

2020

Validation of utilizing the pediatric Sequential Organ Failure Assessment scoring system in patients with congenital heart disease

<https://hdl.handle.net/2144/41152>

"Downloaded from OpenBU. Boston University's institutional repository."

BOSTON UNIVERSITY
SCHOOL OF MEDICINE

Thesis

**VALIDATION OF UTILIZING THE PEDIATRIC
SEQUENTIAL ORGAN FAILURE ASSESSMENT SCORING SYSTEM
IN PATIENTS WITH CONGENITAL HEART DISEASE**

by

NEHA NARAYANAN

B.A., Rutgers University, 2018

Submitted in partial fulfillment of the
requirements for the degree of
Master of Science

2020

Approved by

First Reader

Louis C. Gerstenfeld, Ph.D.
Professor of Pulmonary, Allergy, Sleep & Critical Care Medicine

Second Reader

Dima Daaboul, M.D.
Instructor of Anesthesiology

ACKNOWLEDGMENTS

I would like to thank Dr. Koichi Yuki and all members of the Yuki lab for all of their support. Thank you to my lab partner Zachary Abbate for collaborating on data collection. I would also like to thank my thesis readers, Dr. Louis Gerstenfeld and Dr. Dima Daaboul for providing their time and guidance. Lastly, I would like to thank Dr. Gwynneth Offner for advising and supporting me throughout these two years at Boston University.

**VALIDATION OF UTILIZING THE PEDIATRIC
SEQUENTIAL ORGAN FAILURE ASSESSMENT SCORING SYSTEM
IN PATIENTS WITH CONGENITAL HEART DISEASE**

NEHA NARAYANAN

ABSTRACT

The Sequential Organ Failure Assessment has been used to track a patient's status for over two decades. It essentially provides a numeric value to quantify the severity of organ dysfunction, most commonly used in sepsis (1). This assessment system was primarily developed for adult patients. However, this threshold cannot be applied in pediatric patients as organ function matures over time. A team of researchers published a paper in 2017 describing the SOFA scale adjusted for pediatric populations (Pediatric Sequential Organ Failure Assessment; pSOFA). Furthermore, they conducted a retrospective study to validate the use of their pSOFA scoring system in pediatric patients admitted to the general Intensive Care Unit. This demonstrated a good correlation with the study for adult patients (2). Patients with congenital heart disease (CHD) often have abnormal circulatory patterns, which can significantly affect cardiovascular and respiratory systems at baseline. This thesis project aims to explore the utilization of pSOFA in assessing the severity of illness in critically ill pediatric patients with congenital heart disease (CHD). Retrospective data collection was carried out in a population of patients with CHD during their stay in the Cardiac ICU (CICU) at Boston Children's Hospital. Two pSOFA scores, separated based

on using indirect vs. direct bilirubin values, were assigned each day spent in the CICU for 101 patients. Of these 101 patients, 50 had a diagnosis of cyanotic CHD while 51 patients had acyanotic CHD. pSOFA scores were compared between cyanotic and acyanotic patients with CHD as well as with a cohort of patients without CHD. This was an exploratory study which provides a deeper understanding for future analysis in order to validate the utilization of pSOFA in a population of patients with CHD.

TABLE OF CONTENTS

TITLE.....	i
COPYRIGHT.....	ii
READER APPROVAL.....	iii
ACKNOWLEDGMENTS.....	iv
ABSTRACT	v
TABLE OF CONTENTS	vii
LIST OF TABLES.....	viii
LIST OF FIGURES	x
LIST OF ABBREVIATIONS	xiii
INTRODUCTION	1
METHODS.....	12
RESULTS	16
DISCUSSION	24
LIST OF JOURNAL ABBREVIATIONS	50
REFERENCES.....	51
CURRICULUM VITAE.....	54

LIST OF TABLES

Table	Title	Page
1	Sequential Organ Failure Assessment Score	3
2	Pediatric Sequential Organ Failure Assessment	5
3	Characteristics of Patients who Received HSCT and Admitted to ICU	8
4	Incidence of Mortality of patients who received HSCT and admitted to ICU	9
5	Correlation Between Type of Organ Injury and Mortality	10
6	Values Recorded for pSOFA Score Assignment	13
7	Respiratory Subscore Data Collection	14
8	Subscores & Total Score Data Collection	14
9	Statistics of Patients with Congenital Heart Disease	17
10	pSOFA Scoring of Patients with Acyanotic & Cyanotic Congenital Heart Disease	17
11	Parameters for Correlation Studies – Patients with Acyanotic Congenital Heart Disease	20
12	Comparison of pSOFA Scores in Patients with Congenital Heart Disease and Patients who Underwent HSCT	22

13	Significant and Non-significant Scores Between Patients with Acyanotic and Cyanotic Congenital Heart Disease	26
----	--	----

LIST OF FIGURES

Figure	Title	Page
1	Pulmonary Systemic Blood Flow Ratio	11
2	Diagram of Acyanotic Congenital Heart Disease	11
3	Age of Patient Populations	30
4	Length of Stay in ICU of Patient Populations	30
5	Highest Total Indirect Score	31
6	Lowest Total Indirect Score	31
7	Average Total Indirect Score	32
8	Lowest Total Direct Score	33
9	Highest Total Direct Score	33
10	Average Total Direct Score	34
11	Lowest Total Respiratory Score	34
12	Highest Respiratory Score	35
13	Average Respiratory Score	35
14	Lowest Coagulation Score	36
15	Highest Coagulation Score	36
16	Average Coagulation Score	37
17	Lowest Cardiovascular Score	37
18	Highest Cardiovascular Score	38

19	Average Cardiovascular Score	38
20	Lowest Neurologic Score	39
21	Highest Neurologic Score	39
22	Average Neurologic Score	40
23	Lowest Renal Score	40
24	Highest Renal Score	41
25	Average Renal Score	41
26	Lowest Direct Hepatic Score	42
27	Highest Direct Hepatic Score	42
28	Average Direct Hepatic Score	43
29	Lowest Indirect Hepatic Score	43
30	Highest Indirect Hepatic Score	44
31	Average Indirect Hepatic Score	44
32	Correlation of Lowest Total Indirect and Highest Renal Scores	45
33	Correlation of Lowest Total Indirect and Average Renal Scores	45
34	Correlation of Lowest Total Indirect and Lowest Hepatic Indirect Scores	46
35	HSCT/CHD Total Maximum Score	47
36	HSCT/CHD Respiratory Maximum Score	47
37	HSCT/CHD Coagulation Maximum Score	48

38	HSCT/CHD Cardiovascular Maximum Score	48
39	HSCT/CHD Neurologic Maximum Score	49
40	HSCT/CHD Renal Maximum Score	49
41	HSCT/CHD Hepatic Maximum Score	50

LIST OF ABBREVIATIONS

BU	Boston University
CHD.....	Congenital Heart Disease
HSCT	Hematopoietic Stem Cell Therapy
pSOFA.....	Pediatric Sequential Organ Failure Assessment
SOFA.....	Sequential Organ Failure Assessment

INTRODUCTION

Subsection 1: Summary/Aims

The Sequential Organ Failure Assessment (SOFA) score was originally developed in the 1990s to describe the severity and risk of organ dysfunction. It is frequently used for quantification in critically ill patients with sepsis based on the Sepsis-3 definition (1). SOFA is comprised of six sub-scores for six organ systems which will be explained in more detail in the following section. The SOFA was developed primarily for adult patients; however, since pediatric patients undergo organ development and maturation, it is critical to use different criteria from the SOFA. In 2017, a group of investigators published the SOFA scoring system in which the cardiovascular and renal system scores were adjusted for pediatric patients. The respiratory system score was expanded to account for cases in which only noninvasive measurements were available (1).

This adjusted Pediatric SOFA scoring system will be called the pSOFA. This scoring system was validated by the investigators using data from Intensive Care Unit (ICU) patients in their institution, which demonstrated a good correlation with the original SOFA, particularly in the context of in-hospital mortality. Following this report, Dr. Koichi Yuki's group tested the pSOFA in patients who were admitted to the ICU after receiving hematopoietic stem cell therapy (HSCT). In line with the previous study, higher pSOFA scores correlated well with higher mortality.

This thesis aims to examine the pSOFA scoring system in patients with congenital heart disease (CHD) who were admitted to the Cardiac Intensive Care Unit (CICU). Patients with CHD were further classified into acyanotic CHD and cyanotic CHD. We hypothesized pSOFA scores for patients with cyanotic CHD to be significantly higher than those of patients with acyanotic CHD secondary to presumed higher respiratory scores (23-27). Further background information and details regarding methods are discussed in the following section.

Subsection 2: SOFA & pSOFA

The SOFA scoring system is often used to track the severity and progression of organ dysfunction due to severe sepsis (10). The SOFA score is subdivided into 6 subscores. These include respiratory, coagulation, hepatic, cardiovascular, neurologic, and renal subscores (1). The respiratory score uses $\text{PaO}_2/\text{FiO}_2$ (mmHg) or $\text{SpO}_2/\text{FiO}_2$ values. $\text{PaO}_2/\text{FiO}_2$ is the ratio of partial pressure of arterial oxygen to the percentage of inspired oxygen, while $\text{SpO}_2/\text{FiO}_2$ is the ratio of blood oxygen saturation level to the percentage of inspired oxygen (30). The coagulation subscore uses platelet count values ($\times 10^3/\text{mm}^3$), the hepatic subscore uses total bilirubin values (mg/dL), the cardiovascular subscore uses mean arterial pressure (MAP) in mmHg, the neurologic subscore uses the Glasgow coma score, and the renal subscore is measured by creatinine levels (mg/dL) or urine output (mL/day). The original SOFA system is illustrated Table 1 (1).

SOFA Score	0	1	2	3	4
<i>Respiration</i>					
PaO ₂ /FiO ₂ (mmHg)	>400	≤400	<300	<200 With respiratory support	<100 With respiratory support
<i>Coagulation</i>					
Platelets x 10 ³ /mm ³	>150	<150	<100	<50	<20
<i>Liver</i>					
Bilirubin, mg/dL (μmol/l)	<1.2 <20	1.2-1.9 (20-32)	2.0-5.9 (33-101)	6.0-11.9 (102-204)	>12.0 (< 204)
<i>Cardiovascular</i>					
Hypotension	No hypotension	MAP <70	Dopamine ≤ 5 or dobutamine (any dose) ^a	Dopamine > 5 or epinephrine ≤ 0.1 or norepinephrine ≤ 0.1	Dopamine >15 or Epinephrine > 0.1 or norepinephrine >0.1
<i>CNS</i>					
Glasgow Coma Score	15	13-14	10-12	6-9	<6
<i>Renal</i>					
Creatinine, mg/dL (μmol/l) or urine output (mL/day)	<1.2 (<110)	1.2-1.9 (110-170)	2.0-3.4 (171-299)	3.5-4.9 (300-440) or <500 mL/day	>5.0 (> 440) or <200 mL/day

MAP, mean arterial pressure; CNS, central nervous system

^a Adrenergic agents administered for at least 1 h (doses given in μg/kg/min)

Table 1. Sequential Organ Failure Assessment Score. Primarily developed for adult patients and was used as a basis to develop the modified pediatric version (1).

This SOFA scoring system was developed for adults and does not have age-adjusted value cut-offs which would be more appropriate for children (13). A study conducted in 2001 adjusted the cardiovascular subscore and made a modified SOFA (m/SOFA) scoring system for pediatric patients after cardiac surgery (5). They found that with the m/SOFA system, an initial score of greater than 5 predicted higher postoperative mortality as well as an increased need for intensive care (5). This study however did not have age adjusted measures for the renal subscore (2). This was a concern due to findings that suggested that

there could be increased severity of kidney dysfunction in children admitted to the ICU (15-17). Therefore, the renal subscore in the pSOFA table was adjusted for age as well. Similarly, there have been no modifications of the respiratory subscore either (2). The pSOFA modification in regard to the respiratory subscore includes the option of using SpO₂/FiO₂ when PaO₂/FiO₂ is unavailable. This is due to the lower frequency of having an arterial line or obtaining an arterial sample in pediatric patients (18-20). Given these three modifications in the respiratory, cardiovascular, and renal subscores, the modified pediatric version of SOFA (pSOFA) is presented in **Table 2** (2). The coagulation and neurologic subscores remained from the original SOFA. The hepatic score is calculated with total bilirubin in this chart; however, this thesis also aimed to explore the differences in utilizing indirect and direct bilirubin values. Therefore, two hepatic scores and furthermore two total scores (utilizing indirect and direct bilirubin values) were assigned to each patient in this study. This is further explained in the methods section.

	Score^a				
Variables	0	1	2	3	4
Respiratory					
PaO ₂ /FiO ₂ ^b	≥400	300-399	200-299	100-199 with respiratory support	<100 with respiratory support
or					
SpO ₂ /FiO ₂ ^c	≥292	264-291	221-264	148-220 with respiratory support	<148 with respiratory support
Coagulation					
Platelet count, x10 ³ /μL	≥150	100-149	50-99	20-49	<20
Hepatic					
Bilirubin, mg/dL	<1.2	1.2-1.9	2.0-5.9	6.0-11.9	>12.0
Cardiovascular					

MAP by age group or vasoactive infusion, mmHg or $\mu\text{g}/\text{kg}/\text{min}^{\text{d}}$					
<1mo	≥ 46	<46	Dopamine hydrochloride ≤ 5 or dobutamine hydrochloride (any)	Dopamine hydrochloride <5 or epinephrine ≤ 0.1 or norepinephrine bitartrate ≤ 0.1	Dopamine hydrochloride <15 or epinephrine <0.1 or norepinephrine bitartrate >0.1
1-11mo	≥ 55	<55			
12-23mo	≥ 60	<60			
24-59mo	≥ 62	<62			
60-143mo	≥ 65	<65			
144-216mo	≥ 67	<67			
>216mo ^e	≥ 70	<70			
Neurologic					
Glasgow Coma Score ^f	15	13-14	10-12	6-9	<6
Renal					
Creatinine by age group, mg/dL					
<1mo	<0.8	0.8-0.9	1.0-1.1	1.2-1.5	≥ 1.6
1-11mo	<0.3	0.3-0.4	0.5-0.7	0.8-1.1	≥ 1.2
12-23mo	<0.4	0.4-0.5	0.6-1.0	1.1-1.4	≥ 1.5
24-59mo	<0.6	0.6-0.8	0.9-1.5	1.6-2.2	≥ 2.3
60-143mo	<0.7	0.7-1.0	1.1-1.7	1.8-2.5	≥ 2.6
144-216mo	<1.0	1.0-1.6	1.7-2.8	2.9-4.1	≥ 4.2
>216mo ^e	<1.2	1.2-1.9	2.0-3.4	3.5-4.9	≥ 5

Abbreviations: FiO₂, fraction of inspired oxygen; MAP, mean arterial pressure; pSOFA, pediatric Sequential Organ Failure Assessment; SpO₂, peripheral oxygen saturation.

SI conversion factors: To convert bilirubin to micromoles per liter, multiply by 17.104; creatinine to micromoles per liter, multiply by 88.4; and platelet count to $\times 10^9/\text{L}$, multiply by 1.

^aThe pSOFA score was calculated for every 24-hour period. The worst value for every variable in each 24-hour period was used to calculate the subscore for each of the 6 organ systems. If a variable was not recorded in a given 24-hour period, it was assumed to be normal and a score of 0 was used. Daily pSOFA score was the sum of the 6 subscores (range, 0-24 points; higher scores indicated a worse outcome).

^bPaO₂ was measured in millimeters of mercury.

^cOnly SpO₂ measurements of 97% or lower were used in the calculation.

^dMAP (measured in millimeters of mercury) was used for scores 0 and 1; vasoactive infusion (measured in micrograms per kilogram per minute), for scores 2 to 4. Maximum continuous vasoactive infusion was administered for at least 1 hour.

^eCutoffs for patients older than 18 years (216 months) were identical to the original SOFA score.

^fGlasgow Coma Scale was calculated using the pediatric scale.

Table 2. Pediatric Sequential Organ Failure Assessment. Modified version with measurements and cutoffs adjusted to pediatric patients (2).

Subsection 3: pSOFA with HSCT Recipients

A previous study in this lab evaluated the utilization of the pSOFA scoring system in 2018 with a population of patients who were admitted to the ICU after receiving Hematopoietic Stem Cell Therapy (HSCT) with the attempt to delineate the risk factors associated with mortality. Data collection from this study was used as a non-CHD patient population. This was compared to the CHD patient populations (cyanotic and acyanotic) in order to explore the possibility of pSOFA utilization in two different disease populations. This subsection aims to provide further information regarding this past study as well as information about the data collected from the non-CHD patient population used in this thesis.

HSCT is used to treat many hematological diseases such as lymphoma, leukemia, and immune-deficiency illnesses in the pediatric population with a survival rate of $\geq 80\%$ (21). However, many patients do suffer from complications after receiving HSCT. Some of them are admitted to the ICU, and those admitted to the ICU are associated with high mortality. Therefore, further studies can be done to understand the risk factors that could lead to ICU admission following HSCT as well as the risk factors associated with mortality.

In order to address this, this study was conducted using a retrospective review of the electronic medical records of pediatric patients admitted to the ICU following HSCT at Boston Children's Hospital between January 2010 and June 2018. Data was used from 104 patients and was divided into three groups. Group A ($n_a=75$) is a population of pediatric patients admitted to the ICU after their first

HSCT. Group B ($n_b = 15$) is a population of pediatric patients discharged home following HSCT but re-admitted to the ICU due to post-transplant complications. Group C ($n_c = 14$) who had failed HSCT(s) and were admitted to the ICU after an additional HSCT. pSOFA subscores were assigned to each of the six organ systems, and a pSOFA score was assigned to each day the patient stayed in the ICU in order to assess for organ injury. The mortality rate was calculated and the pSOFA scores were used to determine risk factors associated with mortality using univariable and multivariable statistical analysis. Overall, this study found that higher neurologic and cardiovascular subscores were associated with a higher incidence of mortality. These results are illustrated in the table below.

Group A	Survivor (n=55)	Non-survivor (n=20)	P value	Odds Ratio (95% C.I.)
Age (years)	3.75 [1.00, 9.17]	12.25 [2.48, 16.27]	0.029*	1.09 [1.01- 1.17]
Gender	Male 34 (61.8%)	Male 9 (45.0%)	0.196	0.51 [0.18- 1.42]
Admission pSOFA	7.00 [5.00, 9.00]	8.50 [6.00,11.25]	0.232	1.08 [0.95- 1.23]
Average pSOFA	6.00 [5.19, 7.85]	12.70 [10.14, 15.67]	< 0.001*	2.23 [1.49- 3.33]
Maximum pSOFA	9.00 [7.00, 13.00]	18.00 [15.75, 19.25]	< 0.001*	1.67 [1.32- 2.11]
Duration of ICU Stay	11.00 [5.00, 32.00]	33.50 [11.00, 51.50]	0.446	1.01 [0.99- 1.02]
Group B	Survivor (n=11)	Non-survivor (n=4)	P value	Odds Ratio (95% C.I.)

Age (years)	7.33 [2.25, 9.75]	14.58 [13.46, 15.27]	0.113	1.24 [0.95, 1.62]
Gender	Male 5 (45.5%)	Male 0 (0%)	n/a	n/a
Admission pSOFA	5.00 [2.50, 7.00]	7.25 [5.00, 9.25]	0.541	1.08 [0.84, 1.39]
Average pSOFA	3.75 [2.89, 5.83]	8.60 [7.85, 9.12]	0.074	1.78 [0.95, 3.35]
Maximum pSOFA	5.00 [4.00, 11.0]	11.00 [10.00, 12.75]	0.222	1.17 [0.91, 1.50]
Duration of ICU Stay	4.00 [1.00, 5.00]	4.00 [4.00, 31.50]	0.307	1.04 [0.97, 1.11]
Group C	Survivor (n=55)	Non-survivor (n=20)	P value	Odds Ratio (95% C.I.)
Age (years)	6.42 [2.58, 13.42]	5.50 [2.42, 8.92]	0.428	0.92 [0.74, 1.33]
Gender	Male 7 (77.8%)	Male 4 (80.0%)	0.923	1.14 [0.08, 16.95]
Admission pSOFA	6.00 [4.00, 7.00]	6.00 [5.00, 9.00]	0.816	0.96 [0.68, 1.35]
Average pSOFA	6.21 [5.33, 7.75]	12.31 [8.69, 14.83]	0.111	1.29 [0.99, 1.68]
Maximum pSOFA	10.00 [6.00, 11.00]	18.00 [18.00, 19.00]	0.064	1.29 [0.99, 1.68]
Duration of ICU Stay	9.00 [7.00, 11.00]	29.00 [21.00, 63.00]	0.167	1.03 [0.99, 1.07]

Table 3. Characteristics of patients who received HSCT and admitted to ICU. Profiles of survivors and non-survivors in Groups A, B, and C. Age, admission pSOFA, average pSOFA, maximum pSOFA and duration of ICU stay were shown as median [25th percentile, 75th percentile]. *denotes statistical significant. C.I denotes confidence interval; n/a denotes not available.

	No. of Survivors	No. of Non-survivors	Mortality
Group A (n=75)	55	20	26.7%
Group B (n=15)	11	4	26.7%
Group C (n=14)	9	5	35.7%

Table 4. Incidence of Mortality of patients who received HSCT and admitted to ICU.

Group A				
Type of Organ Injury	Survivor (n=55)	Non-survivor (n=20)	P values	Odds ratio (95% C.I.)
Neurological Injury	0.00 [0.00, 1.00] (0.64)	4.00 [3.00, 4.00] (3.00)	< 0.001*	2.92 [1.86-4.58]
Cardiovascular Injury	0.00 [0.00, 1.00] (0.18)	1.50 [0.00, 3.00] (1.60)	< 0.001*	2.96 [1.66-5.26]
Respiratory Injury	0.00 [0.00, 0.00] (0.65)	1.50 [0.25, 2.75] (1.55)	0.010*	1.74 [1.14-2.65]
Hepatic Injury	0.00 [0.00, 0.00] (0.31)	2.00 [0.00, 2.00] (1.20)	0.003*	2.34 [1.34-4.11]
Renal Injury	0.00 [0.00, 1.00] (0.32)	1.00 [0.00, 2.00] (1.00)	0.019*	1.86 [1.11-3.12]
Hematologic Injury	0.00 [0.00, 0.00] (0.09)	0.00 [-1.00, 1.00] (0.05)	0.847	0.94 [0.50-1.77]
Group C				
Type of Organ Injury	Survivor (n=9)	Non-survivor (n=5)	P values	Odds ratio (95% C.I.)
Neurological Injury	0.00 [0.00, 1.00] (0.44)	3.00 [2.50, 4.00] (3.20)	n/a	n/a

Cardiovascular Injury	0.00 [0.00, 2.00] (0.78)	3.00 [1.00, 3.50] (2.40)	0.100	1.98 [0.88-4.48]
Respiratory Injury	0.00 [0.00, 2.00] (0.89)	3.00 [2.00, 4.00] (3.00)	0.065	5.46 [0.90-33.18]
Hepatic Injury	0.00 [0.00, 1.50] (0.78)	1.00 [0.00, 2.00] (1.00)	0.738	1.17 [0.47-2.88]
Renal Injury	0.00 [0.00, 0.50] (0.78)	1.00 [0.00, 2.00] (1.00)	0.235	2.63 [0.53-12.92]
Hematologic Injury	1.00 [0.00, 1.00] (1.00)	0.00 [-0.50, 1.50] (0.40)	0.416	0.64 [0.21=1.89]

Table 5. Correlation between type of organ injury and mortality. Correlation between progression of organ injury and mortality was examined using multivariable and univariable analysis for Group A and C (only multivariable analysis is presented here). $d(\text{subscore})$ defined as [maximum pSOFA – admission pSOFA] was used for this purpose and shown as median [25th percentile, 75th percentile] (mean). *denotes statistical significance. C.I., confidence interval.

For the purpose of this thesis, scores from Group A were used as non-CHD comparison. This was due to the fact that Group A was more homogenous from disease progression than Groups B and C. Further background information about the cohort of patients with congenital heart disease is discussed in the following subsection.

Subsection 4: Congenital Heart Disease

This thesis examines a population of pediatric patients diagnosed with congenital heart disease admitted to the CICU, focusing on acyanotic CHD. Congenital heart disease encompasses various structural malformations of the heart present at birth. A structural abnormality can present in the heart walls, valves or, nearby arteries or veins which could disrupt normal blood flow.

Depending on how normal blood flow is disrupted, CHD can be categorized into acyanotic and cyanotic CHD (22). In acyanotic CHD, biventricular circulation exists; however, a left to right shunt increases pulmonary blood flow, decreasing the efficiency of the system. In cyanotic CHD, a right to left shunt decreases overall O₂ levels (22).

$$\frac{Q_p}{Q_s} = \frac{[SaO_2 - SvO_2]}{[SpvO_2 - SpaO_2]}$$

Fig 1. Pulmonary Systemic Blood Flow Ratio. Q_p (L/min) = pulmonary blood flow. Q_s (L/min) = systemic blood flow. SaO₂ = O₂ saturation of aorta. SvO₂ = O₂ saturation of SVC. SpaO₂ = O₂ saturation of pulmonary artery. SpvO₂ = O₂ saturation of pulmonary vein.

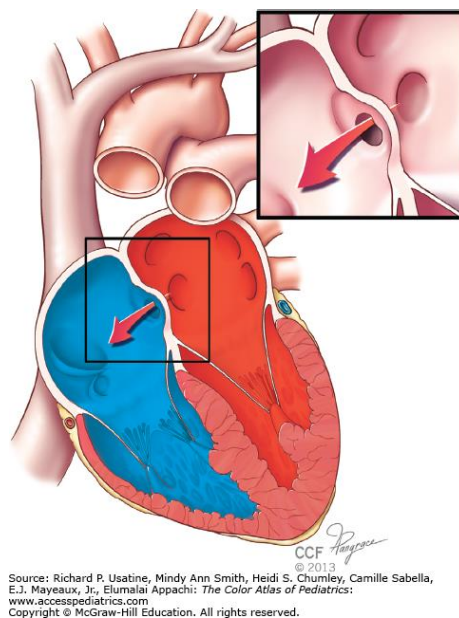


Fig 2. Diagram of Acyanotic Congenital Heart Disease. (23)

METHODS

Subsection 1: Retrospective Research Review

Patients with congenital heart disease were extracted and filtered for acyanotic CHD. pSOFA scores were assigned for each of the six organ systems which were summed to obtain a pSOFA total score. A total score was calculated for each day a patient stayed in the ICU. Data from electronic medical records of 51 patients diagnosed with acyanotic congenital heart disease were extracted and organized. Each patient's medical records number, age (months), sex, and length of stay (days) in the ICU were recorded. Values and assigned subscores were recorded throughout their ICU stay.

According to the pSOFA scoring table, values corresponding to each subscore category were recorded every day of ICU stay. In order to calculate the respiratory subscore, PaO₂ values and FiO₂ values were recorded for each day. Only the highest ratio for the day was recorded as that would be the highest pSOFA subscore. If PaO₂ was not available, SpO₂ was used instead and the highest SpO₂/FiO₂ ratio for the day was recorded. SpO₂ was not recorded for every day, it was only recorded if PaO₂ was not available. In order to differentiate PaO₂ and SpO₂ during data collection, cells were highlighted green when SpO₂ had to be utilized as illustrated in **Table 6**. Utilizing SpO₂ was differentiated using highlighting during data collection in order to explore potential differences between using the two values in further analysis. Potential differences in respiratory subscores and total scores between PaO₂ and SpO₂ not be discussed

in this thesis but, was noted as a potential limiting factor for future studies. The remaining subscores are explained in the table below.

pSOFA Subscore	Recorded value utilized to assigned pSOFA subscore
Respiratory	Explained in text.
Coagulation	Lowest platelet count/day
Hepatic (indirect score)	Highest indirect value/day
Hepatic (direct score)	Highest direct value/day
Cardiovascular	Lowest MAP/day & administered medications according to pSOFA
Neurologic	Lowest Glasgow coma score/day
Renal	Highest creatinine value/day

Table 6. Values Recorded for pSOFA Score Assignment.

Each patient received two hepatic subscores and therefore, two total scores in order to account for utilizing indirect versus direct bilirubin values. This was done in order to account for any hemolytic events that may increase the hepatic (indirect) subscore which can be potentially determined using indirect bilirubin values. Templates used to record and organize patient data taken from Power Chart is presented in **Table 7** and **Table 8** below.

MRN			
Date	Day 1	Day 2	Day 3
Time			
PaO ₂			
FiO ₂			
Ratio			
pSOFA Score			

Table 7. Respiratory Subscore Data Collection. Date, time, PaO₂, and FiO₂ values are recorded in this table. PaO₂/FiO₂ ratios were calculated and the highest ratio was recorded. pSOFA score was then assigned. A green highlighted ratio cells indicates the use of SpO₂/FiO₂ for the respiratory subscore.

MRN	Date	Highest Hepatic Value (direct bilirubin)	Hepatic Score	pSOFA Score (direct bilirubin)	Highest Hepatic Value (indirect bilirubin)	Hepatic Score	pSOFA Score (indirect bilirubin)

Table 8. Subscores & Total Score Data Collection.

Subsection 2: Statistical Analysis

Statistical analysis was carried out using Prism software (GraphPad Software, San Diego, CA) and Excel (correlation, regression). Patient demographics such as mortality, age, sex, and length of stay are expressed with percentage and number. For each patient, the lowest, highest, and average score from their whole ICU stay was used to perform analysis. These 3 scores (low, high, average) were recorded for each subscore and total scores. This culminates in 21 subscores for each patient (3*7 subscores due to utilizing indirect and direct bilirubin values for two hepatic subscores) and 6 total scores

for each patient (3*2 total scores due to utilizing indirect and direct bilirubin values). **Table 10** illustrates this breakdown. Subscores and total scores are expressed as median and interquartile range. Mann Whitney (non-parametric) tests were carried out to determine significant differences between acyanotic and cyanotic CHD pSOFA scores. Results are shown with median, interquartile ranges, and whether p-values are greater than or less than 0.05 or with a confidence interval of 95%. $p < 0.05$ was considered to be significant.

The Kruskal-Wallis test was used in Prism software to do a three-way comparison of both CHD populations with HSCT patients within parameters including the Highest or Maximum Cardiovascular, Coagulation, Hepatic Indirect, Neurologic, Renal, Respiratory, and Total Indirect Scores. Their means were compared and significance is indicated with alpha values used. The specific p-values of each comparison are not given. Graphs of the three-way analysis are displayed with median and interquartile ranges.

RESULTS

Subsection 1: Comparison of Acyanotic and Cyanotic Patients

Table 9 summarizes some demographic data as well as ICU length of stay and mortality rate of patients with CHD and compares cyanotic versus acyanotic patients. **Table 10** presents statistical analysis including median, interquartile range, and p-values of pSOFA scores assigned to patients with cyanotic and acyanotic CHD. “Low” scores indicate the lowest or minimum total score and subscore for each patient. “High” indicates the highest or maximum total score and subscores for each patient. “Average” indicates the average pSOFA score for each patient. “Direct” indicates the usage of direct bilirubin values from Power Chart. “Indirect” indicates the usage of indirect bilirubin values from Power Chart. These two CHD populations were compared to determine any potential differences in pSOFA scores.

We speculated the patients with acyanotic CHD would have lower respiratory and cardiovascular subscores leading to higher total pSOFA scores. However, these subscores and total scores were not significantly different from patients with cyanotic CHD. Results display that there were significant differences between the two groups for Highest Total Direct Score (<0.0001), Average Total Direct Score (0.013), Lowest Total Indirect Score (0.0172), Highest Total Indirect Score (0.0008), Average Total Indirect Score (0.0035), Highest Neurologic Score (<0.0001), Average Neurologic Score (<0.0001),

Highest Renal Score (<0.0001), Average Renal Score (<0.0001), and Lowest Hepatic Indirect Score (0.0006).

	Acyanotic (n=51)	Cyanotic (n=50)	p-value
Male (% , no.)	66.67%, 34	62%, 31	n/a
Age in mo. (median, IQR(Q3-Q1))	23, 28 (45.5-17.5)	26, 21.5 (37.75-16.25)	0.9744
Length of ICU Stay in Days (median, IQR(Q3-Q1))	5.4, 0.7 (5.8-5.1)	3, 2.525 (4.625-2.1)	<0.0001*
Mortality (% , no.)	0%, 0	4%, 2	n/a

Table 9. Statistics of Patients with Congenital Heart Disease. Comparison of age, sex, length of ICU stay and mortality rate in patients with CHD. *Indicates statistical significance, $\alpha = 0.05$

Parameters		Acyanotic (n-51)		Cyanotic (n=50)		p-value
		Median	IQR (Q3-Q1)	Median	IQR (Q3-Q1)	
Total Direct Score	Lowest	3	3 (4-1)	2	2 (3-1)	0.1120
	Highest	6	2 (7-5)	9	4 (11-7)	<0.0001*
	Average	4.43	2.185 (5.5-3.135)	5.25	2.6025 (7-4.3975)	0.013*

Total Indirect Score	Lowest	3	4 (5-1)	2	2 (3-1)	0.0172*
	Highest	7	3.5 (8.5-5)	9.5	4.75 (11.75-7)	0.0008*
	Average	7	2.57 (6.155-3.585)	5.3125	2.58575 (7-4.41425)	0.0035*

Respiratory Score	Lowest	1	2 (2-0)	0	2 (2-0)	0.5537
	Highest	3	1 (4-3)	4	1 (4-3)	0.1420
	Average	2	1.42 (2.75-1.33)	2.25	1.79225 (3.12525-1.333)	0.8272

Coagulation Score	Lowest	0	0 (0-0)	0	0 (0-0)	0.3002
	Highest	0	1 (1-0)	1	2 (2-0)	0.3678
	Average	0	0.77 (0.77-0)	0.354	1 (1-0)	0.1901

Cardiovascular Score	Lowest	1	1 (1-0)	1	1 (1-0)	>0.9999
	Highest	2	2 (3-1)	3	2 (3-1)	0.2328
	Average	1.29	0.585 (1.585-1)	1.333	0.75 (1.75-1)	0.1842

Neurologic Score	Lowest	0	0 (0-0)	0	0 (0-0)	0.1120
	Highest	0	0 (0-0)	4	2 (4-2)	<0.0001*
	Average	0	0 (0-0)	1.333	1.18 (1.95-0.77)	<0.0001*

Renal Score	Lowest	0	0 (0-0)	0	0 (0-0)	0.0597
	Highest	0	1 (1-0)	0	0 (0-0)	<0.0001*
	Average	0	0.62 (0.62-0)	0	0 (0-0)	<0.0001*

Hepatic Direct Score	Lowest	0	0 (0-0)	0	0 (0-0)	0.4950
	Highest	0	0 (0-0)	0	0 (0-0)	0.2999
	Average	0	0 (0-0)	0	0 (0-0)	0.1472

Hepatic Indirect Score	Lowest	0	1 (1-0)	0	0 (0-0)	0.0006*
	Highest	0	2 (2-0)	0	1 (1-0)	0.4496
	Average	0	1.855 (1.855-0)	0	0.32225 (0.32225-0)	0.3376

Table 10. pSOFA Scoring of Patients with Acyanotic & Cyanotic Congenital Heart Disease. Summary of all parameter data for both patient populations with congenital heart disease. *Indicates statistical significance, $\alpha = 0.05$

Subsection 2: Aycanotic CHD Correlation Studies

Table 11 presents acyanotic congenital heart disease patients' scores for Lowest Total Indirect Score, Highest Renal Score, Average Renal Score, and Lowest Hepatic Indirect Score. Correlation studies performed between Renal and Total Scores as well Hepatic and Total scores did not show any strong correlations. Lowest Total Indirect Score is not correlated with Highest Renal Score ($r^2 = 0.443$), Lowest Total Indirect Score is not correlated with Average Renal Score ($r^2 = 0.542$), and Lowest Total Indirect Score is not correlated with Lowest Hepatic Indirect Score ($r^2 = 0.294$).

Patient	Lowest Total Indirect Score	Highest Renal Score	Average Renal Score	Lowest Hepatic Indirect Score
1	2	0	0	0
2	2	1	0.33	0
3	1	0	0	0
4	4	0	0	0
5	2	0	0	0
6	5	1	0.33	0
7	1	1	0.17	0
8	3	3	2.33	0
9	2	1	0.33	0
10	4	1	0.5	0
11	3	0	0	2
12	6	1	0.67	3

13	0	0	0	0
14	3	2	0.83	0
15	3	2	1.22	2
16	1	0	0	0
17	3	0	0	2
18	0	1	0.17	0
19	0	0	0	0
20	1	0	0	0
21	1	0	0	0
22	0	1	0.17	0
23	1	1	0.17	0
24	3	3	2.5	0
25	7	2	2	2
26	6	1	0.83	3
27	1	0	0	0
28	4	0	0	0
29	9	3	2.43	2
30	1	0	0	0
31	4	1	0.43	0
32	1	0	0	11
33	5	0	0	0
34	4	0	0	0
35	2	0	0	0
36	4	0	0	0
37	3	0	0	0
38	6	1	0.83	0
39	9	2	1.29	3
40	8	2	2	4
41	2	1	0.57	0
42	3	0	0	0
43	3	0	0	0
44	8	0	0	2
45	0	0	0	0
46	6	2	1.29	2
47	2	0	0	0
48	5	0	0	0
49	5	0	0	0

50	5	2	1.43	2
51	2	0	0	0

Table 11. Parameters for Correlation Studies – Patients with Acyanotic Congenital Heart Disease. Summary of all data used to conduct correlation analysis. Scores significantly higher than scores of patients with cyanotic CHD were chosen for correlation studies.

Subsection 3: Comparison of Patients with Congenital Heart Disease (Acyanotic & Cyanotic) and Patients who underwent HSCT (non-CHD):

Table 12 summarizes statistical analysis performed between both congenital heart disease populations and HSCT patients who were admitted to the ICU after one treatment. The Kruskal-Wallis test done in Prism software did not have an output of specific p-values but, determined significance and indicated the alpha used. All parameters are compared using the highest or maximum scores.

Parameters	Acyanotic CHD & Cyanotic CHD	Acyanotic CHD & HSCT	Cyanotic CHD & HSCT
Total (Indirect)	Significant, p<0.0001	Significant, p<0.0001	Significant, p<0.0001
Respiratory	Not significant	Not significant	Significant, p<0.05
Coagulation	Not significant	Significant, p<0.05	Significant, p<0.05
Cardiovascular	Not significant	Not significant	Significant, p<0.05

Neurologic	Significant, p<0.05	Significant, p<0.05	Not significant
Renal	Significant, p<0.0001	Significant, p<0.0001	Significant, p<0.0001
Hepatic	Significant, p<0.05	Significant, p<0.05	Significant, p<0.05

Table 12. Comparison of pSOFA Scores in Patients with Congenital Heart Disease & Patients who Underwent HSCT. Summary of significant and nonsignificant differences between all three populations across the parameters listed.

DISCUSSION

Subsection 1: Comparison of Patients with Acyanotic and Cyanotic CHD

This discussion will focus on the differences in pSOFA scores between the two patient populations with CHD. We hypothesized that we would observe higher scores associated with in-hospital mortality in patients with cyanotic CHD. Patients with acyanotic CHD did not have any mortality while patients with cyanotic CHD only had 2 cases of in-hospital mortality.

This was an exploratory study and discussion of significant and nonsignificant differences have led to understanding further measures to be taken when conducting future studies. Overall, the pSOFA scoring system did present significant differences between the two CHD patient populations in assessing the risk of organ failure since there were total higher scores in the cyanotic CHD population compared to the acyanotic CHD population. The hypothesis in expecting higher respiratory subscores in patients with cyanotic CHD was not met, which may be due to the inconsistent use of PaO₂ and SpO₂ values. Details regarding each of the subscores are provided in the follow tables. Further analysis should be conducted with stricter filtering of patients based on the data available in PowerChart according to the following parameters:

- PaO₂ values: Using SpO₂ values when PaO₂ was not available may have introduced a confounding variable. Future studies should select for patient data when one value is consistently available, preferably PaO₂. Another option is selecting for patient data when both values are consistently

available. This would provide for score comparisons between utilizing PaO₂ versus SpO₂.

- Type of malformation: Future studies should separate patients based on the type of heart malformation. This would provide for further comparison rather than overall comparisons between acyanotic and cyanotic CHD.
- Total bilirubin level calculation and scoring: This study broke down hepatic subscores into one subscore using indirect bilirubin and one subscore using direct bilirubin. Future studies should also calculate total bilirubin and assign one hepatic and one total score. It would be interesting to explore potential differences in scores between the CHD cohorts when total bilirubin values are used.
- Glasgow coma scores: Glasgow coma scores were not available for all patients. Future studies should select for patients who have Glasgow coma scores available.
- Underlying renal conditions: Future studies should separate patients who have underlying renal conditions in order to understand potential differences seen in the renal subscores.
- Surgery history: Future studies should record surgery history for each selected patient as this information may be needed to understand higher scores seen in patients with acyanotic CHD.
- Length of stay: In this study, the length of stay in the CICU of patients with acyanotic CHD was significantly higher than that of patients with cyanotic

CHD. This could be used to explain some of the higher pSOFA subscores in the acyanotic CHD population. They could have had underlying complications that required a longer CICU stay, which could have affected the scores as well.

	Significant Difference	Non-significant Difference
Total Direct	Highest Average	Lowest
Total Indirect	Lowest ^{*(M)} Highest Average	
Respiratory		Lowest Highest Average
Coagulation		Lowest Highest Average
Cardiovascular		Lowest Highest Average
Neurologic	Highest Average	Lowest
Renal	Highest ^{*(Q3)} Average ^{*(Q3)}	Lowest
Hepatic Direct		Lowest Highest Average
Hepatic Indirect	Lowest ^{*(Q3)}	Average Highest

Table 13. Significant and Non-significant Scores Between Patients with Acyanotic and Cyanotic CHD. ^{*(M)} denotes patients with acyanotic CHD have a higher median than patients with cyanotic CHD. ^{*(Q3)} denotes patients with acyanotic CHD have a higher 75th percentile than patients with cyanotic CHD.

Absence of * denotes patients with cyanotic CHD have higher scores than patients with acyanotic CHD.

Patients with cyanotic CHD had significantly higher Highest & Average Total Direct Scores, Highest & Average Total Indirect Scores, as well as Highest & Average Neurologic Scores. These were expected to be higher in patients with cyanotic CHD because they have overall lower O₂ levels. Patients with acyanotic CHD had significantly higher Lowest Total Indirect Score, Lowest Hepatic Indirect Score, and Highest & Average Renal Scores. This was not expected and could be explained due to potential hemolytic events or surgical histories of some patients in this cohort. Some patients could have had underlying renal issues which could have caused the renal scores to be higher. Future studies should record this information for each patient to gain a better understanding of these scores.

Subsection 2: Aycanotic CHD Correlation Studies

No correlations were found between the variables observed. This could mean there was no link between the scores that were higher than those of the cyanotic population. More data would need to be collected to understand the reasoning behind higher acyanotic CHD scores as discussed in the previous subsection.

Subsection 3: Comparison of Patients with Congenital Heart Disease (Acyanotic & Cyanotic) and HSCT Recipients

Patients who underwent HSCT had significantly higher hepatic, renal, respiratory, and total scores as seen in **Graphs 32 - 38**. This could be due to the fact that patients who underwent HSCT had a higher incidence of mortality however; further information and a larger sample size is needed to understand this result.

These comparisons between patients with CHD and patients without CHD provide a step into understanding whether pSOFA can be used across different pediatric disease populations. Further data collection and analysis are needed to gain a better understanding of whether pSOFA can be utilized across different pediatric disease populations.

Conclusion:

The results and discussion based on comparisons between acyanotic and cyanotic CHD could mean that pSOFA is a promising scoring assessment that can be used to assess risk of organ dysfunction within one type of pediatric disease population. Further data collection and analysis, accounting for stricter parameters found from this study, is needed to begin validating pSOFA for this utilization in CHD populations.

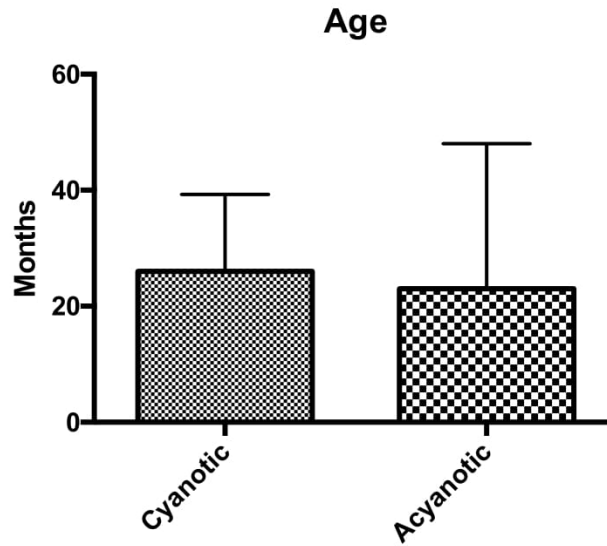


Figure 3. Age of Acyanotic (median = 23, Q3 = 45.5) and Cyanotic (median = 26, Q3 = 37.75) patient populations. There is no significant difference ($p = 0.9744$, $\alpha = 0.05$).

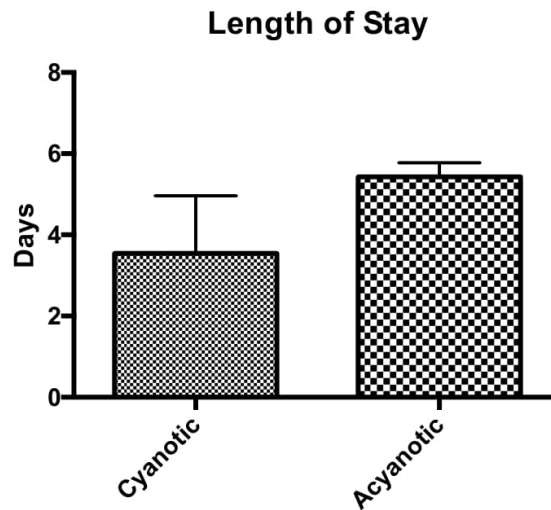


Figure 4. Length of ICU stay of Acyanotic (median = 5.4, Q3 = 5.8) and Cyanotic (median = 3, Q3 = 4.625) patient populations. There is a significant difference ($p < 0.0001$, $\alpha = 0.05$).

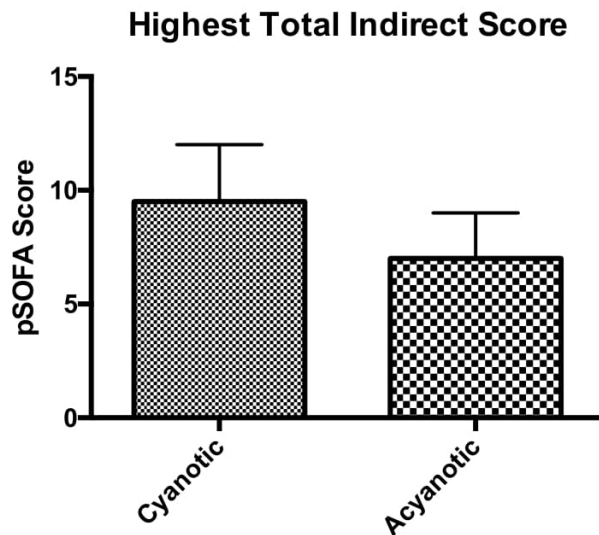


Figure 5. Highest Total Indirect Scores of Acyanotic (median = 7, Q3 = 8.5) and Cyanotic (median = 9.5, Q3 = 11.75) patient populations. There is a significant difference ($p = 0.0008$, $\alpha = 0.05$).

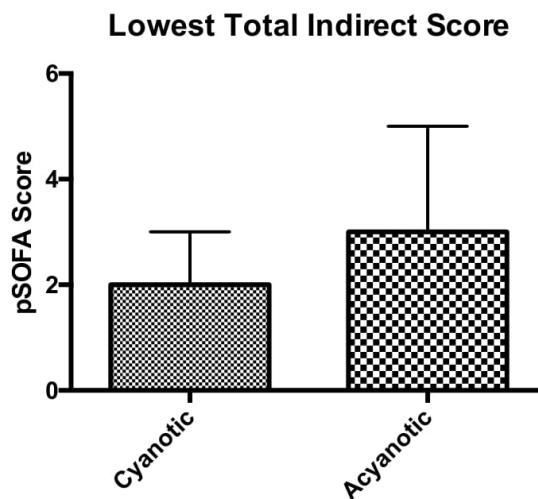


Figure 6. Lowest Total Indirect Scores of Acyanotic (median = 3, Q3 = 5) and Cyanotic (median = 2, Q3 = 3) patient populations. There is no significant difference ($p = 0.0172$, $\alpha = 0.05$).

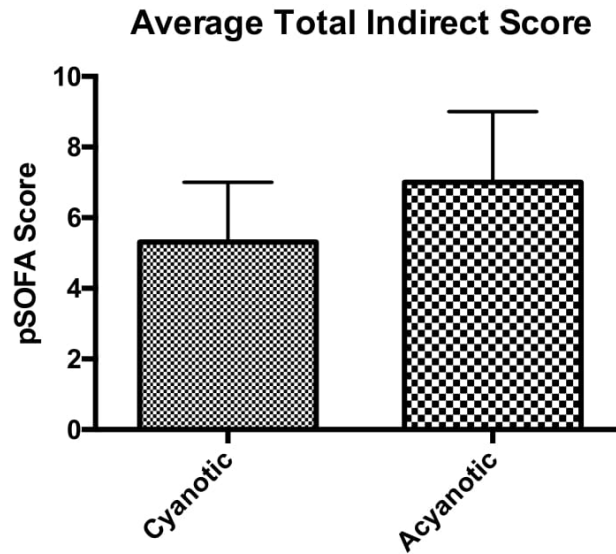


Figure 7. Average Total Indirect Scores of Acyanotic (median = 7, Q3 = 6.155) and Cyanotic (median = 5.3, Q3 = 7) patient populations. There is a significant difference ($p = 0.0035$, $\alpha = 0.05$).

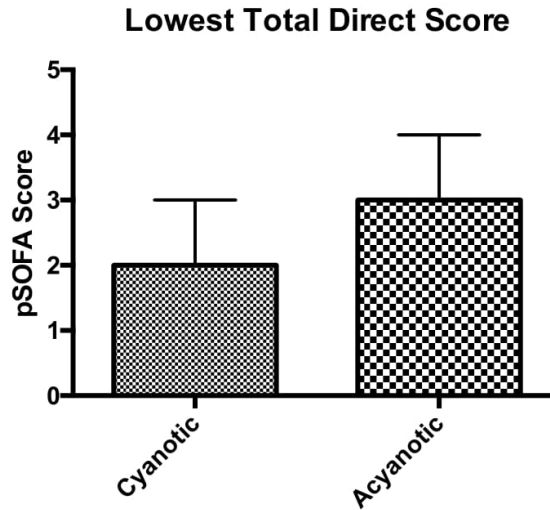


Figure 8. Lowest Total Direct Scores of Acyanotic (median = 3, Q3 = 4) and Cyanotic (median = 2, Q3 = 3) patient populations. There is no significant difference ($p = 0.1120$, $\alpha = 0.05$).

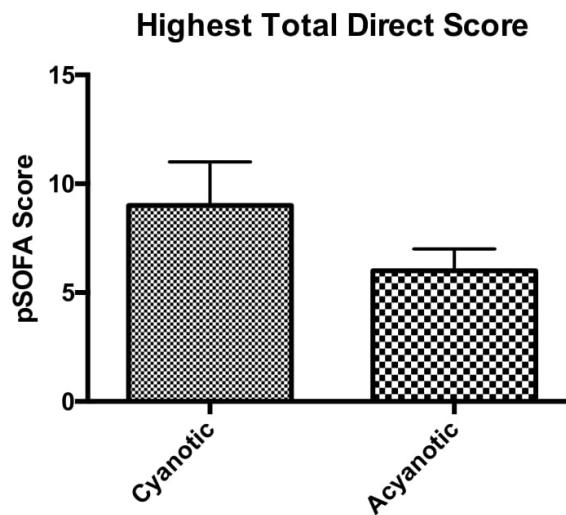


Figure 9. Highest Total Direct Scores of Acyanotic (median = 6, Q3 = 7) and Cyanotic (median = 9, Q3 = 11) patient populations. There is a significant difference ($p < 0.0001$, $\alpha = 0.05$).

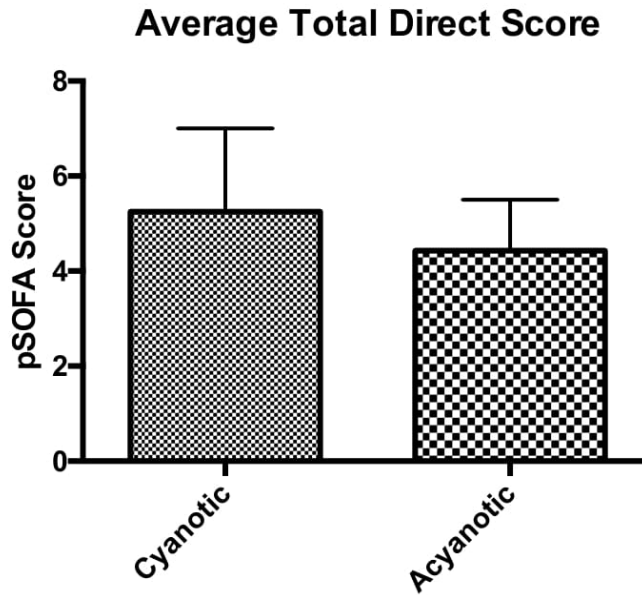


Figure 10. Average Total Direct Scores of Acyanotic (median = 4.43, Q3 = 5.5) and Cyanotic (median = 5.25, Q3 = 7) patient populations. There is a significant difference ($p = 0.013$, $\alpha = 0.05$).

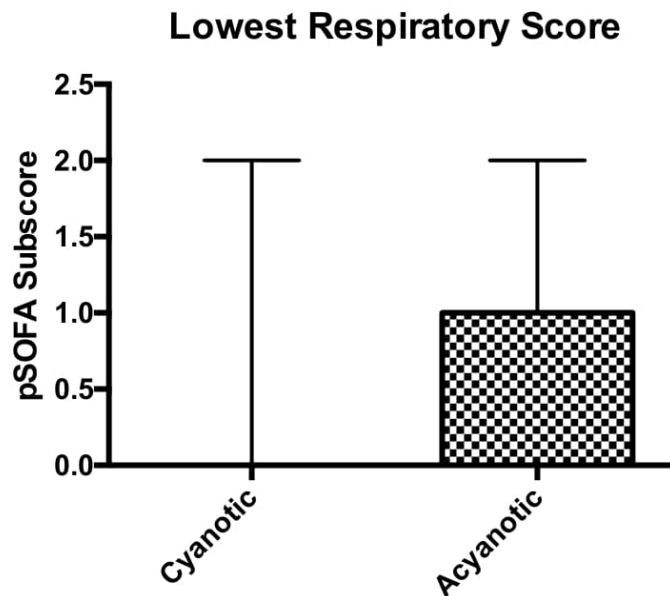


Figure 11. Lowest Respiratory Scores of Acyanotic (median = 1, Q3 = 2) and Cyanotic (median = 0, Q3 = 2) patient populations. There is no significant difference ($p = 0.5537$, $\alpha = 0.05$).

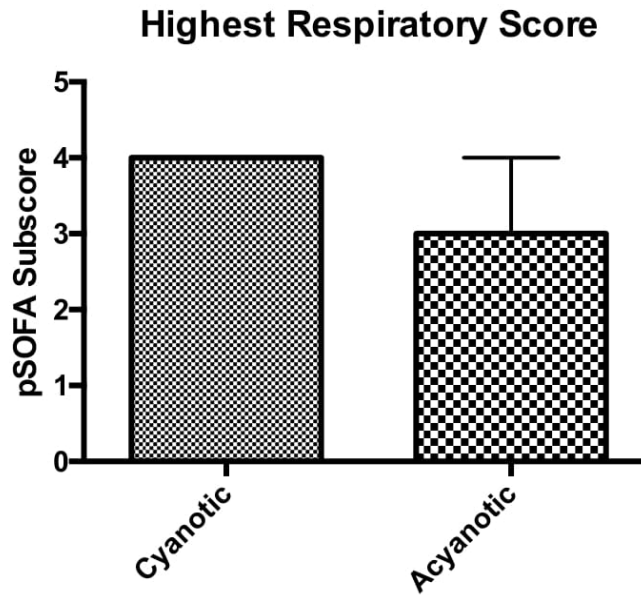


Figure 12. Highest Respiratory Scores of Acyanotic (median = 3, Q3 = 4) and Cyanotic (median = 4, Q3 = 4) patient populations. There is no significant difference ($p = 0.1420$, $\alpha = 0.05$).

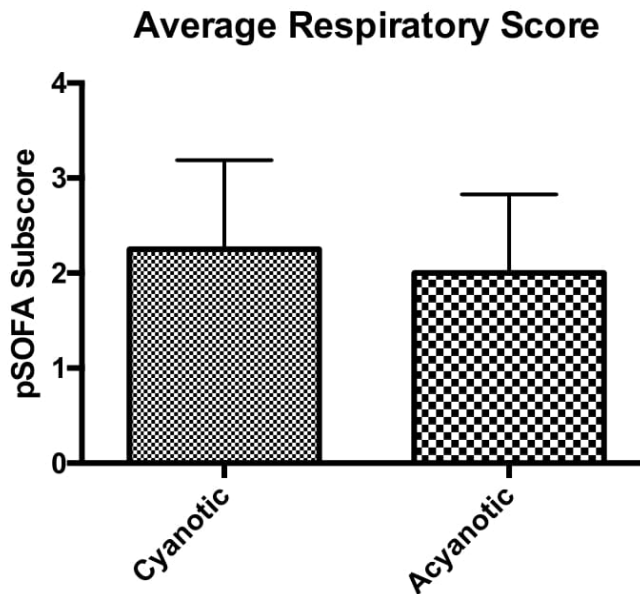


Figure 13. Average Respiratory Scores of Acyanotic (median = 2, Q3 = 2.75) and Cyanotic (median = 2.25, Q3 = 3.13) patient populations. There is no significant difference ($p = 0.8272$, $\alpha = 0.05$).

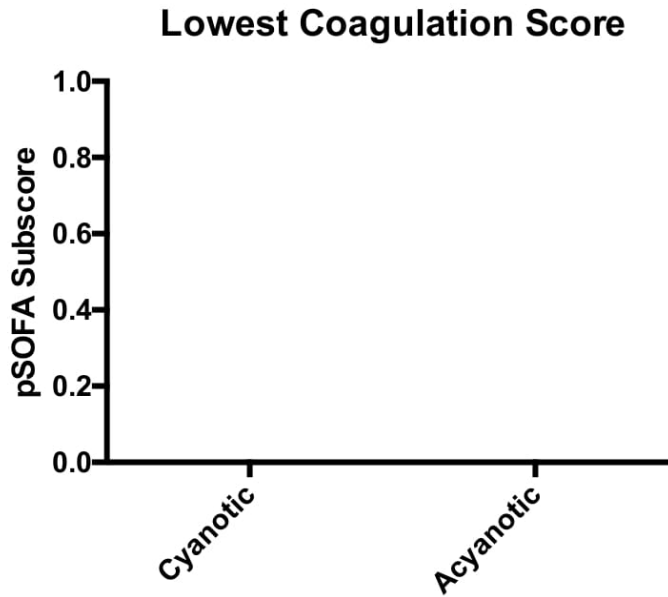


Figure 14. Lowest Coagulation Scores of Acyanotic (median = 0, Q3 = 0) and Cyanotic (median = 0, Q3 = 0) patient populations. There is no significant difference ($p = 0.3002$, $\alpha = 0.05$).

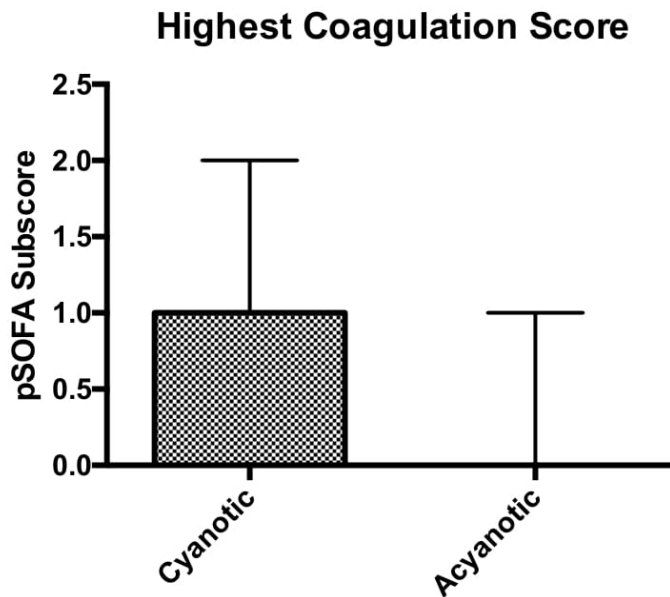


Figure 15. Highest Coagulation Scores of Acyanotic (median = 0, Q3 = 1) and Cyanotic (median = 1, Q3 = 2) patient populations. There is no significant difference ($p = 0.1420$, $\alpha = 0.05$).

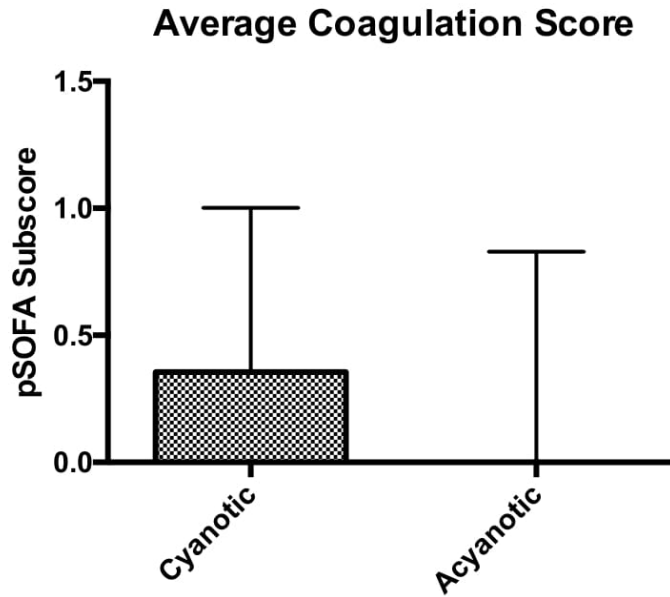


Figure 16. Average Coagulation Scores of Acyanotic (median = 0, Q3 = 0.77) and Cyanotic (median = 0.354, Q3 = 1) patient populations. There is no significant difference ($p = 0.1901$, $\alpha = 0.05$).

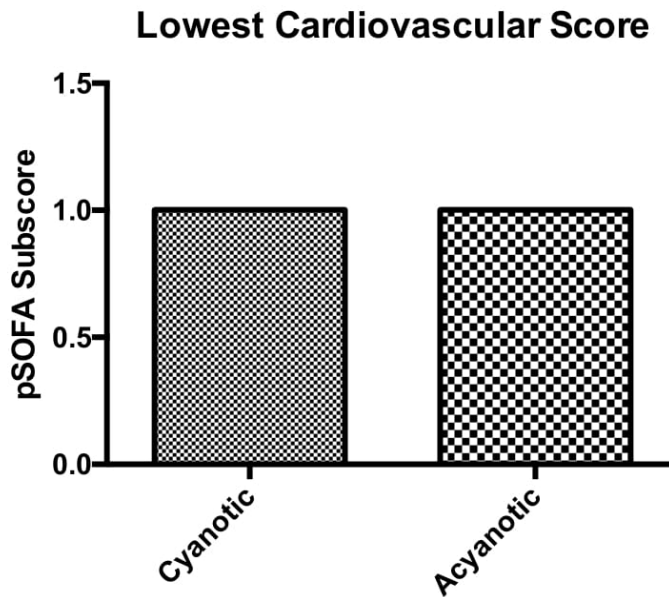


Figure 17. Lowest Cardiovascular Scores of Acyanotic (median = 1, Q3 = 1) and Cyanotic (median = 1, Q3 = 1) patient populations. There is no significant difference ($p > 0.9999$, $\alpha = 0.05$).

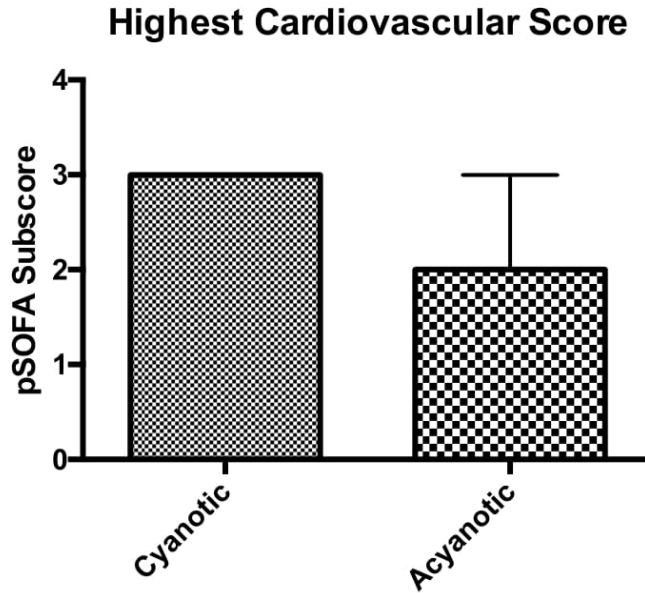


Figure 18. Highest Cardiovascular Scores of Acyanotic (median = 2, Q3 = 3) and Cyanotic (median = 3, Q3 = 3) patient populations. There is no significant difference ($p = 0.2328$, $\alpha = 0.05$).

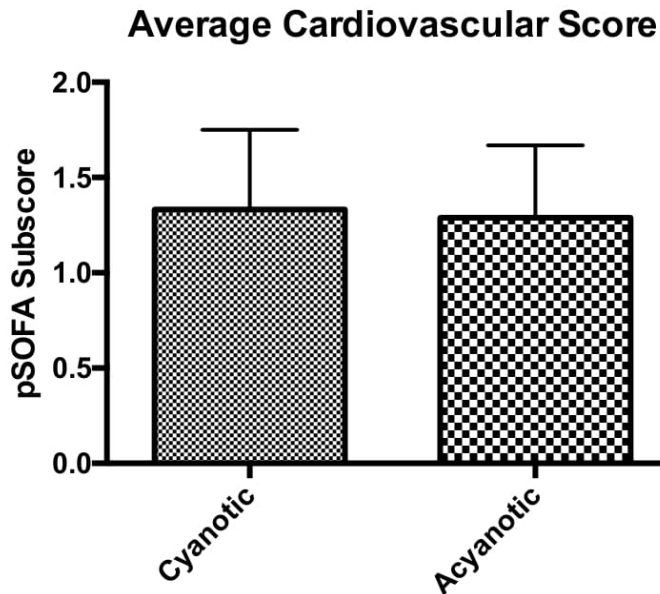


Figure 19. Average Cardiovascular Scores of Acyanotic (median = 1.29, Q3 = 1.585) and Cyanotic (median = 1.33, Q3 = 1.75) patient populations. There is no significant difference ($p = 0.1842$, $\alpha = 0.05$).

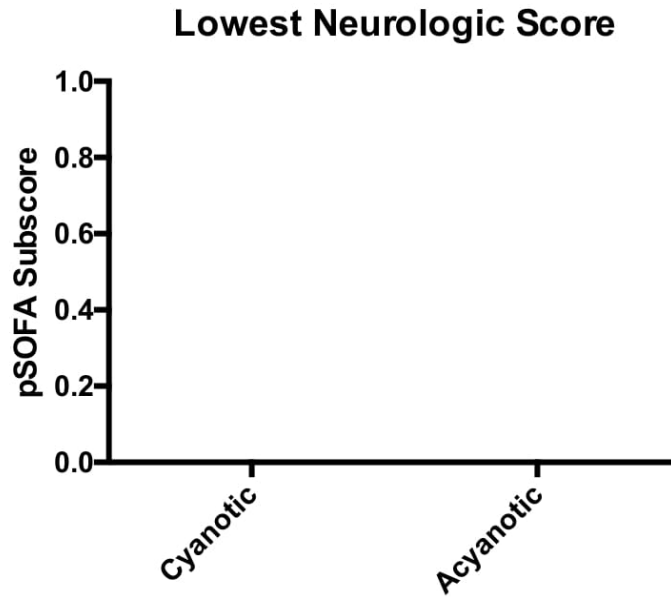


Figure 20. Lowest Neurologic Scores of Acyanotic (median = 0, Q3 = 0) and Cyanotic (median = 0, Q3 = 0) patient populations. There is no significant difference ($p = 0.1120$, $\alpha = 0.05$).

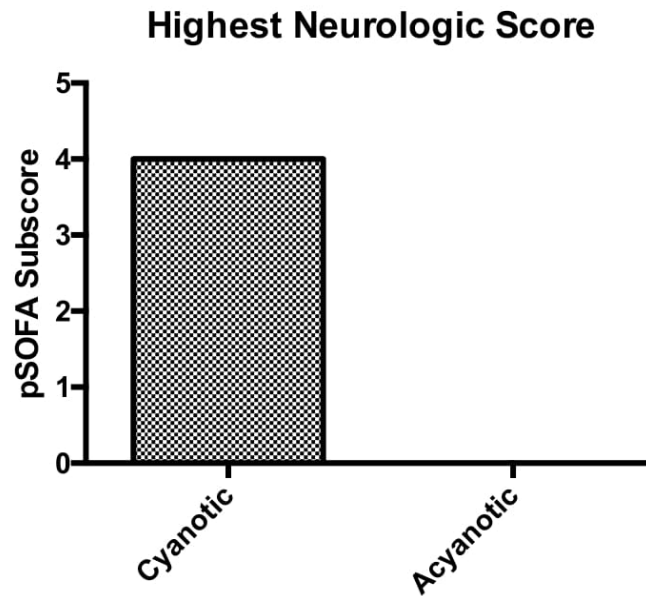


Figure 21. Highest Neurologic Scores of Acyanotic (median = 0, Q3 = 0) and Cyanotic (median = 4, Q3 = 4) patient populations. There is a significant difference ($p < 0.0001$, $\alpha = 0.05$).

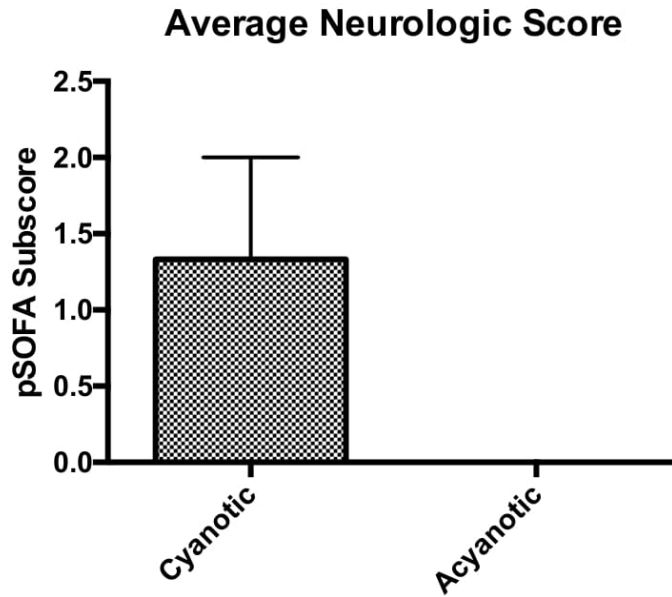


Figure 22. Average Neurologic Scores of Acyanotic (median = 0, Q3 = 0) and Cyanotic (median = 1.33, Q3 = 1.95) patient populations. There is a significant difference ($p < 0.0001$, $\alpha = 0.05$).

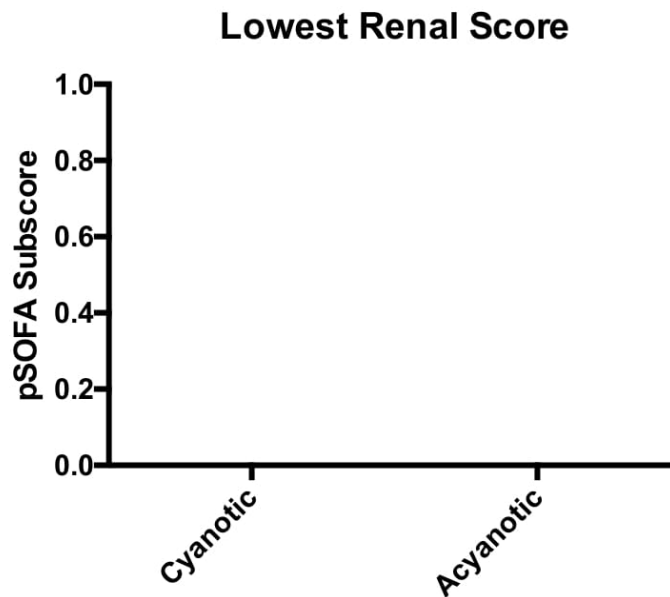


Figure 23. Lowest Renal Scores of Acyanotic (median = 0, Q3 = 0) and Cyanotic (median = 0, Q3 = 0) patient populations. There is no significant difference ($p = 0.597$, $\alpha = 0.05$).

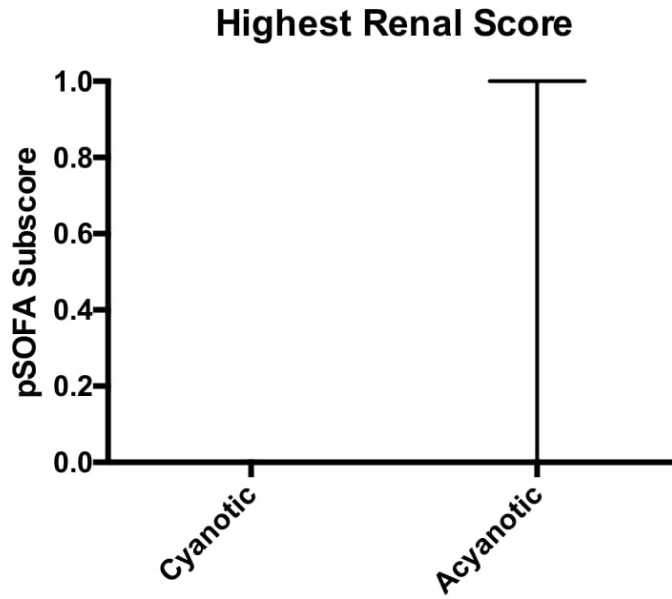


Figure 24. Highest Renal Scores of Acyanotic (median = 0, Q3 = 1) and Cyanotic (median = 0, Q3 = 0) patient populations. There is a significant difference ($p < 0.0001$, $\alpha = 0.05$).

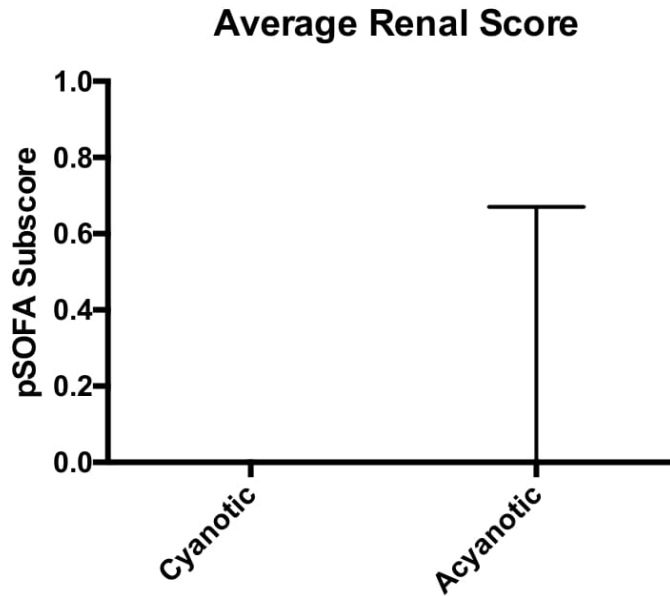


Figure 25. Average Renal Scores of Acyanotic (median = 0, Q3 = 0.62) and Cyanotic (median = 0, Q3 = 0) patient populations. There is a significant difference ($p < 0.0001$, $\alpha = 0.05$).

Lowest Direct Hepatic Score

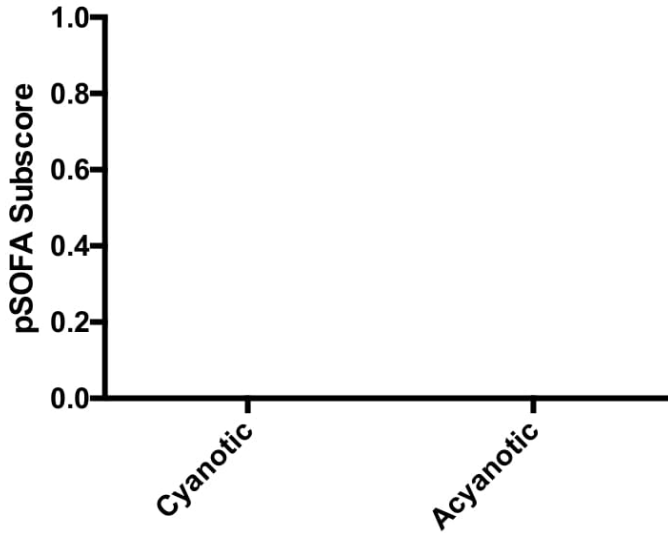


Figure 26. Lowest Direct Hepatic Scores of Acyanotic (median = 0, Q3 = 0) and Cyanotic (median = 0, Q3 = 0) patient populations. There is no significant difference ($p = 0.4950$, $\alpha = 0.05$).

Highest Direct Hepatic Score

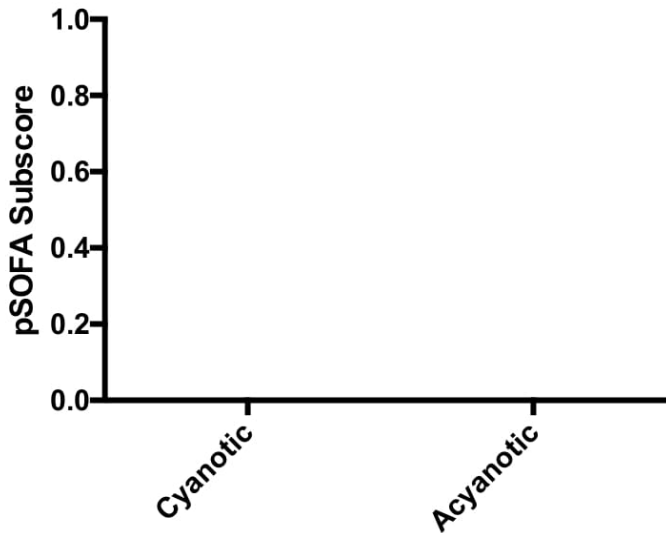


Figure 27. Highest Direct Hepatic Scores of Acyanotic (median = 0, Q3 = 0) and Cyanotic (median = 0, Q3 = 0) patient populations. There is no significant difference ($p = 0.2999$, $\alpha = 0.05$).

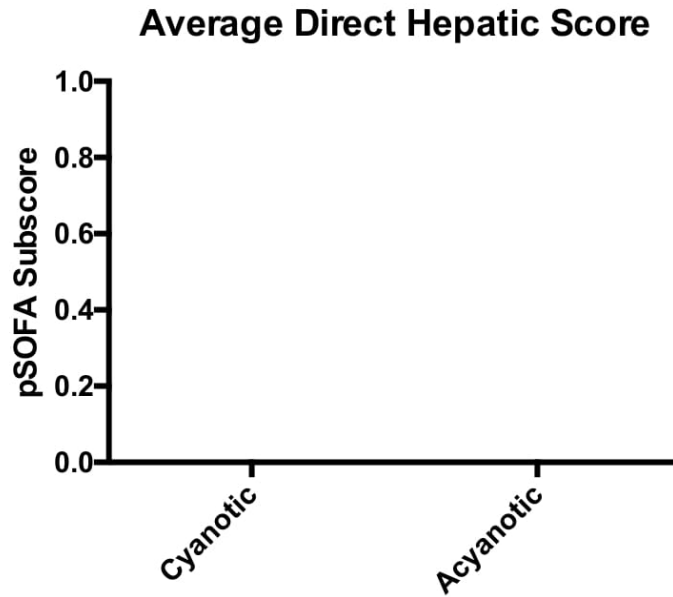


Figure 28. Average Direct Hepatic Scores of Acyanotic (median = 0, Q3 = 0) and Cyanotic (median = 0, Q3 = 0) patient populations. There is no significant difference ($p = 0.1472$, $\alpha = 0.05$).

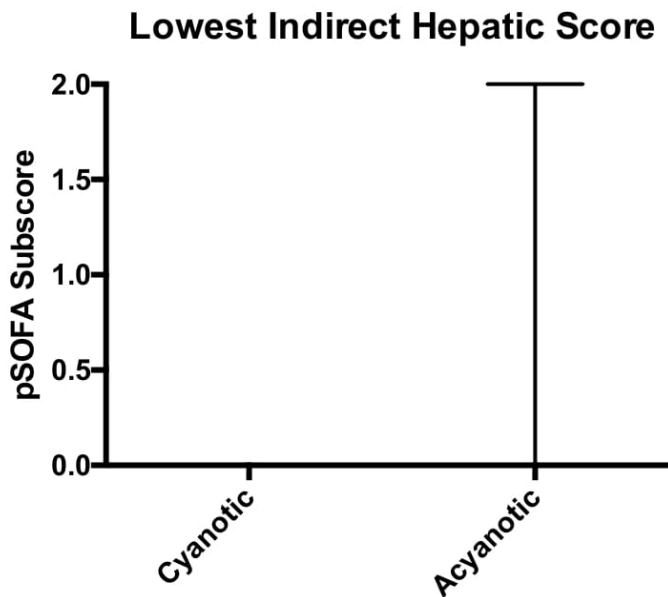


Figure 29. Lowest Indirect Hepatic Scores of Acyanotic (median = 0, Q3 = 1) and Cyanotic (median = 0, Q3 = 0) patient populations. There is a significant difference ($p = 0.0006$, $\alpha = 0.05$).

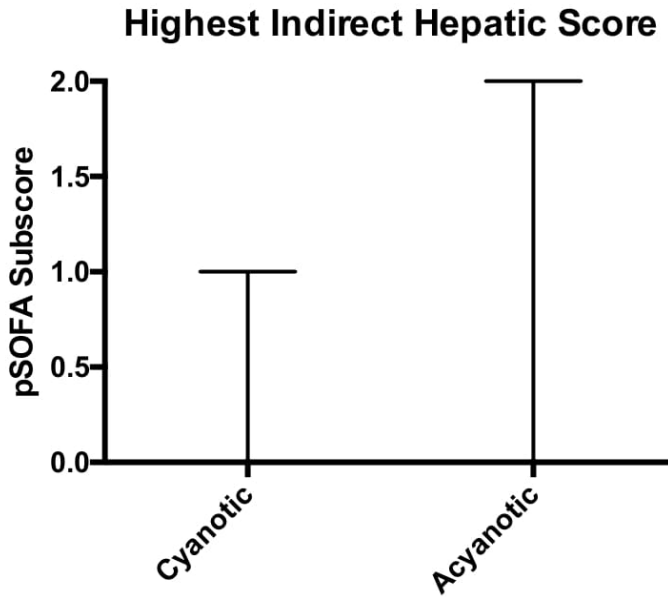


Figure 30. Highest Indirect Hepatic Scores of Acyanotic (median = 0, Q3 = 2) and Cyanotic (median = 0, Q3 = 1) patient populations. There is no significant difference ($p = 0.4496$, $\alpha = 0.05$).

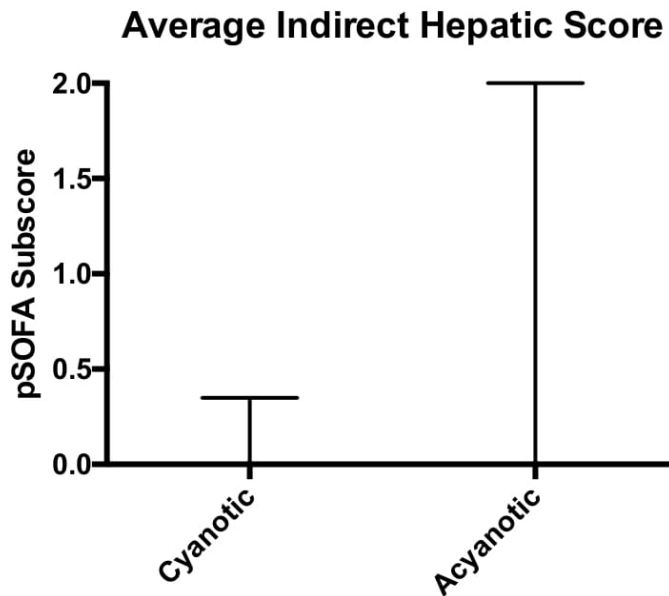


Figure 31. Average Indirect Hepatic Scores of Acyanotic (median = 0, Q3 = 1.855) and Cyanotic (median = 0, Q3 = 0.323) patient populations. There is no significant difference ($p = 0.3376$, $\alpha = 0.05$).

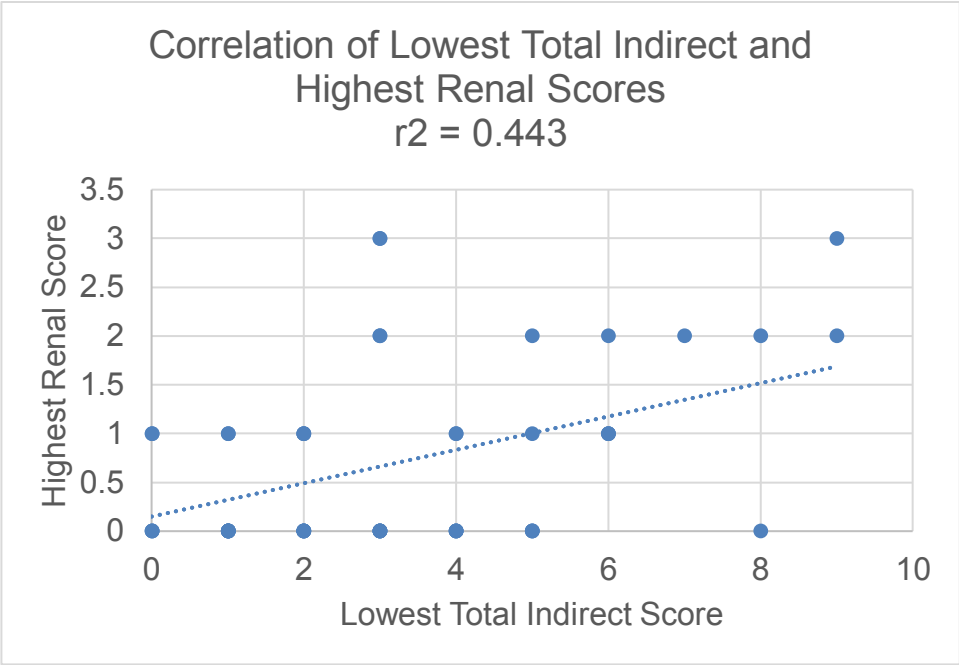


Figure 32. There is no correlation between Highest Renal and Lowest Total Indirect Scores, $r^2 = 0.443$.

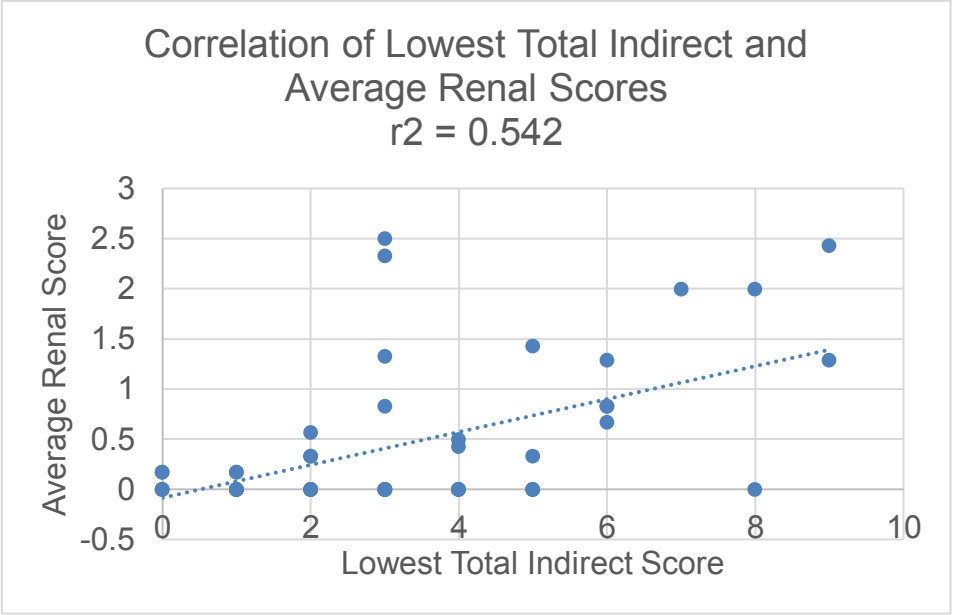


Figure 33. There is no correlation between Average Renal and Lowest Total Indirect Scores, $r^2 = 0.542$.

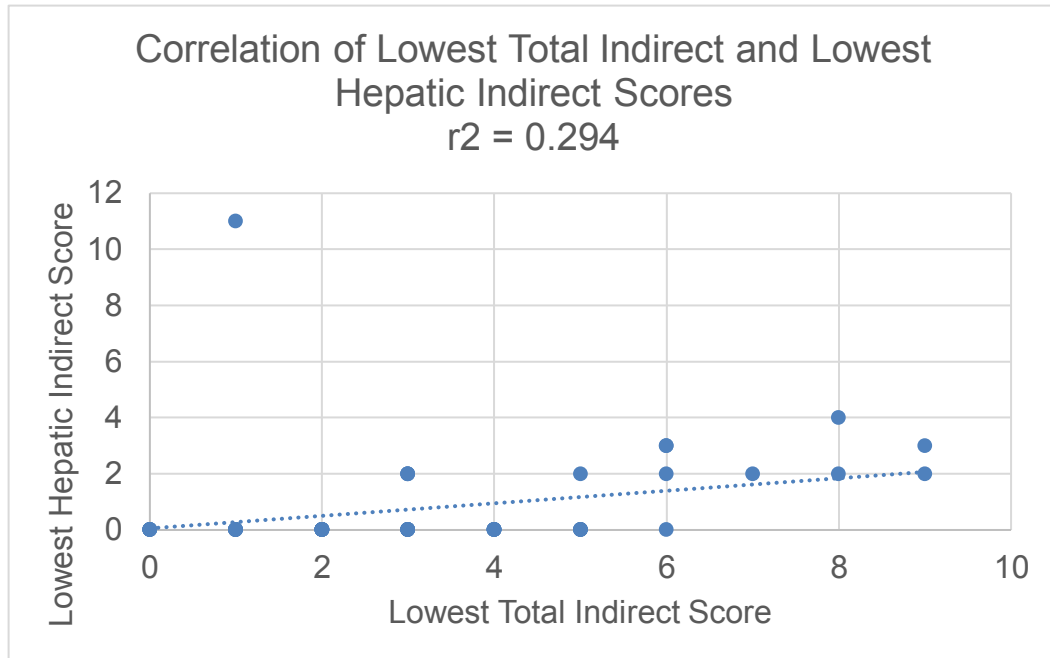


Figure 34. There is no correlation between Lowest Hepatic Indirect and Lowest Total Indirect Scores, $r^2 = 0.294$.

HSCT/ CHD Total Maximum Score

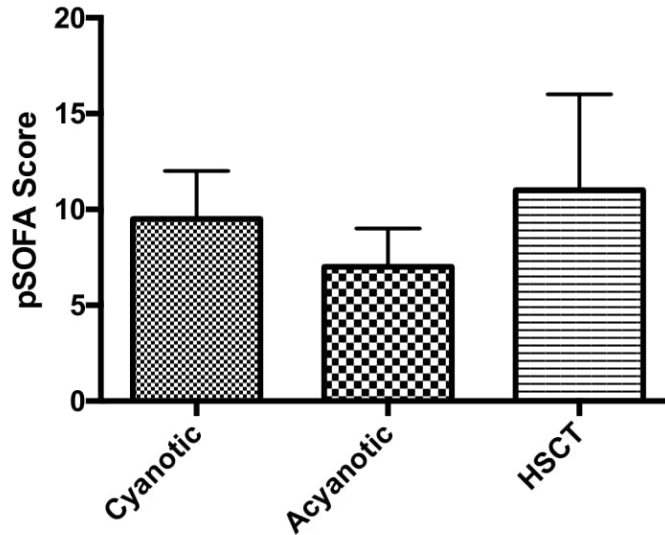


Figure 35. There is a significant difference between HSCT & Cyanotic CHD patients ($p < 0.0001$). There is a significant difference between HSCT & Acyanotic CHD patients ($p < 0.0001$).

HSCT/ CHD Respiratory Maximum Score

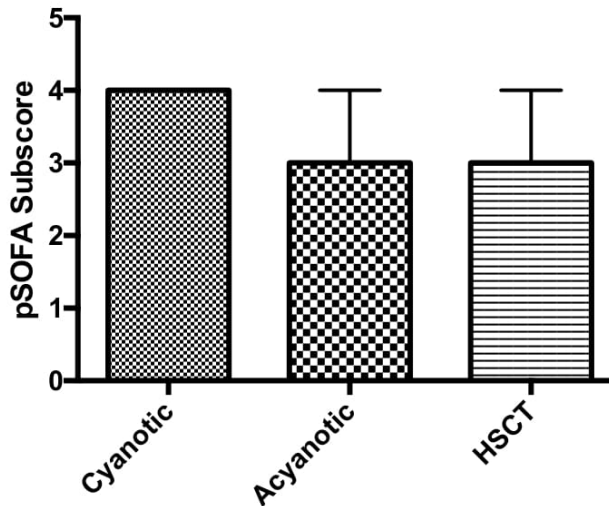


Figure 36. There is a significant difference between HSCT & Cyanotic CHD patients ($p < 0.05$). There is no significant difference between HSCT & Acyanotic CHD patients.

HSCT/ CHD Coagulation Maximum Score

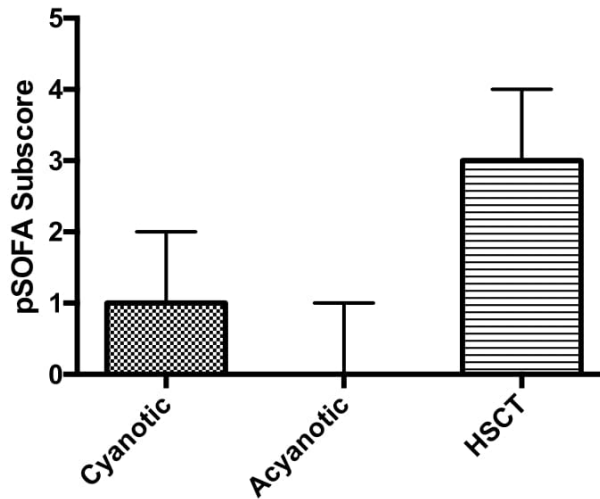


Figure 37. There is a significant difference between HSCT & Cyanotic CHD patients ($p < 0.05$). There is a significant difference between HSCT & Acyanotic CHD patients ($p < 0.05$).

HSCT/ CHD Cardiovascular Maximum Score

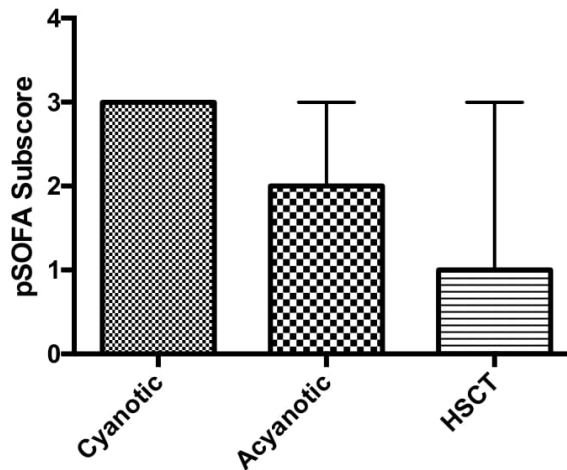


Figure 38. There is a significant difference between HSCT & Cyanotic CHD patients ($p < 0.05$). There is no significant difference between HSCT & Acyanotic CHD patients.

HSCT/ CHD Neurologic Maximum Score

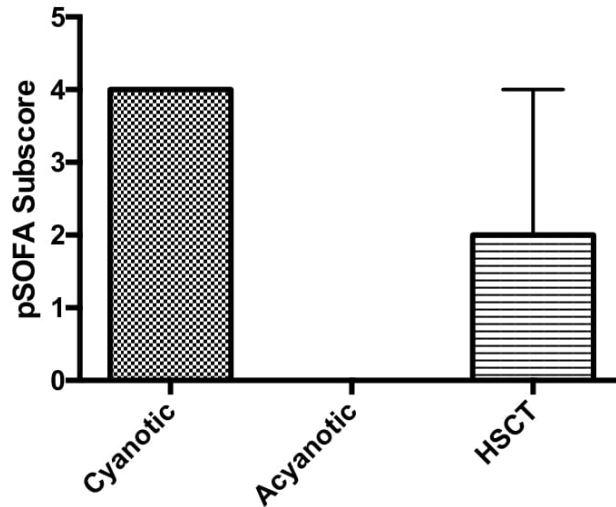


Figure 39. There is no significant difference between HSCT & Cyanotic CHD patients. There is a significant difference between HSCT & Acyanotic CHD patients ($p < 0.05$).

HSCT/ CHD Renal Maximum Score

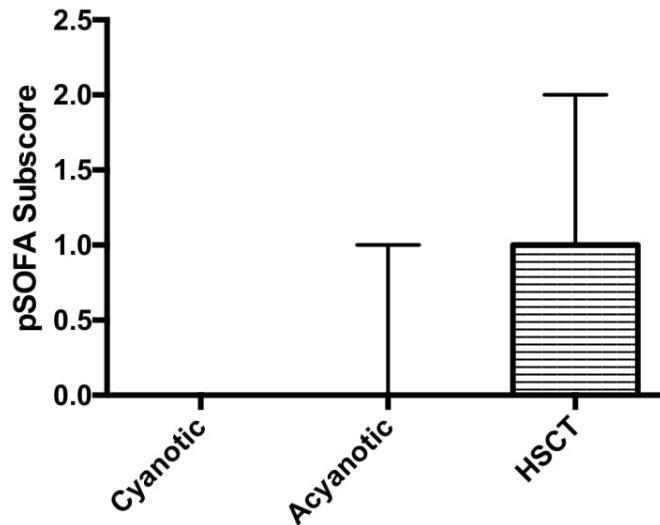


Figure 40. There is a significant difference between HSCT & Cyanotic CHD patients ($p < 0.0001$). There is a significant difference between HSCT & Acyanotic CHD patients ($p < 0.0001$).

HSCT/ CHD Hepatic Maximum Score

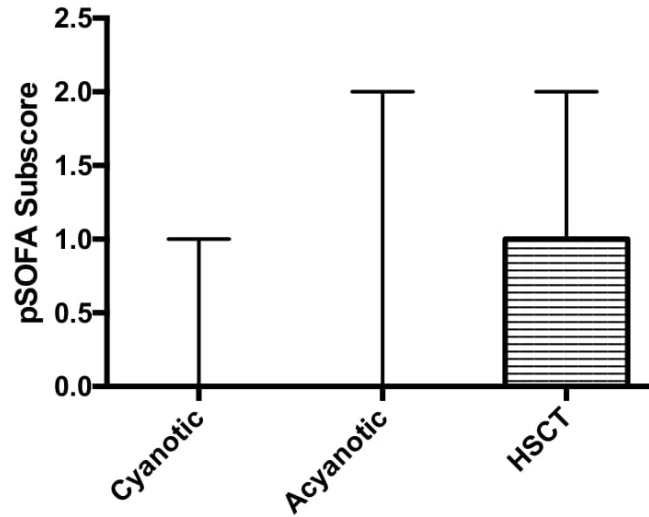


Figure 41. There is a significant difference between HSCT & Cyanotic CHD patients ($p < 0.05$). There is a significant difference between HSCT & Acyanotic CHD patients ($p < 0.05$).

LIST OF JOURNAL ABBREVIATIONS

Ann Transl Med	Annals of Translational Medicine
Childs Nerv Syst	Child's Nervous System
Crit Care Med	Critical Care Medicine
Curr Cardiol Rev	Current Cardiology Reviews
Intensive Care Med	Intensive Care Medicine
JAMA	JAMA: The Journal of the American Medical Association
J Cardiothorac Vasc Anesth	Journal of Cardiothoracic Vascular Anesthesiology
Yale J Biol Med	Yale Journal of Biology and Medicine

REFERENCES

1. Vincent JL, de Mendonca A, Cantraine F, Moreno R, Takala J, Suter P, Spring C, Colardyn F, Blecher, S. Use of the SOFA score to assess the incidence of organ dysfunction/failure in intensive care units: Results of a multicenter, prospective study. *Critical Care Medicine*. 1998; 26(11): 1793-1800
2. Matics TJ, Sanchez-Pinto N. Adaptation and Validation of a Pediatric Sequential Organ Failure Assessment Score and Evaluation of the Sepsis-3 Definitions in Critically Ill Children. *JAMA Pediatrics*. 2017; 171(10); e172352
3. Leteurtre S, Martinot A, Duhamel A, Proulx F, Grandbastien B, Cotting J, Gottesman R, Joffe A, Pfenninger J, Hubert P, Lacroix J, Leclerc F. Validation of the paediatric logistic organ dysfunction (PELOD) score: prospective, observational, multicentre study. *Lancet*. 2006; 367(9514): 902
4. Graciano AL¹, Balko JA, Rahn DS, Ahmad N, Giroir BP. The Pediatric Multiple Organ Dysfunction Score (P-MODS): development and validation of an objective scale to measure the severity of multiple organ dysfunction in critically ill children. *Crit Care Med*. 2005; 33(7): 1484-91
5. Shime N¹, Kageyama K, Ashida H, Tanaka Y. Application of modified sequential organ failure assessment score in children after cardiac surgery. *J Cardiothorac Vasc Anesth*. 2001; 15(4): 463-8.
6. Shime N¹, Kawasaki T, Nakagawa S. Proposal of a New Pediatric Sequential Organ Failure Assessment Score for Possible Validation. *Pediatric Crit Care Med*. 2017; 18(1): 98-99.
7. Schwartz GJ, Brion LP, Spitzer A. The use of plasma creatinine concentration for estimating glomerular filtration rate in infants, children, and adolescents. *Pediatric Clinics of North America*. 1987; 34(3): 571-90.
8. Reilly PL¹, Simpson DA, Sprod R, Thomas L. Assessing the conscious level in infants and young children: a paediatric version of the Glasgow Coma Scale. *Childs Nerv Syst*. 1988; 4(1): 30-3.
9. Ferreira FL¹, Bota DP, Bross A, Mélot C, Vincent JL. Serial evaluation of the SOFA score to predict outcome in critically ill patients. *JAMA*. 2001; 286(4): 1754-8.

10. Caraballo C, Jaimes F. Organ Dysfunction in Sepsis: An Ominous Trajectory From Infection To Death. *Yale J Biol Med.* 2019;92(4):629–640.
11. World Health Organization. Fact Sheets: Sepsis. Retrieved February 10, 2019, from <https://www.who.int/news-room/fact-sheets/detail/sepsis>.
12. McLymont N, Glover GW. Scoring systems for the characterization of sepsis and associated outcomes. *Ann Transl Med.* 2016;4(24):527.
13. Singer M, Deutschman CS, Seymour CW, et al. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). *JAMA.* 2016;315(8):801–810.
14. Singer M, Deutschman CS, Seymour CW, et al. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). *JAMA.* 2016;315(8):801–810.
15. Sanchez-Pinto LN¹, Khemani RG. Development of a Prediction Model of Early Acute Kidney Injury in Critically Ill Children Using Electronic Health Record Data. *Pediatr Crit Care Med.* 2016; 17(6): 508-15.
16. Hassinger AB¹, Garimella S, Wrotniak BH, Freudenheim JL. The Current State of the Diagnosis and Management of Acute Kidney Injury by *Pediatric Critical Care* Physicians. *Pediatric Critical Care Medicine.* 2016; 17(8): e362-70.
17. Sanchez-Pinto LN¹, Goldstein SL, Schneider JB, Khemani RG. Association Between Progression and Improvement of Acute Kidney Injury and Mortality in Critically Ill Children. *Pediatric Critical Care.* 2015; 16(8): 703-10.
18. Khemani RG¹, Smith LS, Zimmerman JJ, Erickson S; Pediatric Acute Lung Injury Consensus Conference Group. Pediatric acute respiratory distress syndrome: definition, incidence, and epidemiology: proceedings from the Pediatric Acute Lung Injury Consensus Conference. *Pediatric Critical Care.* 2015; 16(5 Suppl 1):S23-40.
19. Khemani RG¹, Thomas NJ, Venkatachalam V, Scimeme JP, Berutti T, Schneider JB, Ross PA, Willson DF, Hall MW, Newth CJ; Pediatric Acute Lung Injury and Sepsis Network Investigators (PALISI). Comparison of SpO₂ to PaO₂ based markers of lung disease severity for children with acute lung injury. *Crit Care Med.* 2012;40(4):1309-16.

20. Leteurtre S¹, Dupré M, Dorkenoo A, Lampin ME, Leclerc F. Assessment of the Pediatric Index of Mortality 2 with the Pao₂/Fio₂ ratio derived from the Spo₂/Fio₂ ratio: a prospective pilot study in a French pediatric intensive care unit. *Pediatric Critical Care Medicine*. 2011;12(4):e184-6.
21. Hierlmeier S, Eyrich M, Wolfl M, Schlegel PG, Wiegering V. Early and late complications following hematopoietic stem cell transplantation in pediatric patients - A retrospective analysis over 11 years. *PLoS ONE*. 2018.
22. Hoffman, Julien I. E., Moller, James H., Benson, D. Woodrow, Van Hare, George F., and Wren, C. *Pediatric Cardiovascular Medicine*. Second ed. Chichester, West Sussex, U.K.: Wiley-Blackwell, a John Wiley & Sons,, Publication, 2012. Web.
23. Usatine R, Smith M, Chumley H, Sabella C, Mayeux EJ, Appachi E. *The Color of Atlas of Pediatrics*. www.accesspediatrics.com
24. Sommer RJ, Hijazi ZM, Rhodes JF. Pathophysiology of Congenital Heart Disease in the Adult. *Circulation*. 2008; 117:1090-1099.
25. UF College of Medicine. Cath Lab Hemodynamics. Retrieved on February 10 from <https://neonatology.pediatrics.med.ufl.edu/files/2016/04/Cardiac-Hemodynamics.pdf>.
26. University of Rochester Medical Center. Direct Bilirubin. Retrieved on February 10 from https://www.urmc.rochester.edu/encyclopedia/content.aspx?contenttypeid=167&contentid=bilirubin_direct.
27. Perloff JK. Cyanotic congenital heart disease the coronary arterial circulation. *Curr Cardiol Rev*. 2012;8(1):1–5.
28. Pruitt AA, Graus F, Rosenfeld MR. Neurological complications of transplantation: part I: hematopoietic cell transplantation. *Neurohospitalist*. 2013;3(1):24–38.

CURRICULUM VITAE

