

78014_Auto_Edited.docx

Name of Journal: *World Journal of Clinical Cases*

Manuscript NO: 78014

Manuscript Type: MINIREVIEWS

Early diagnostic value of liver stiffness measurement in hepatic sinusoidal obstruction syndrome induced by hematopoietic stem cell transplantation

Tan YW *et al.* LSM in HSCT-SOS

You-Wen Tan, Yi-Chun Shi

Abstract

Hematopoietic stem cell transplantation (HSCT)-sinusoidal obstruction syndrome (SOS), also known as veno-occlusive disease, is a clinical syndrome characterized by symptoms, such as right upper quadrant pain, jaundice, fluid retention, and hepatomegaly, and is caused by pre-treatment-related hepatotoxicity during the early stages after HSCT. Clinical diagnosis of HSCT-SOS is based on the revised Seattle or Baltimore standards. The revised standard by the European Society for Bone Marrow Transplantation in 2016 has good practicability and can be used in combination with these two standards. Eight studies have shown the value of liver stiffness measurement (LSM) in the early diagnosis of HSCT-SOS. Four studies investigated LSM specificity and sensitivity for the early diagnosis of HSCT-SOS. LSM can distinguish SOS from other post-HSCT complications, enabling a clear differential diagnosis. It has been shown that median LSM of patients with SOS is significantly higher than that of patients with other treatment-related liver complications (*e.g.*, acute cholecystitis, cholangitis, antifungal drug-related liver injury, liver graft-versus-host disease, isolated liver biochemical changes, and fulminant Epstein Barr virus related hepatitis reactivation). Therefore, the above data confirmed the utility of LSM and strongly suggested that LSM improves the positive predictive value of the SOS diagnostic clinical score after allogeneic HSCT. Early diagnosis of SOS is beneficial in preventing severe HSCT complications.

Key Words: Hematopoietic stem cell transplantation; Sinusoidal obstruction syndrome; Liver stiffness measurement; Stem cell

Tan YW, Shi YC. Early diagnostic value of liver stiffness measurement in hepatic sinusoidal obstruction syndrome induced by hematopoietic stem cell transplantation. *World J Clin Cases* 2022; In press

Core Tip: Clinical diagnosis of hematopoietic stem cell transplantation (HSCT)-sinusoidal obstruction syndrome (SOS) is based on the revised Seattle or Baltimore

standards. Eight studies have shown the value of liver stiffness measurement (LSM) in the early diagnosis of HSCT-SOS. Four studies investigated the specificity and sensitivity of LSM for the early diagnosis of HSCT-SOS. Therefore, LSM can distinguish SOS from other post-HSCT complications, enabling a clear differential diagnosis. The early diagnosis of SOS is beneficial in preventing severe HSCT complications.

INTRODUCTION

10 Hepatic sinusoidal obstruction syndrome (HSOS), also known as hepatic veno-occlusive disease (VOD), is a hepatic vascular disease characterized by hepatic sinusoidal, hepatic venule, and interlobular venous endothelial cell injuries, leading to lumen stenosis or occlusion and eventually resulting in intrahepatic congestion, liver injury, and intrahepatic retrosinusoidal portal hypertension. Hepatic sinusoidal obstruction syndrome (SOS) manifests clinically as liver pain, jaundice, ascites, and hepatomegaly, and is a severe liver complication commonly observed in patients undergoing hematopoietic stem cell transplantation (HSCT)^[1].

DEFINITION AND EPIDEMIOLOGY

HSCT-SOS is a clinical syndrome characterized by symptoms, such as right upper quadrant pain, jaundice, fluid retention, and hepatomegaly, and is caused by pre-treatment-related hepatotoxicity in the early stages after HSCT. In the early stages, mortality rate of severe cases can be as high as 80%^[2-4]. In recent years, defibrotide and defibrinopolysaccharide are the only approved drugs for SOS treatment^[5,6]. The overall survival rates of patients with SOS at 100 d, 1 year, and 5 years after HSCT were 62%, 46%, and 27%, respectively, while those of patients without SOS were 92%, 77%, and 66% ($P < 0.001$), respectively with significant decreased in mortality rates^[7-9].

The incidence of SOS varies greatly in studies, owing to factors, such as differences in patient characteristics, pre-treatment schemes, transplantation center experience, and diagnostic criteria. A meta-analysis showed that in 135 studies conducted between June **3** 1979 and October 2007, the overall average incidence of SOS was 13.7% [95% confidence

interval (CI): 13.3%-14.1%]. The average incidence of SOS between 1979 and 1994 was significantly lower than that between 1994 and 2007 [11.5% (95%CI: 10.9%-12.1%) vs 14.6% (95%CI: 14.0%-15.2%); $P < 0.05$]^[10]. Overall, the incidence of autologous HSCT (auto-HSCT) was 3.1%-8.7% and 8.9%-14.0% in allogeneic HSCT (allo-HSCT)^[10-13]. The incidence of SOS is high in pediatric populations^[14,15]. SOS is common in young patients (1-2-year-olds) with lower body weight, primary hemophagocytic lymphohistiocytosis, adrenal leukodystrophy osteolithiasis, severe thalassemia, or neuroblastoma undergoing autologous HSCT^[16,17]. In recent years, the overall incidence and severity of this disease has decreased. However, the use of certain drugs, such as monoclonal antibodies (CD 33 and 22), raising the pre-treatment intensity, as well as secondary transplantation in these patients increases the risk to some extent. The severity of SOS ranges from remission within a few weeks to multiple organ failure and high mortality (> 80%). Therefore, a high index of suspicion along with early diagnosis and treatment is important.

Baixiaoan (1,4-bis[¹⁵methanesulfonyl-¹³y]butane) is a bifunctional alkylating compound. Over the past 20 years, baixiaoan has been widely used in combination with cyclophosphamide (CY) for the pre-treatment of HSCT. The therapeutic index of busulfan (BU) is very narrow, and acute toxicity may be related to the absorption and disposal of drugs and metabolites. Unstable gastrointestinal absorption can affect precise delivery of oral preparations, particularly in infants and young children. Nearly 40 years after oral preparation was approved, the formula for intravenous BU was approved. It has been reported that BU levels higher than 1500 $\mu\text{m}/\text{min}$ increase the risk of SOS, whereas low levels may lead to implantation failure or disease recurrence. Measuring individual plasma BU levels during oral or intravenous administration may provide necessary protection for monitoring drug disposal, thereby ensuring efficacy and preventing toxicity in patients receiving HSCT^[18].

Monitoring of therapeutic drug concentrations of BU began in 2000, and liver-supporting drugs, such as ursodeoxycholic acid and N-acetyl-L-cysteine (NAC) were used in 2002 and 2009, respectively. However, NAC is not routinely recommended for the treatment of venous occlusive disease^[19]. This prospective randomized study

included 160 patients. N-acetyl-L-cysteine showed no significant benefit in reducing post-HSCT hepatotoxicity^[20].

Busulfan and CY are commonly used as chemotherapeutic drugs for allogeneic and autologous HSCT^[21]. The BU-CY regimen is a commonly used HSCT pre-treatment regimen, but studies have found that administering CY immediately after BU treatment increases the active metabolites of CY^[22]. The interval between CY and BU administration negatively correlated with the incidence of SOS^[21]. A multicenter randomized controlled trial was designed by Seydoux *et al*^[23] who showed that a 24-h interval between BU and CY administration reduced the incidence of SOS. According to recently published randomized controlled trials and other retrospective studies, the CY-BU protocol is recommended instead of BU-CY^[24]. In a systematic evaluation of the efficacy and toxicity characteristics of busulfonamide-fludarabine (BU-flu) and BU-CY preparation program in patients undergoing allogeneic HSCT, patients in the BU-flu program had a lower risk of developing SOS and microbial record infections [risk ratio (RR), 0.34; 95% CI: 0.19-0.62; 8 trials: RR, 0.79; 95% CI: 0.64-0.97]^[24].

PATHOPHYSIOLOGY

The pathogenesis of SOS remains unclear. However, the central role of SOS pathogenesis is the loss of endothelial cell cohesion caused by sinusoidal endothelial injury^[25]. Gaps appear between endothelial cells, and red blood cells infiltrate the Disse space and aggregate followed by retrosinusoidal obstruction^[26]. There are many reasons for sinusoidal endothelial cell (SEC) injury, including pre-treatment regimen^[27], cytokines^[28], endogenous microbial products^[29], drugs [calcineurin inhibitor (CNI), monoclonal antibodies, and hematopoietic growth factor], heteroreactive T cells, mutations in glutathione (GSH) transferase-related genes, migration of endogenous microbial metabolites, hematopoietic implantation produced by tissue injury can also cause or aggravate secondary injury^[28,30-33], and the implantation process itself^[33]. Conditioning regimens play a crucial role in the pathogenesis, which highlights that the increased risk of SOS is associated with higher levels of cytotoxic drugs in the plasma, such as

metabolites of BU^[34] or CY^[35]. Chemotherapeutic drugs are metabolized by the cytochrome P450 complex to produce toxic metabolites, which are then transformed into nontoxic metabolites and eliminated by the GSH enzyme system^[36]. The central area of the hepatic lobule (hepatic acinus 3) is more vulnerable to injury, owing to the lack of GSH^[21,27,37]. This also explains the pathological basis of serious damage to the central area of the hepatocytes^[38,39]. Additionally, the GSH S-transferase M1 deletion genotype reduces the detoxification ability of the liver parenchyma and is prone to SOS^[40]. The reduced detoxification ability caused by an immature enzyme system can at least partially explain the high incidence of SOS.

After HSCT, increased levels of endothelial activation markers, such as endothelial procoagulant factors and adhesion molecules^[28], circulating endothelial cells^[41], endothelial progenitor cells^[42], and microparticles^[43] were found in the circulatory system, and these pathophysiological changes suggested that endothelial cells showed signs of damage in pro-coagulant and pro-inflammatory states. Nitric oxide deficiency is also a promoter of endothelial cell isolation. Nitric oxide deficiency leads to an increase in matrix metalloproteinase-9, which is associated with isolation of SOS-formed endothelial cells. Metalloproteinase-9 inhibitors completely prevents its occurrence *in vivo*^[44,45].

Damage to SEC leads to destruction of the endothelial cell barrier, loss of sinus wall integrity, infiltration of red blood cells into the Disse space, separation of endothelial cells, and obstruction of the hepatic sinus space^[46]. Additionally, an imbalance in the coagulation fibrinolysis system can cause microthrombosis, aggravate obstruction of the central lobular vein, and ultimately result in retrosinus portal hypertension^[47]. Central lobular necrosis, fibrosis, and liver failure may occur in severe cases. In view of the central role of endothelial cell injury in pathogenesis, some researchers have included SOS in the category of HSCT-related endothelial injury syndromes (Figure 1)^[48].

RISK FACTORS

Risk factors for SOS are divided into two categories: patient- and transplantation-related factors. The former mainly includes females (children)^[34,49], physical condition, pre-

transplant liver history, abnormal liver function, disease progression status, thalassemia, abdominal radiotherapy history, and use of targeted cancer drugs, such as gemtuzumab ozogamicin, or inotuzumab ozogamicin (IO)^[50-52]. Transplantation-related risk factors include allo-HSCT *vs* auto-HSCT^[53]. Some clinical observations have shown that allo-reactivity plays a role in SOS. Compared to autologous HSCT, the incidence of SOS was higher after allogeneic transplantation and in patients receiving mismatched unrelated donor transplantation. These observations are supported by experimental models in which endothelial cells are the targets of allo-reactive T cells^[54]. Human leukocyte antigen incompatibility, haplotype transplantation, secondary transplantation, graft non-T cell removal, pre-treatment with BU or total-body radiotherapy (TBI), fludarabine, and CNI combined with sirolimus to prevent graft-versus-host disease (GVHD)^[55-57].

In the past 7-10 years, studies assessing the risk factors of SOS in large HSCT recipients were inconsistent with previous data, which revealed potential risk factors that had not been noticed before^[1,11,14,58-60]. In many of these studies, the total number of patients ranged between 75 and 5072, and the incidence of SOS ranged between 2.0% [the lowest incidence diagnosed ¹ according to the European Society for Bone Marrow Transplantation (EBMT) criteria] and 30.7%. After multivariate analysis, ² transplantation-related factors associated with an increased risk of SOS in adult HSCT recipients included the use of horse antithymocyte globulin^[60], oral and intravenous serum level-adjusted administration of BU (adults and adolescents)^[60], myeloablative pre-treatment (based on whole-body irradiation and BU), and two or more HSCTs^[58]. Busulfan thiotepa conditioning^[60] was used in adults with SOS who needed at least analgesic or diuretic drug treatment, and the ² serum tacrolimus level increased (above the target range of 5-10 ng/mL).

Liver disease is a major risk factor of SOS. For example, abnormal liver function indicators, or the existence of chronic liver disease (cirrhosis, chronic viral hepatitis, *etc.*)^[13,61]. These liver diseases can be completely asymptomatic, but are risk factors for SOS during previous hepatotoxic treatment with gituzumab and ozone histamine,

including iron overload. Identifying risk factors or building a forward-looking risk assessment model is helpful for early prediction and prevention of SOS^[62].

DIAGNOSIS AND GRADING OF SOS

Typical SOS usually occurs within 21 d after HSCT, whereas delayed SOS can occur after 21 d. The disease onset can be insidious or rapidly progressing. The main clinical manifestations include right upper abdominal tenderness, jaundice, painful hepatomegaly, ascites, weight gain, and edema. Laboratory examination revealed hyperbilirubinemia, elevated transaminase levels, and unexplained thrombocytopenia. Imaging (Doppler ultrasound is recommended) can detect hepatomegaly, ascites, gallbladder wall edema, slow or reverse flow of portal venous blood, and portal vein widening^[63,64]. The mild symptoms of the syndrome are self-limiting. Patients with severe disease may exhibit multiple organ failure in the kidneys, lungs, and heart with a poor prognosis. Ultrasound can easily detect ascites, hepatomegaly, slow or narrow hepatic venous flow, and thickening of the gallbladder wall; although non-specifically, it may be helpful in the diagnosis of SOS^[19]. Precise techniques to confirm the diagnosis of SOS, such as measurement of hepatic venous gradient pressure through the jugular vein and liver biopsy, are invasive and difficult to perform in routine practice.

Currently, there are no biological markers of predictive or diagnostic significance. Bearman *et al*^[65] established a model to predict the risk of SOS. However, this model is limited to myeloablative conditioning (TBI, CY, BU, or etoposide). Therefore, its utility is limited. Plasminogen activator inhibitor-1 and other hemagglutination markers have a predictive value. Markers of endothelial cell injury and inflammation are still being explored^[34,66-68], and routine detection is not yet recommended^[69].

The diagnosis of SOS is based on the presence of clinical manifestations within the first three weeks after HSCT and is not attributable to any other possible cause. However, neither set of criteria considers the late onset of SOS after 21 or 40-50 d. Additionally, the use of these criteria may be problematic when only edema and weight gain are present.

The clinical diagnosis of HSCT-SOS was based on the revised Seattle^[61] or Baltimore standards^[70]. The SOS standard revised by the EBMT in 2016 has good practicability^[3], and can be used in conjunction with these two standards. The diagnostic criteria used are listed in Table 1.

The EBMT diagnostic criteria for SOS in children mention that the onset does not have an age limit and is based on the occurrence of at least two of the following manifestations^[15]: (1) Unexplained consumptive thrombocytopenia and ineffective infusion; (2) Unexplained body weight gain for three consecutive days, or weight gain > 5% of the baseline value, irrespective of the use of diuretics; (3) Liver enlargement above the baseline (confirmation using imaging is recommended); (4) Ascites above the baseline (confirmation using is recommended); and (5) Higher bilirubin levels than the baseline value for three consecutive days or values ≥ 2 mg/dL within 72 h. It is worth noting that 16%-20% of children with SOS have late onset, and nearly 30% have no jaundice^[71,72].

Severity classification according to the EBMT classification standard is presented in Table 2.

VALUE OF LIVER STIFFNESS MEASUREMENT DURING EARLY HSCT-SOS DIAGNOSIS

The above diagnostic norms and standards depend on clinical symptoms, biochemical findings, and imaging data. However, acquiring all these data can take weeks, which could delay diagnosis and result in a poor prognosis. Liver biopsy is the gold standard; however, its invasive nature precludes its use in severe cases, which along with the risk of hemorrhage in severe thrombocytopenia, effectively limits its usability. Several non-invasive models have been developed for the diagnosis of SOS using clinical indicators^[1,73]; however, it is still difficult to promote its application owing to its limitations^[74]; less than half of those who met the SOS criteria were definitively diagnosed. The subjective difference in ultrasound examination is related to the operator's identification technology, especially in the early stage of SOS, and it is difficult to distinguish specific ultrasonic changes from other liver lesions. Elastography has been

widely used to determine liver hardness in recent years, and it can effectively detect liver fibrosis and cirrhosis^[75,76]. Liver stiffness measurement (LSM) includes transient elastic imaging, point shear waves with acoustic radiation force impulse (ARFI), and two-dimensional real-time shear wave elastography (2D-SWE)^[77,78].

Value of ARFI and SWE in early diagnosis of HSCT-SOS

The elastography techniques used in clinical LSM mainly include TE, ARFI, and strain elastography (SE). Acoustic radiation force impulse technology includes point SWE (P-SWE) and 2D-SWE. Fontanilla *et al*^[79] reported the use of quantitative ARFI elastography in two cases of HSCT-SOS, and described that when SOS was accurately diagnosed by ultrasound, acoustic radiation force pulse elastography showed medium and high shear wave velocities (case one, 2.75 m/s and case two, 2.58 m/s), which returned to normal after specific treatment. Therefore, ARFI elastography provides quantitative information to help diagnose this condition and monitor the treatment responses. In one of the above cases, contrast-enhanced ultrasound showed patch enhancement of the liver, which was related to high-speed patch distribution on ARFI elastography, whereas in the second case, nonhomogeneous images on contrast-enhanced computed tomography were noted. During the follow-up period after a specific treatment, the contrast-enhanced mode gradually returned to normal, demonstrating the role of ARFI elastography in early diagnosis and clinical follow-up of the disease.

Traditional ultrasonography has poor sensitivity and specificity. Two-dimensional-SWE is an ultrasound-based technique for staging liver fibrosis by measuring the liver stiffness. At present, it is widely used to evaluate fibrosis in various liver diseases^[80-83]. The early diagnostic value of the SOS was unexpected. This single-center prospective cohort study evaluated 25 patients who underwent HCT. Five patients developed an SOS. Patients were evaluated using 2D-SWE at three predetermined time points. On day +5 of HSCT, SWE velocity in patients with SOS increased by 0.25 ± 0.21 m/s, while that in patients without SOS increased by 0.02 ± 0.18 ($P = 0.020$). On day +14, the SWE velocity increased significantly by $0.91 \text{ m/s} \pm 1.14 \text{ m/s}$ in patients with SOS compared with 0.03

⁴ m/s \pm 0.23 m/s in patients without SOS ($P = 0.010$). The SWE diagnosis was made 9 and 11 d before the clinical and routine ultrasound diagnoses, respectively. Patients with SOS had increased liver stiffness compared with those without SOS. Thus, SWE changes occur before other imaging and clinical findings of SOS^[84].

Early diagnostic value of FibroScan LSM for SOS

Inotuzumab ozogamicin is an effective treatment for acute lymphoblastic leukemia (ALL) and is a risk factor for SOS. Ravaoli *et al*^[85] observed 21 patients with ALL during their treatment period and 17.2 mo of follow-up. They observed a significant increase ($P < 0.001$) in median LSM from 6.7 kPa to 9.5 kPa after the IO cycle and > 8 kPa at the end of the second IO cycle in a dose-dependent kinetic model. Two patients developed SOS, and the LSM exceeded 21 kPa. Another prospective single-center study observed 78 patients receiving HSCT, four of whom developed SOS and found that LSM had good early diagnostic value^[86]. It should be noted that increase in LSM after HSCT occurred 2-12 d earlier than that before HSCT. Compared to previous measurements, the increase in LSM value was significantly correlated with the diagnosis of SOS. ¹ In a prospective study of adult HSCT recipients, the increase in LSM value after HSCT was assessed using TE, and identified as an accurate predictor of SOS development for the first time. Colecchia *et al*^[87] observed 22 children who underwent HSCT, for whom LSM was performed between 7-10 (T1), 17-20 (T2), and 27-30 (T3) d after the procedure. They reported that there were four individuals who developed SOS for whom LSM values were 4-6 kPa at baseline level, which sharply increased to > 12 -20 kPa at T2. Alterations in LSM values were observed 3-6 d before the SOS diagnosis. Transient elastography-FibroScan quantitatively evaluates liver fibrosis by measuring LSM using a shear wave technique^[88]. Its non-invasive diagnostic efficacy for liver fibrosis has been verified in a variety of causes of chronic liver disease^[85,89].

The high LSM values reported in HSOS are not the result of increased liver hardness due to liver fibrosis and cirrhosis, but the result of liver congestion caused by congestion in the hepatic sinuses, occlusion of hepatic venules, and obstruction of hepatic venous

reflux following damage to the hepatic SEC. Increase in LSM has been proven to be caused by inflammation, cholestasis, and congestion^[90]. Ravaioli *et al*^[85] found that LSM significantly increased in patients with ALL undergoing IO treatment. This observed trend was difficult to explain because liver fibrosis occurred in these patients. Thus, an inflammatory injury to the liver may be a plausible explanation.

1 LSMs have shown that the median LSM of patients with SOS is significantly higher than that of patients with other treatment-related liver complications (e.g., acute cholecystitis, cholangitis, antifungal drug-related liver injury, liver GVHD, isolated liver biochemical changes, and fulminant Epstein-Barr virus-related hepatitis reactivation)^[85,91].

Sensitivity and specificity of LSM in diagnosing HSCT-SOS

Four studies investigated the specificity and sensitivity of early diagnosis of HSCT-SOS using LSM (details are shown in Table 3)^[84,86,92,93]. Two studies used SWE to detect LSM. In a prospective study, 5 of 25 HSCT patients developed SOS with an area under the curve (AUC) of 0.7762, sensitivity of 80%, and specificity of 67%^[84]. Another retrospective study included 161 adult patients who underwent HCT for > 2 years, and 146 patients were analyzed. The ultrasound and 2D-SWE measurements were performed +7 and +14 d after the HCT. Within the first 100 days of the allo-HSCT, 81 patients (55%) developed liver injury. Baseline 2D-SWE could not predict the overall occurrence of liver abnormalities. Six patients were diagnosed with SOS, and we found a significant increase in 2D-SWE on day 14 (AUC = 0.84), with a 2D-SWE measurement greater than 8.1 kPa, increasing sensitivity (75%), specificity (99%), and positive predictive value (60%) in the Seattle criteria. Therefore, it is considered a promising and reproducible method for early diagnosis of SOS^[93].

1 In two other prospective studies, a FibroScan was used to detect LSM. Seventy-eight adult patients with indications for allogeneic HSCT were prospectively enrolled. LSM was performed before HSCT and +9/10, +15/17, and +22/24 d after HSCT. Four patients (5.1%) developed SOS during the study period, and the median duration of SOS after the

HSCT was +17 d. A sudden increase in LSM was observed in all patients with SOS compared with the values previously evaluated and those before HSCT. The LSM increased 2–12 days before the occurrence of clinical SOS. Compared to the pre-HSCT evaluation, the SOS diagnostic performance of LSM showed that the AUC of the patients was 0.997 (sensitivity, 75%; specificity, 98.7%). After a successful SOS-specific treatment, the LSM gradually decreased. Interestingly, except for SOS, there was no significant increase in LSM in the patients with hepatobiliary complications. The measurement of liver stiffness is considered a promising method for early diagnosis^[86].

Another prospective study included 31 adult patients with two or more LSM values. SOS occurred in 2 of the 31 patients (6.4%) who received allogeneic HSCT. Very high LSM values were detected in patients with SOS with an AUC of 0.569, sensitivity of 100%, and specificity of 55.17%. Early and specific VOD/SOS processing can improve LSM values and other related characteristics^[92].

CONCLUSION

The current HSCT-SOS diagnosis depends on the revised EBMT, Seattle, or Baltimore criteria, critically aiding which play an important role in the diagnosis and treatment of such potential serious complications of HSCT, but its though a serious disadvantage lies in its inaccuracy (inability) of an is that it is difficult to diagnose early diagnosis. As a non-invasive detection technology, LSM can detect abnormalities before clinical symptoms, which providing the possibility for an early diagnosis of SOS. Limitations of the current study is still a small sample study include its small size, thus further multi-center, prospective, large-sample studies are needed to verify our findings.

10%

SIMILARITY INDEX

PRIMARY SOURCES

- 1 Antonio Colecchia, Federico Ravaioli, Mariarosaria Sessa, Vanessa Alemanni Luigina et al. "Liver Stiffness Measurement Allows Early Diagnosis of Venous Occlusive Disease/Sinusoidal Obstruction Syndrome in Adult Patients Who Undergo Hematopoietic Stem Cell Transplantation: Results from a Monocentric Prospective Study", *Biology of Blood and Marrow Transplantation*, 2019
Crossref 83 words — 2%
- 2 Selim Corbacioglu, Elias J. Jabbour, Mohamad Mohty. "Risk Factors for Development of and Progression of Hepatic Venous Occlusive Disease/Sinusoidal Obstruction Syndrome", *Biology of Blood and Marrow Transplantation*, 2019
Crossref 42 words — 1%
- 3 www.science.gov
Internet 40 words — 1%
- 4 scholarlyexchange.childrensmemory.org
Internet 39 words — 1%
- 5 link.springer.com
Internet 27 words — 1%
- 6 Sıdıka Gülkan Özkan, Cengiz Pata, Alphan Şekuri, Yasemin Çınar, Hasan Atilla Özkan. "Transient elastography of liver: Could it be a guide for diagnosis and management strategy in hepatic venous occlusive disease 22 words — 1%

(sinusoidal obstruction syndrome)?", Transfusion and Apheresis Science, 2022

Crossref

7 Teresa Fontanilla, Concepción González Hernando, Juan Cristóbal Valenzuela Claros, Guiomar Bautista et al. "Acoustic Radiation Force Impulse Elastography and Contrast-Enhanced Sonography of Sinusoidal Obstructive Syndrome (Veno-occlusive Disease)", Journal of Ultrasound in Medicine, 2011

21 words — 1%

Crossref

8 www.nature.com

Internet

21 words — 1%

9 pubmed.ncbi.nlm.nih.gov

Internet

20 words — < 1%

10 assets.researchsquare.com

Internet

19 words — < 1%

11 Dan Lv, Zepu Wang, Shuai Ji, Xiaoxi Wang, Huiqing Hou. "Plasma Levels of Homocysteine is Associated with Liver Fibrosis in Health Check-Up Population", International Journal of General Medicine, 2021

16 words — < 1%

Crossref

12 www.ncbi.nlm.nih.gov

Internet

16 words — < 1%

13 N. Krivoy, E. Hoffer, A. Tabak, R. Elhasid, M. Weyl Ben Arush, J. Stein, I. Yaniv, J. M. Rowe. "THERAPEUTIC MONITORING OF BUSULFAN IN PEDIATRIC BONE MARROW TRANSPLANTATION", Pediatric Hematology and Oncology, 2009

13 words — < 1%

Crossref

14 Daniele Zama, Gianluca Bossù, Federico Ravaioli, Riccardo Masetti, Arcangelo Prete, Davide Festi, Andrea Pession. "Longitudinal evaluation of liver stiffness in three pediatric patients with veno - occlusive disease", *Pediatric Transplantation*, 2019

11 words — < 1%

Crossref

15 Brett Glotzbecker, Christine Duncan, Edwin Alyea, Bonnie Campbell, Robert Soiffer. "Important Drug Interactions in Hematopoietic Stem Cell Transplantation: What Every Physician Should Know", *Biology of Blood and Marrow Transplantation*, 2012

10 words — < 1%

Crossref

16 haematologica.org
Internet

10 words — < 1%

EXCLUDE QUOTES ON
EXCLUDE BIBLIOGRAPHY ON

EXCLUDE SOURCES < 10 WORDS
EXCLUDE MATCHES < 10 WORDS