone Marrow Transplant.* 2018;53(2):138-145. **6.** Coppell JA, Richardson PG, Soiffer R, et al. Hepatic veno-occlusive disease following stem cell transplantation: incidence, clinical course, and outcome. *Biol Blood Marrow Transplant.* 2010;16(2):157-168. **7.** Jones RJ, Lee KS, Beschorner WE, et al. Venooclusive disease of the liver following bone marrow transplantation. *Transplantation.* 1987;44(6):778-783. **8.** McDonald GB, Sharma P, Matthews DE, et al. Venooclusive disease of the liver after bone marrow transplantation: diagnosis, incidence, and predisposing factors. *Hepatology.* 1984;4(1):116-122. **9.** Cairo MS, Cooke KR, Lazarus HM, et al. Modified diagnostic criteria, grading classification and newly elucidated pathophysiology of hepatic SOS/VOD after haematopoietic cell transplantation. *Br J Haematol.* 2020;190(6):822-836. **10.** Mahadeo KM, Bajwa R, Abdel-Azim H, et al; Pediatric Acute Lung Injury and Sepsis Investigators (PALISI) Network; Pediatric Diseases Working Party of the European Society for Blood and Marrow Transplantation. Diagnosis, grading, and treatment recommendations for children, adolescents, and young adults with sinusoidal obstructive syndrome: an international expert position statement. *Lancet Haematol.* 2020;7(1):e61-e72.



**Devastating—no matter
how you look at it.**

VOD Identification and Diagnosis Checklist

Patient's initials: _____ Date: _____

Consider preexisting VOD risk factors (check all that apply to patient)

Patient- and disease-related risk factors	Pediatric-specific patient- and disease-related risk factors
<input type="checkbox"/> Advanced disease (beyond second CR or relapse/refractory) <input type="checkbox"/> Female receiving norethindrone <input type="checkbox"/> Older age (in adult patients) <input type="checkbox"/> Karnofsky score <90% <input type="checkbox"/> Adult metabolic syndrome <input type="checkbox"/> Thalassemia <input type="checkbox"/> Deficit of AT III or t-PA	<input type="checkbox"/> Low weight <input type="checkbox"/> Age <2 years <input type="checkbox"/> Lansky score <90 History of any of the following diseases: <input type="checkbox"/> Osteopetrosis <input type="checkbox"/> High-dose auto-HSCT for neuroblastoma <input type="checkbox"/> Hemophagocytic lymphohistiocytosis (HLH) <input type="checkbox"/> Adrenoleukodystrophy (ALD) <input type="checkbox"/> Juvenile myelomonocytic leukemia (JMML) <input type="checkbox"/> Hemoglobinopathies <input type="checkbox"/> Sickle cell disease <input type="checkbox"/> Thalassemia
Hepatic-related risk factors	Transplant-related risk factors
<input type="checkbox"/> Previous use of gemtuzumab ozogamicin or inotuzumab ozogamicin <input type="checkbox"/> Transaminase levels >2.5 ULN <input type="checkbox"/> Serum bilirubin >1.5 x ULN <input type="checkbox"/> Cirrhosis <input type="checkbox"/> Hepatic fibrosis <input type="checkbox"/> Active viral hepatitis <input type="checkbox"/> Abdominal or hepatic irradiation <input type="checkbox"/> Use of hepatotoxic drugs <input type="checkbox"/> Iron overload	<input type="checkbox"/> Allogeneic HSCT <input type="checkbox"/> Second HSCT <input type="checkbox"/> Myeloablative conditioning regimen <input type="checkbox"/> Non-T-cell-depleted graft <input type="checkbox"/> Unrelated donor/HLA mismatch <input type="checkbox"/> Oral or high-dose BU-based conditioning regimen <input type="checkbox"/> High-dose TBI-based conditioning regimen

Vigilant monitoring is important regardless of risk factors, as VOD can occur in any patient following HSCT

Although VOD generally emerges within the first 21 days post HSCT, it can occur later. Consider daily monitoring at the start of the conditioning regimen.

Date conditioning regimen was started: _____ Date of HSCT: _____

Has VOD monitoring started? Date that monitoring started: _____

Daily monitoring (check appropriate box after monitoring for each of the following 10 signs/symptoms is completed)

1 Platelet-refractory thrombocytopenia	Day + ____	Day + ____	Day + ____	Day + ____	Day + ____	Day + ____	Day + ____
Is the patient receiving excessive platelet transfusions consistent with refractory thrombocytopenia?	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes

2 Weight gain	Day + ____	Day + ____	Day + ____	Day + ____	Day + ____	Day + ____	Day + ____
Patient's baseline weight _____							
Patient's weight	____ AM ____ PM	____ AM ____ PM	____ AM ____ PM	____ AM ____ PM	____ AM ____ PM	____ AM ____ PM	____ AM ____ PM
Is weight gain >5% compared to baseline weight pre-HSCT OR has patient gained weight on 3 consecutive days despite use of diuretics?	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes

3 Edema and ascites*	Day + ____	Day + ____	Day + ____	Day + ____	Day + ____	Day + ____	Day + ____
Is edema present?	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes
Is abdominal distension/ascites present?	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes
Is patient experiencing shortness of breath?	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes
Has a change from baseline been confirmed by ultrasound or physical exam?	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes

*Consider monitoring during the AM and PM.

AT III=antithrombin III; BU=busulfan; CR=complete remission; HLA=human leukocyte antigen; HSCT=hematopoietic stem-cell transplantation; TBI=total body irradiation; t-PA=tissue plasminogen activator; ULN=upper limit of normal; VOD=veno-occlusive disease (also known as sinusoidal obstruction syndrome, or SOS).

4 Abdominal discomfort/pain*	Day + ____	Day + ____	Day + ____	Day + ____	Day + ____	Day + ____	Day + ____
Is patient experiencing abdominal discomfort/pain?	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes
Is pain localized to right upper quadrant?	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes
Is there liver tenderness?	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes

5 Hepatomegaly*	Day + ____	Day + ____	Day + ____	Day + ____	Day + ____	Day + ____	Day + ____
Is hepatomegaly present?	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes

6 Jaundice*	Day + ____	Day + ____	Day + ____	Day + ____	Day + ____	Day + ____	Day + ____
Have bilirubin levels increased from baseline?	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes

7 Liver function	Day + ____	Day + ____	Day + ____	Day + ____	Day + ____	Day + ____	Day + ____
Are any liver function tests elevated?	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes
Alkaline phosphatase	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes
Aspartate aminotransferase (AST)	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes
Alanine aminotransferase (ALT)	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes
Gamma-glutamyl transpeptidase (GGT)	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes

8 Fluid retention*	Day + ____	Day + ____	Day + ____	Day + ____	Day + ____	Day + ____	Day + ____
Is fluid retention present?	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes

9 Renal function	Day + ____	Day + ____	Day + ____	Day + ____	Day + ____	Day + ____	Day + ____
Has urinary output decreased?	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes
Is serum creatinine elevated relative to the start of conditioning regimen?	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes
Does patient require dialysis?	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes
Is glomerular filtration below normal?	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes

10 Pulmonary function	Day + ____	Day + ____	Day + ____	Day + ____	Day + ____	Day + ____	Day + ____
Does patient have blood oxygen saturation below normal?	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes
Does patient require oxygen support?	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes
Does patient require mechanical ventilation?	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes

*Consider monitoring during the AM and PM.

Patient Health Information: For healthcare provider use only and not to be returned to Jazz or any third parties. Documentation may be added to patient medical record.