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Critical Rounds

MICRO LABS LIMITED

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Inside This Issue

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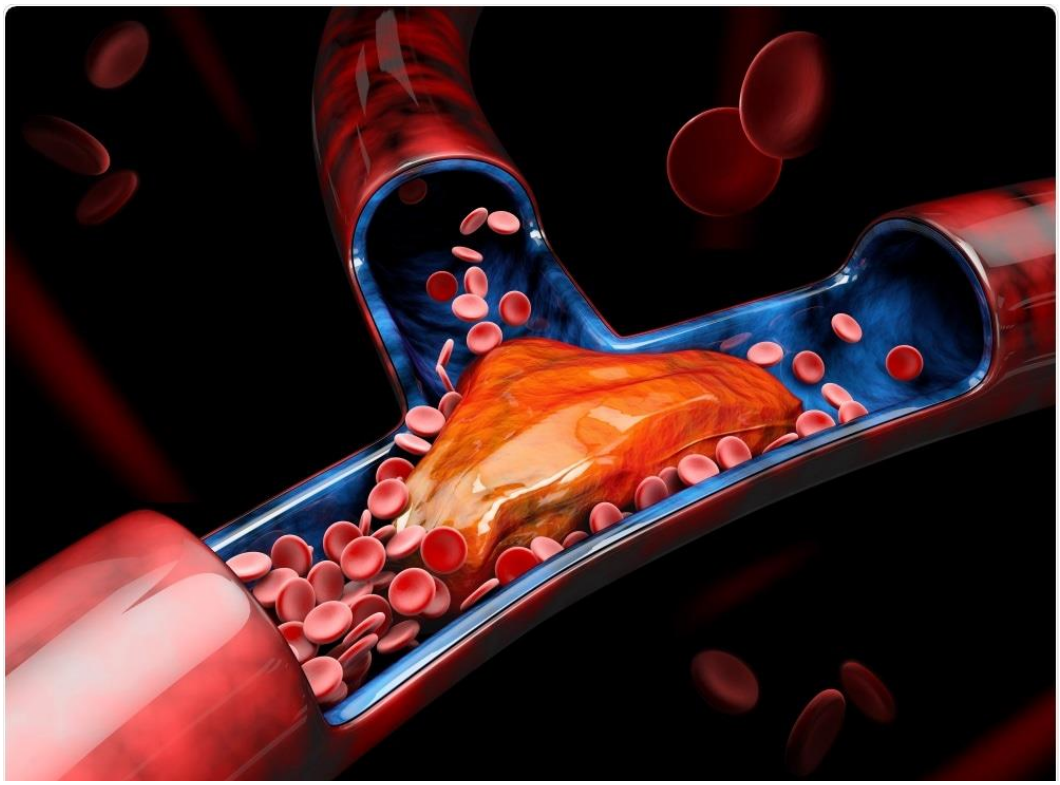
Best Regards,
Medical Team, Micro Labs Ltd

Deep vein thrombosis common in moderate to severe COVID-19 patients

Researchers from Russia have shown that patients with moderate and severe coronavirus disease (COVID-19) have a high incidence of deep vein thrombosis – indicating that anticoagulation therapy may need to be given early as part of their treatment regimen.



Amid the COVID-19 pandemic, a potentially fatal respiratory disease caused by severe coronavirus 2 (SARS-CoV-2) acute respiratory syndrome, data on various complications caused by this virus are still emerging and evolving in real-time. One of the potential complications is deep vein thrombosis, which is a condition that occurs in a large vein following the formation of a blood clot, most often in the calf. There may be pain, swelling, and sometimes pulmonary embolism (or a sudden lung blockage), making deep vein thrombosis a life-threatening condition. To date, several studies have shown a high incidence of venous thromboembolic complications in patients with severe and critical COVID-19; however, there is a lack of data on moderate to severe (but not critical) diseases. This is why researchers at the Federal State Clinical Research Hospital and Burnasyan Federal Medical Biophysical Center of the Federal Medical Biological Agency in Russia aimed to investigate the incidence of deep-vein thrombosis in patients with moderate to severe COVID-19 but also to evaluate its prevalence using imaging methods, clinical information and laboratory data.

This study explored 75 consecutive patients with moderate to severe COVID-19 during the first half of May 2020. They all underwent venous ultrasonography within seven days of admission to hospital, the standard imaging test used in patients suspected of having acute deep venous thrombosis. The analysis excluded critical COVID-19 patients admitted to the intensive care unit, patients with a known history of deep vein thrombosis, patients with more than 75 percent lung damage and patients with recent hip or leg trauma.

In 71 per cent of patients, detailed vein ultrasonography revealed spontaneous echo contrast in common femoral veins, indicating a decreased venous flow rate and blood stasis. Additionally, 16 patients had vein thrombosis; one of them had superficial thrombosis, while 15 patients developed deep vein thrombosis. Most patients had thrombi only in the veins of the calf, whereas two patients had ileofemoral thrombosis and floating thrombi with increased pulmonary embolism risk. Most of the thrombi were occlusive and located in the peroneal veins, tibial posterior veins and sinuses. Despite intensive anticoagulant therapy, the results were limited with low molecular weight heparins, and basically all thrombi persisted. In two of the cases, the alleged ileofemoral thrombosis posed a strong risk of pulmonary embolism, but early diagnosis tended to avoid the grim scenario.

In fact, two patients with deep vein thrombosis had thrombi in upper extremity veins, which illustrates the risk of significant thrombi development in patients with only mild COVID-19. Based on the findings of this report, we should understand the American Society of Hematology 's guidelines for controlling platelet concentration, partial thromboplastine duration, partial thromboplastin duration triggered, fibrinogen and D-dimer in all COVID-19 patients.

In addition, it may make sense to follow these patients even after recovery, and to carry out venous ultrasonography at some point in the future to rule out deep vein thrombosis. In the future, doctors around the world will need to consider adequate prevention of deep vein thrombosis in patients with moderate to severe COVID-19 by ordering early detection screening tests and making appropriate referrals for patients requiring prophylactic treatment.

Source: Kerbikov OB, Orekhov PY, Borskaya, EN, et al. High Incidence of Venous Thrombosis in Patients with Moderate to Severe COVID-19. medRxiv 2020 [Published online]. https://doi.org/10.1101/2020.06.12.20129536.

Immunosuppressive Phase of Septic Shock Patients with Alterations of B Cells

INTRODUCTION

Worldwide, 20 to 30 million patients are diagnosed with sepsis or septic shock each year, of which more than 8 million are killed. Worse still, over the next 20 years' overall mortality is projected to begin to increase at an unprecedented pace. More than 30 separate clinical trials have struggled to minimize sepsis-related mortality for the hyperinflammatory sepsis stage.

Sepsis is currently appreciated as leading to severe immunosuppression, and most deaths associated with sepsis occur during the immunosuppressive phase. Studies of septic patients and experimental animals have shown the causes of sepsis-induced immunosuppression, among which lymphocyte abnormalities are a significant one. The population of B-lymphocytes interacts with cells within the innate immune system and other adaptive immune system cells. The exhaustion of the B-cells inevitably contributes to sepsis immunosuppression. However, the role of B cells in sepsis was not well studied until recently and some studies have shown that they are more important than previously believed.

It has been shown that septic shock, a subset of sepsis associated with acute circulatory failure, has a crude mortality rate of more than 45 percent, but less studies of B cells have been carried out on it. In addition to the lineage-defined markers of CD19, CD20, as well as immunoglobulin M (IgM) and immunoglobulin D, a unique set of surface markers was shown to assist in the classification of mature human circulating B cells and was intensively used by HIV-1 investigators. In this study, five subsets of peripheral blood B cells were classified as follows, according to these markers: immature / transitional B cells, naive B cells, tissue like memory B cells, resting B cells and activated B cells. In HIV-1 infection the shifts in these B-cell subsets are closely linked to the development of the epidemic, viral replication, and therapeutic impact. During the immunosuppressive phase of septic shock, the alterations in B-cell subset counts and the principal function of B cells, antibody secretion, were investigated in this study. The differences were compared between healthy controls and patients with septic shock, as well as survivors of septic shock and nonsurvivors.

METHODS

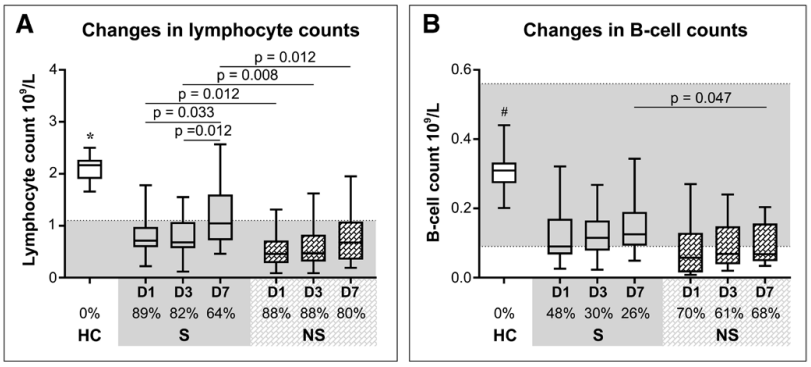
Design: Prospective cohort study.

Setting: Adult ICUs at a university hospital.

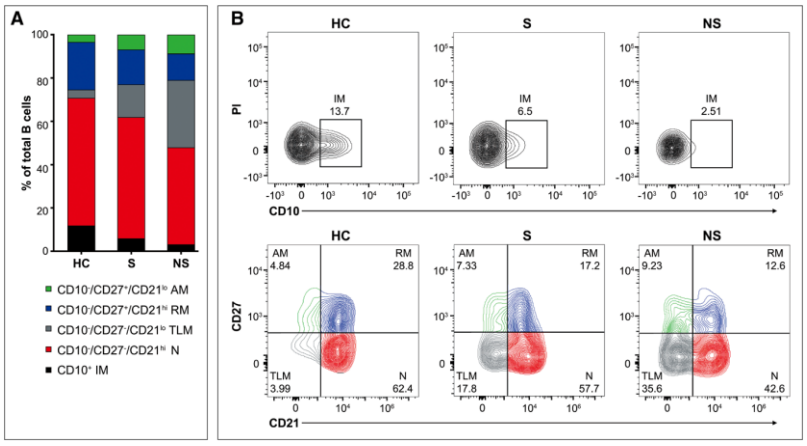
Patients: Adult septic shock patients without any documented immune comorbidity.

RESULTS

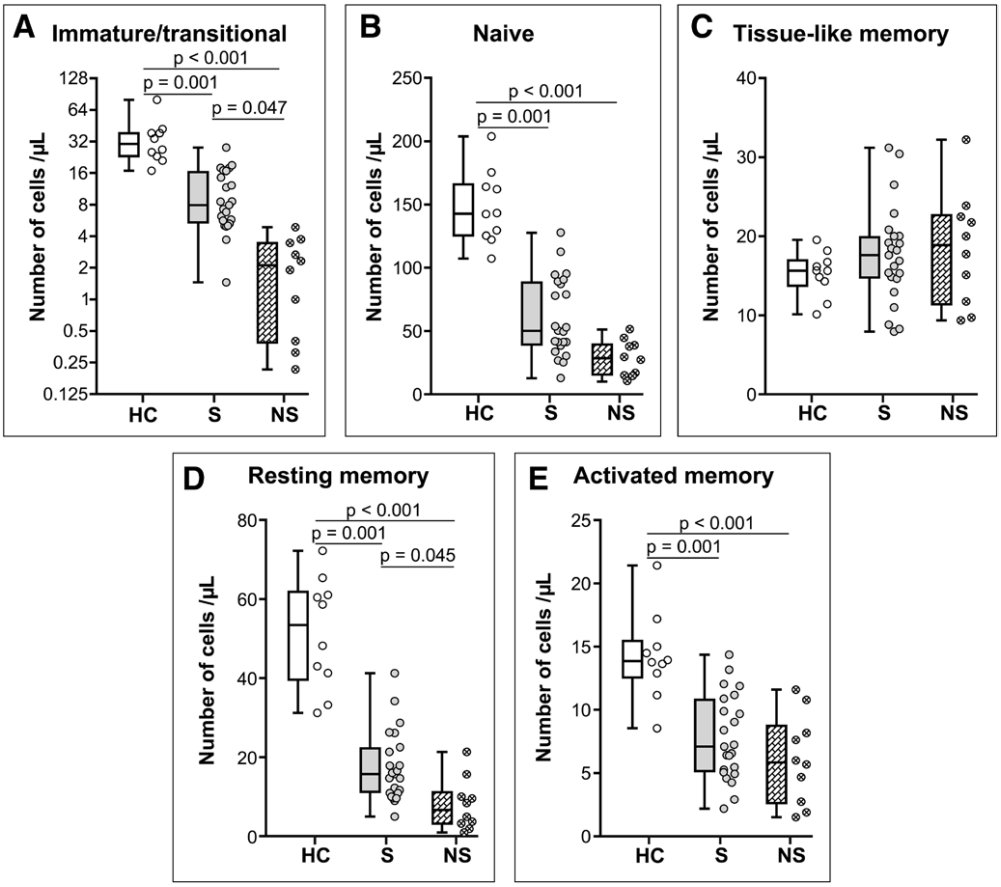
The absolute counts of lymphocytes and B cells of 81 patients and 13 healthy controls, and serum immunoglobulin levels of 64 patients and 10 healthy controls were determined by clinical laboratory. The percentages and counts of B-cell subsets of 33 patients and 10 healthy controls and the immunoglobulin M expression on B-cell subsets of 20 patients and five healthy controls were quantified by flow cytometry. Immunoglobulin levels produced by B cells after stimulation in vitro of 20 patients and five healthy controls were tested by enzyme-linked immunosorbent assay. Redistribution and selective depletion of B-cell subsets in septic shock patients were discovered, and a decrease in immunoglobulin M levels was associated with a reduction in resting memory B-cell counts. These alterations were more pronounced in nonsurvivors compared with survivors. Additionally, receiver operating characteristic curve analysis showed that the data of B-cell subsets had the best predictive value for mortality risk.



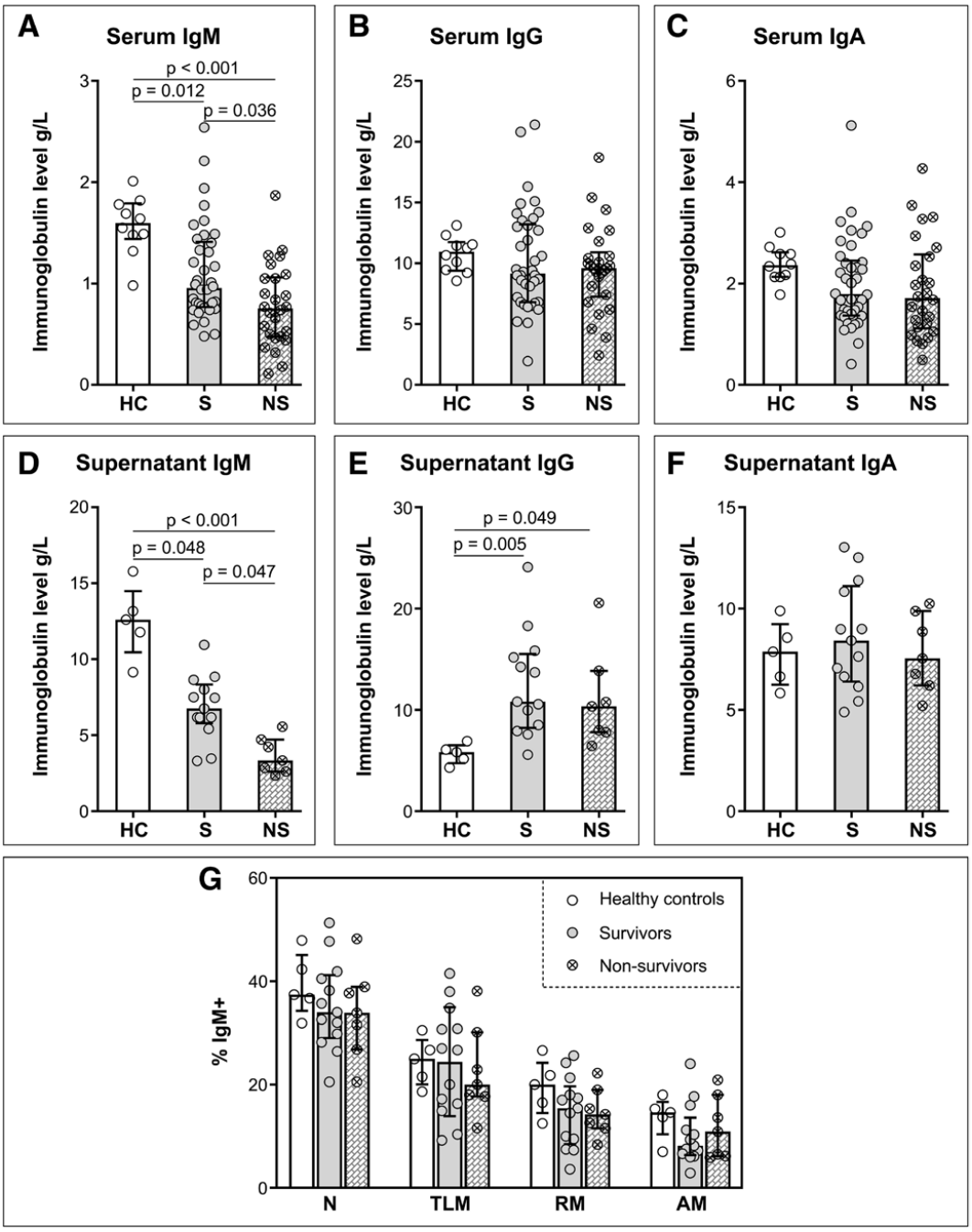
Lymphopenia, including B-lymphocyte population in septic shock patients. The proportions of people with lymphopenia (shaded area) are shown on the x-axis (A). The proportions of people with B-cell counts below the lower limit of the normal range (shaded area) are shown on the x-axis (B), and the proportions of nonsurvivors (NS, n = 24) with B-cell counts below lower limit of the normal range were higher than those of survivors (S, n = 57) (D1 = 70% vs 48%, D3 = 61% vs 30%, and D7 = 68% vs 22%, respectively; no statistical differences were made)



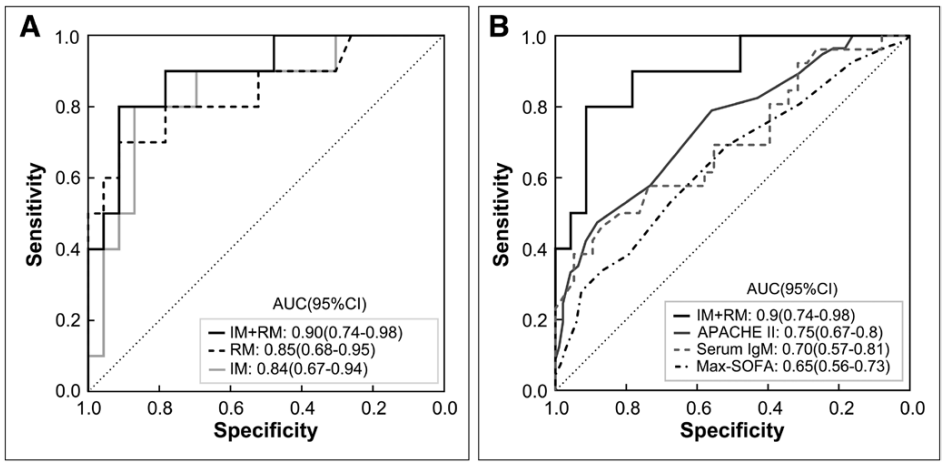
B-cell subset profiles in peripheral blood. Distribution of B-cell subsets in healthy controls (HCs) and septic shock patients. HCs = (n = 10), survivors (S) = (n = 23), and nonsurvivors (NS) = (n = 10) (A). A representative result reflecting the changing trend of the percentages of the five B-cell subsets among HCs, S, and NS (B).



Absolute counts of immature/transitional B cells (A), naive B cells (B), tissue-like memory B cells (C), resting memory B cells (D), and activated memory B cells (E) in peripheral blood of healthy controls (HCs, n = 10), survivors (S, n = 23) and nonsurvivors (NS, n = 10).



Serum and supernatant immunoglobulin levels and the expression of immunoglobulin M (IgM) on B-cell subsets. Serum immunoglobulin levels are measured in a total of 64 septic shock patients (including 13 patients who had been studied for total B-cell counts on day 1, 3, and 7 and the 33 patients who had been studied for B-cell subsets on day 7). Healthy controls (HCs) = (n = 10), survivors (S) = (n = 38), and nonsurvivors (NS) = (n = 26) (A–C). Supernatant immunoglobulin levels are measured in 20 septic shock patients who had been studied for B-cell subsets on day 7. HC (n = 5), S (n = 13), and NS (n = 7) (D–F). IgM expression levels on B-cell subsets are determined in another 20 patients. HC (n = 5), S (n = 13), and NS (n = 7) (G).



Receiver operating characteristic (ROC) curve analysis to compare the values of various indicators in predicting 60-d mortality risk of septic shock patients. Areas under the ROC curve (AUC) are presented with 95% CIs.

CONCLUSIONS

In the immunosuppressive process of septic shock patients, there was redistribution and systematic loss of subsets in terms of B-cell numbers, a decrease in IgM rates in terms in B-cell activity. Many anomalies of nonsurvivors were more severe. In addition, decreased levels of IgM may be linked to reduced counts of RM B-cells. Additionally, B-cell subset evidence exerted a strong predictive benefit for septic shock patient mortality event. Those results shed light on the significance of septic shock B-cell subsets.

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Pediatric Cardiopulmonary Resuscitation for Bradycardia and Poor Perfusion Versus Pulseless Cardiac Arrest: Survival and Hemodynamics

INTRODUCTION

More than 15,000 children are undergoing cardiopulmonary resuscitation (CPR), despite being treated daily in the United States. In comparison to adult cardiac arrests in the hospital (IHCAs), the bulk of pediatric IHCAs arise in the ICU and the original pulse is not shockable at more than 85 per cent. Most are the result of a systemic shock or respiratory collapse, as in adult IHCAs. Bradycardia and poor perfusion in children is a life-threatening response to hypoxemia and/or deep circulatory shock that often advances into pulseless cardiac arrest within minutes. As such, Pediatric Advanced Life Support protocols prescribe that children with bradycardia and low perfusion be given CPR. Bradycardia and poor perfusion are the initial rhythm of cardiac arrest in most occurrences in several contemporary studies. Compared with children with pulseless non-shockable rhythms, these children have higher survival rates to hospital discharge. In comparison, a new review of the registry showed that 31 per cent of children with bradycardia and weak perfusion also were pulseless during CPR. These patients had lower hospital discharge survival rates than either those with initial pulselessness or those with bradycardia that never became pulseless. The precise mechanisms that drive these differences in survival are not fully known, but perhaps superior hemodynamics during CPR have been speculated because CPR is initiated in the process of cardiorespiratory collapse at an earlier stage.

The study Pediatric Intensive Care Quality of CPR (PICqCPR) was a multicenter, prospective cohort study that found that mean diastolic blood pressure (DBP) values greater than or equal to 25 mm Hg for infants during CPR and greater than or equal to 30 mm Hg for older children were associated with higher survival rates for hospital discharge and favorable neurological outcome survival. The study Pediatric Intensive Care Quality of CPR (PICqCPR) was a multicenter, prospective cohort study that found that mean diastolic blood pressure (DBP) values greater than or equal to 25 mm Hg for infants during CPR and greater than or equal to 30 mm Hg for older children were associated with higher survival rates for hospital discharge and favorable neurological outcome survival. Additionally, among patients with bradycardia and poor perfusion, the authors aimed to compare patients with and without subsequent pulselessness during CPR.

METHODS

Design: Prospective, multicenter observational study.

Setting: PICUs and cardiac ICUs of the Collaborative Pediatric Critical Care Research Network.

Patients: Children (< 19 yr old) who received greater than or equal to 1 minute of cardiopulmonary resuscitation with invasive arterial blood pressure monitoring in place.

RESULTS

Of 164 patients, 96 (59%) had bradycardia and poor perfusion as the initial cardiopulmonary resuscitation rhythm. Compared to those with initial pulseless rhythms, these children were younger (0.4 vs 1.4 yr; p = 0.005) and more likely to have a respiratory etiology of arrest (p < 0.001). Children with bradycardia and poor perfusion were more likely to survive to hospital discharge (adjusted odds ratio, 2.31; 95% CI, 1.10–4.83; p = 0.025) and survive with favorable neurologic outcome (adjusted odds ratio, 2.21; 95% CI, 1.04–4.67; p = 0.036). There were no differences in diastolic or systolic blood pressures or event survival (return of spontaneous circulation or return of circulation via extracorporeal cardiopulmonary resuscitation). Among patients with bradycardia and poor perfusion, 49 of 96 (51%) had subsequent pulselessness during the cardiopulmonary resuscitation event. During cardiopulmonary resuscitation, these patients had lower diastolic blood pressure (point estimate, –6.68 mm Hg [–10.92 to –2.44 mm Hg]; p = 0.003) and systolic blood pressure (point estimate, –12.36 mm Hg [–23.52 to –1.21 mm Hg]; p = 0.032) and lower rates of return of spontaneous circulation (26/49 vs 42/47; p < 0.001) than those who were never pulseless.

Outcome	Adjusted Estimate[a] (95% CI)	*p*
Event hemodynamics[b]		
Above DBP targets[c]	0.92 (0.44–1.92)[d]	0.817
DBP, mm Hg	–3.28 (–7.49 to 0.94)[e]	0.129
Systolic blood pressure, mm Hg	3.33 (–6.36 to 13.02)[e]	0.501
Survival outcomes		
Survival to hospital discharge	2.31 (1.10–4.83)[d]	0.025
Survival with favorable neurologic outcome[f]	2.21 (1.04–4.67)[d]	0.036

Multivariable Models of Initial Rhythm with Hemodynamic and Survival Outcomes

Outcome	Overall ($n = 164$)	Bradycardia and Poor Perfusion ($n = 96$)	Pulseless ($n = 68$)	p
Event hemodynamics[a]				
Above DBP targets[b], *n* (%)	101 (61.6)	60 (63)	41 (60)	0.871[c]
DBP, mm Hg, median (IQR)	29.3 (22.8–37.9)	29.5 (22.0–36.4)	29.0 (24.9–39.0)	0.502[d]
Systolic blood pressure, mm Hg, median (IQR)	74.4 (54.9–98.2)	72.8 (55.0–97.4)	77.6 (54.0–99.1)	0.716[d]
Outcome of cardiopulmonary resuscitation event, *n* (%)				0.658[c]
Return of spontaneous circulation ≥ 20 min	112 (68)	68 (71)	44 (65)	
Return of circulation via extracorporeal cardiopulmonary resuscitation	36 (22)	19 (20)	17 (25)	
Died	16 (10)	9 (9)	7 (10)	
Survival outcomes, *n* (%)				
24-hr survival	135 (82)	80 (83)	55 (81)	0.684[c]
Survival to hospital discharge	77 (47)	52 (54)	25 (37)	0.039[c]
Survival with favorable neurologic outcome[e]	70 (43)	48 (50)	22 (32)	0.026[c]
Outcomes among survivors, *n* (%)				
New morbidity[f]	22/77 (29)	16/52 (31)	6/25 (24)	0.600[c]
New domain morbidity[g]	30/77 (39)	21/52 (40)	9/25 (36)	0.805[c]

Associations Between Hemodynamic and Survival Outcomes by Initial Rhythm

CONCLUSIONS

Bradycardia and poor perfusion were the initial CPR rhythm in 59 per cent of arrests in this multicenter observational study of pediatric IHCA. Children with bradycardia and low perfusion were more likely to continue through hospital release and live with beneficial neurological effects relative through pulseless rhythms, but there were no variations in the immediate result of the incident or intra-arrest hemodynamics. Upon initiation of CPR, patients who advanced to pulselessness had lower intraarrest hemodynamics and lower ROSC levels than those who were never pulseless during CPR.

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