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Critical Rounds

MICRO LABS LIMITED

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Best Regards,
Medical Team, Micro Labs Ltd

Umbilical cord mesenchymal stem cells in patients with severe COVID-19 pneumonia

No new medication treatments or vaccinations are required for the 2019 coronavirus disease pandemic (COVID-19), which is linked with substantial mortality. When handling patients with serious COVID-19 pneumonia, attenuating or eliminating the cytokine surge is key. It has been shown that mesenchymal stem cells (MSCs) have active immunoregulation and reparative properties with strong protection in damaged tissue. This study is intended to examine whether the therapy with umbilical cord MSC (UC-MSC) enhances the results of 31 patients with serious or essential COVID-19 pneumonia. At Taikangtongji Hospital in Wuhan, China, the authors would like to share their experience using UC-MSCs for treating serious COVID-19 pneumonia. Patient data were collected including demographics, clinical data, laboratory indices, treatment outcomes and outcomes in hospital. Severe acute respiratory coronavirus syndrome 2 (SARS-CoV-2) polymerase chain reaction (PCR) tests were favorable in both patients before infusion of UC-MSCs. Patients were diagnosed according to national guidelines and treated accordingly. UC-MSCs were suspended in 100 ml of normal saline before the intravenous drip was established. They record numbers (percentages) for categorical variables, and for continuous variables the median (interquartile range [IQR]) or mean ± standard deviation (SD). Comparisons of the intergroups is rendered with combined t checks. They diagnosed 31 patients with UC-MSCs who had COVID-19. The mean age was 70 years; it was male in 25 cases (80.6 per cent). The largest percentage of oxygen therapy was (31 [100%]), accompanied by antivirals, intravenous immunoglobulin (8 [25.8%]), intravenous albumin (8 [25.8%]), and methylprednisolone (6 [19.4%]).

The median volume (IQR) of infused UC-MSCs was around 200 mL (100–300 mL). Several adverse effects were due to intravenous UC-MSC transplants. After the first infusion of UC-MSCs, the tests of 30 patients (96.8 percent) on SARS-CoV-2 PCR were negative after a 10.7-day mean period. Laboratory parameters tended to improve after UC-MSC therapy, including elevated counts of lymphocytes, decreased levels of creactive protein, decreased levels of procalcitonin, decreased levels of interleukin-6, decreased levels of D-dimer and increased levels of PaO2 / FiO2. Their experience has shown that UC-MSC therapy in patients hospitalized with extreme COVID-19 without an infusion reaction will improve oxygenation and downregulate cytokine storms.

Characteristics	Before UC-MSC therapy	After UC-MSC therapy	*P* value
White blood cell count, $\times 10^9$/mL (normal range, 3.5–9.5)	6.72 ± 2.62	6.43 ± 1.72	0.346
Lymphocyte count, $\times 10^9$/mL (normal range, 1.1–3.2)	1.09 (0.68–1.35)	1.43 (1.02–2.20)	**< 0.001**
C-reactive protein, mg/L (normal range, < 10)	13.39 (1.30–38.86)	0.50 (0.50–6.40)	**0.003**
Procalcitonin, ng/mL (normal range, < 0.05)	0.07 (0.05–0.09)	0.04 (0.03–0.06)	**< 0.001**
Interleukin-6, pg/mL (normal range, < 7)	13.78 (5.69–25.26)	4.86 (2.13–8.19)	**< .001**
D-dimer, ng/mL (normal range, < 243)	495 (320–727)	288 (197–537)	**0.010**
PaO_2/FiO_2	242 (200–294)	332 (288–364)	**< 0.001**

UC-MSCs umbilical cord mesenchymal stem cells, *PaO_2/FiO_2 ratio* ratio of the partial pressure of arterial oxygen to the percentage of inspired oxygen

Comparison of laboratory parameters before and after UC-MSC therapy

That approach is a promising candidate for severe COVID-19 treatment. The number of patients rose rapidly during the outbreak of COVID-19 in Wuhan, China. The hospital capacity was, however, limited, and many patients were unable to be admitted to hospital. Therefore, days were long between the start of symptoms and referral to hospital. UC-MSCs may enhance the lung microenvironment, pulmonary fibrosis and lung quality, potentially attributable to inflammatory response control and tissue repair and regeneration promotion. A new study of 7 patients reported MSC therapy with the bone marrow to be a successful cure for extreme COVID-19. In addition, another recent research found that bone marrow MSC therapy in patients with extreme COVID-19 could boost hypoxia, immune reconstitution and cytokine storms, which was compatible with their findings. In order to confirm their results in the future, further large multicenter prospective trials are required.

Source: Guo Z, Chen Y, Luo X, et al. Administration of umbilical cord mesenchymal stem cells in patients with severe COVID-19 pneumonia. Critical Care 2020; 24:420.

A predictive biomarker for moderate-severe ARDS in severe COVID-19 patients

INTRODUCTION

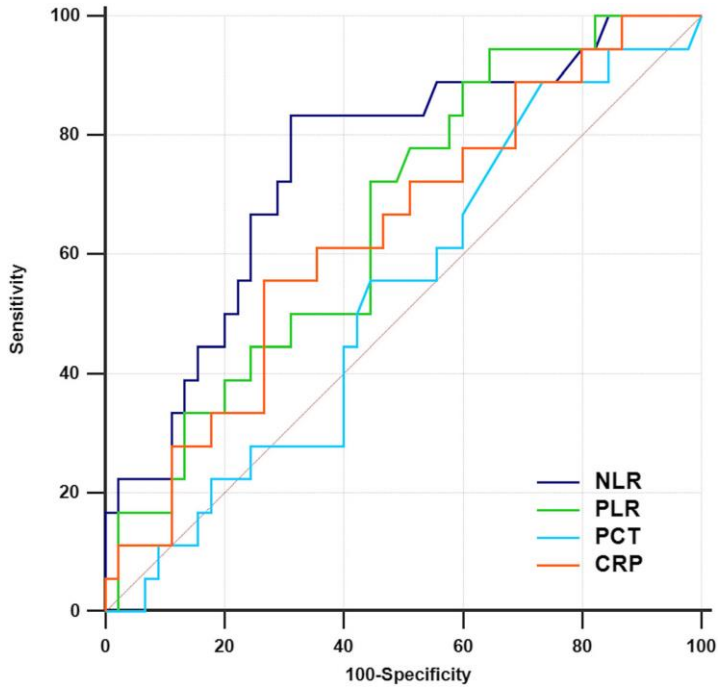
The COVID-19 pandemic has expanded exponentially around the world and has exhausted the supply of intensive care beds and ventilators; judicious distribution of ICU services is now one of the main problems for clinicians and administrators. The increased frequency of ARDS is the primary explanation that ventilator machinery is burdened. In the ICU, early prediction of the occurrence and worsening of ARDS helps clinicians to prepare for respiratory support equipment due to the lack of effective treatment strategies. In addition, V-V ECMO, which is a relatively scarce critical care resource, could successfully support early selected patients with severe ARDS who do not benefit from conventional treatment. Early warning of moderate-serious ARDS will also enable clinicians properly distribute limited ICU services for COVID-19 crisis. The neutrophil-to-lymphocyte ratio (NLR) is a simple inflammation biomarker that is measurable during routine hematology. Previous research has shown that higher NLR in COVID-19 patients are correlated with psychiatric decline and mortality. The degree to which NLR 's importance will forecast the frequency of ARDS and ICU ventilator specifications for the COVID-19 crisis remains uncertain, however.

METHODS

Patients diagnosed with severe COVID-19 from 21 hospitals in Sichuan Province between January 16 and March 15 were included in the analysis (ChiCTR2000029758). The maximum value of NLR, PLR, PCT, and CRP during the first 3 days after being diagnosed as severe COVID-19 was included in the analysis. Severe COVID-19 and ARDS were defined according to previous study and Berlin definition, respectively. Multivariate logistic regression analysis and the area under the receiver operating characteristic (ROC) curve were used to analyze the ability of NLR in predicting ARDS.

RESULTS

Of totally 81 patients defined as severe COVID-19, 44 were diagnosed as ARDS. The area under the ROC curve for ARDS was 0.71, 0.591, 0.494, and 0.625 for NLR, PLR, PCT, and CRP, respectively. They used the median as the cutoff value to divide the patients into two groups. The high NLR group (NLR > 9.8) showed a higher incidence of ARDS (P = 0.005) and higher rate of noninvasive (P = 0.002) and invasive (P = 0.048) mechanical ventilation. Further, they defined moderate severe ARDS as ARDS patients with oxygenation index less than 150. The area under the ROC curve for moderate-severe ARDS was 0.749, 0.660, 0.531, and 0.635 for NLR, PLR, PCT, and CRP, respectively; the cutoff value of NLR for moderate-severe ARDS is 11.



Moderate-severe ARDS prediction biomarkers in severe COVID-19 patients: NLR (0.749, 95% CI 0.624–0.850), PLR (0.660, 95% CI 0.530–0.775), PCT (0.531, 95% CI 0.401–0.658), and CRP (0.635, 95% CI 0.504–0.752)

CONCLUSIONS

NLR is an exceedingly popular laboratory method in which the initial NLR value may be used to distinguish patients with moderate-serious ARDS with an acceptable threshold value of 11. This biomarker can be useful in assessing respiratory equipment allocation in ICU patients and early ECMO assessment. Further clinical trials are, however, needed to determine the effects of NLR in ARDS.

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Importance of Family Members in Detecting Delirium in Critically Ill Patients

INTRODUCTION

Delirium is a disruption in awareness marked by an abrupt occurrence and fluctuating pattern in inattention, followed with either visual hallucinations or a loss in comprehension where a patient's capacity to acquire, process, store, and remember knowledge becomes affected. Delirium exists in one-third of ICU-admitted seriously ill patients and

For ICU patients it is correlated with adverse effects, including extended hospital visits, decreased likelihood of long-term neurological decline and death. Given its high incidence and adverse consequences, delirium can stay undetected at the ICU or be believed to be a common part of the clinical history of a patient. While clinical delirium detection tools such as the Intensive Care Delirium Screening Checklist (ICDSC) and the Confusion Assessment Method for ICU (CAM-ICU) have been implemented worldwide, there is no perfect screening approach and a high degree of variability in reported prevalence and occurrence rate estimates; up to 66 percent of delirium cases are missed using non-standardized clinical apps. Members of the family also know a patient best and will note small shifts in Cognition and actions in patients faster than an inexperienced professional analyst of the case. Many tools have been developed for detecting delirium in adults, including two familial tools identified in a recent systematic review: The Family Confusion Assessment Method (FAM-CAM) and Sour Seven, which have not been validated in the ICU.

By working with family members of patients to identify delirium, and as tools to measure sudden improvement in mental health, we can potentially be able to enhance patient and family treatment interactions and results. In a pilot test, their team investigated the viability and acceptability of using family-administered delirium diagnosis at ICU; Following modifications to the recruitment procedure, including the addition of a former ICU patient's family member to the study team, they determined that the study was both feasible and acceptable for patients and families. This research aimed to evaluate the diagnostic efficacy of two family-administered devices (FAM-CAM and Sour Seven) in order to diagnose delirium in critically ill patients.

METHODS

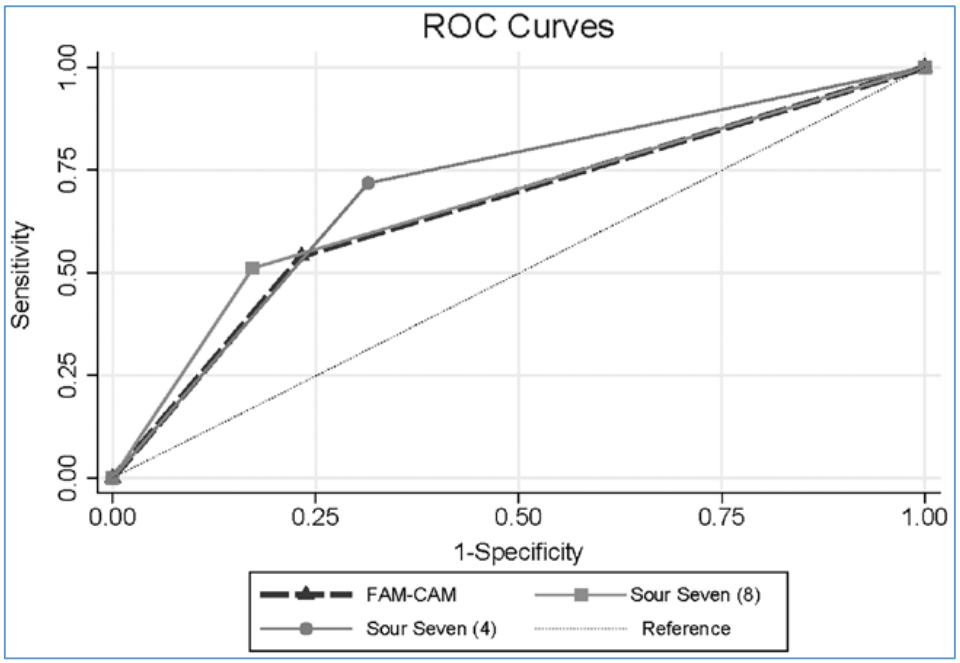
Design: Diagnostic accuracy study.

Setting: Large, tertiary care academic hospital in a single-payer health system.

Patients: Consecutive, eligible patients with at least one family member present (dyads) and a Richmond Agitation-Sedation Scale greater than or equal to –3, no primary direct brain injury, the ability to provide informed consent (both patient and family member), the ability to communicate with research staff, and anticipated to remain admitted in the ICU for at least a further 24 hours to complete all assessments at least once.

RESULTS

Family-administered delirium assessments (Family Confusion Assessment Method and Sour Seven) were completed once daily. A board-certified neuropsychiatrist and team of ICU research nurses conducted the reference standard assessments of delirium (based on Diagnostic and Statistical Manual for Mental Disorders, Fifth Edition, criteria) once daily for a maximum of 5 days. The mean age of the 147 included patients was 56.1 years, 61% of whom were male. Family members (n = 147) were most commonly spouses (n = 71, 48.3%) of patients. The area under the receiver operating characteristic curve on the Family Confusion Assessment Method was 65.0% (95% CI, 60.0–70.0%), 71.0% (95% CI, 66.0–76.0%) for possible delirium (cutpoint of 4) on the Sour Seven and 67.0% (95% CI, 62.0–72.0%) for delirium (cutpoint of 9) on the Sour Seven. These areas under the receiver operating characteristic curves were lower than the Intensive Care Delirium Screening Checklist (standard of care) and Confusion Assessment Method for ICU. Combining the Family Confusion Assessment Method or Sour Seven with the Intensive Care Delirium Screening Checklist or Confusion Assessment Method for ICU resulted in area under the receiver operating characteristic curves that were not significantly better, or worse for some combinations, than the Intensive Care Delirium Screening Checklist or Confusion Assessment Method for ICU alone. Adding the Family Confusion Assessment Method and Sour Seven to the Intensive Care Delirium Screening Checklist and Confusion Assessment Method for ICU improved sensitivity at the expense of specificity.



Receiver operating characteristic (ROC) curves for family administered delirium detection tools compared to the reference standard. FAM-CAM = Family Confusion Assessment Method.

CONCLUSIONS

Detection of delirium by family is possible and has reasonable, albeit poorer, diagnosis quality than clinical tests using the ICU's Intensive Care Delirium Screening Checklist and Uncertainty Appraisal process. Assessments of family relations are important for assessing cognitive capacity at the baseline. Having families of critically ill patients engaged and empowered warrants further study.

REFERENCES

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