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Dear Doctor,

Greetings from Micro Labs limited. We are happy to bring **"CRITICONNECT"** containing latest information in the field of Critical care medicine.

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Looking forward to your valuable feedback

Best Regards,
Medical Team, Micro Labs Ltd



Clinical trial begins on alpha-1-antitrypsin for critically ill COVID-19 patients

Clinician scientists at RCSI University of Medicine and Health Sciences have launched a clinical trial of a novel treatment for intensive care patients with seriously ill COVID-19. The team, headed by RCSI professors Gerry McElvaney and Ger Curley, explains improvements in the typical inflammatory response of the body in patients diagnosed with COVID-19 in a paper published in the American Journal of Respiratory and Critical Care Medicine, in particular for those that need admission to intensive care.

The researchers began a randomized double-blind placebo managed study of alpha-1-antitrypsin to treat medically ventilated critically ill patients with COVID-19 related ARDS in ICU. Alpha-1-antitrypsin is a naturally occurring human protein formed by the liver and released into the bloodstream that usually serves to shield the lungs from infectious disease disruptive behavior. Dr. Ger Curley, RCSI Professor of Anaesthesia and Critical Care and Consultant in Anaesthesia and Intensive Care explained that they are conscious from in-hospital trials that often ICU COVID-19 patients experience extreme inflammation in the body with a relatively high risk of progression to acute respiratory distress syndrome, acute kidney dysfunction, shock and cardiac arrhythmia.

A team of clinical scientists headed by Prof. McElvaney and Prof. Curley, in a partnership between the Departments of Medicine and Critical Care and Anaesthesia, tried to assess the form of inflammation involving the COVID-19 patient in ICU, and to evaluate if there was a association between this sort of inflammation and the need for intubation and mechanical ventilation. The research found that a variety of extremely inflamed proteins in compromised patients have both elevated when opposed to stable controls.

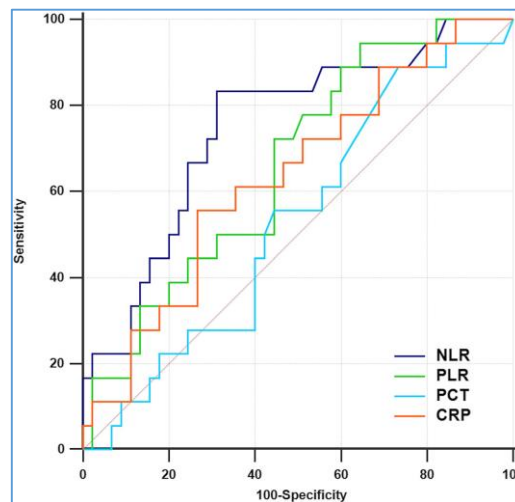
The demographics of patients at ICU and those who were contaminated but healthy often varied. Nevertheless, Prof. Curley clarified that the main unexpected differentiating factor between patients with stable and serious disease was not the degree of rise in inflammatory proteins, but instead the relative decline in anti-inflammatory protein rates, which suggests that the anti-inflammatory pathways of the patients had collapsed. Prof. Curley clarified that this result indicates that a treatment that improves the body's own activation and eliminates pathways may have a beneficial effect. During acute pulmonary infection Alpha-1 protects the airway from injury. This also serves as a effective anti-inflammatory and strengthens the immune system. Modulation of the production and activity of several key pro-inflammatory proteins has been shown to be of particular relevance to COVID-19. And that they are optimistic this clinical trial would show Alpha-1's ability to boost results for patients with the most serious respiratory problems caused by COVID-19. This is the first Ireland-approved investigational medicine product trial to test a therapy to treat COVID19. The research is funded by RCSI Medical and Health Sciences University and is conducted by RCSI Clinical Research Centre.

Neutrophil-to-lymphocyte ratio as a predictive biomarker for moderate-severe ARDS in severe COVID-19 patients

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 why ventilator machinery is burdened. In the ICU, early detection of the incidence and deterioration of ARDS allows physicians to plan for respiratory assistance devices owing to the lack of appropriate care approaches. In fact, V-V ECMO, which is a fairly unavailable critical care option, may effectively help early chosen patients with serious ARDS that may not benefit from traditional therapy. Early warning of moderate-serious ARDS will also enable clinicians properly distribute limited ICU services for COVID-19 crisis.

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. Study involved patients infected with extreme COVID-19 from 21 hospitals in the province of Sichuan between 16 January and 15 March (ChiCTR2000029758). The highest amount of NLR, PLR, PCT, and CRP was included in the study during the first 3 days since being classified as extreme COVID-19. Severe COVID-19 and ARDS were defined according to the definition of earlier study and Berlin, respectively. In the study of NLR 's capacity to forecast ARDS, multivariate logistic regression analysis and the field under the receiver operating characteristic (ROC) curve have been used. Of the total of 81 identified as extreme COVID-19 patients, 44 were classified as ARDS. The area under ARDS 'ROC curve was 0.71, 0.591, 0.494, and 0.625, respectively, for NLR, PLR, PCT, and CRP. To split the patients into two categories, we used the median as the cutoff number. The high NLR group ($NLR > 9.8$) showed a higher incidence of mechanical ventilation in ARDS ($P = 0.005$) and a higher incidence of noninvasive ($P = 0.002$) and invasive ($P = 0.048$). We have described moderate severe ARDS as patients with an oxygenation index of less than 150. The area for moderately severe ARDS under the ROC curve was 0.749, 0.660, 0.531, and 0.635 for NLR, PLR, PCT, and CRP, respectively; the NLR cutoff value for moderately severe ARDS is 11.

Our data revealed that NLR could be a valuable biomarker for recognizing severe COVID-19 patients with moderate-severe ARDS, which made it easier for clinicians to provide effective breathing support strategies and quickly identify moderate-severe ARDS patients with high V-V ECMO indication.



Moderate-severe ARDS prediction biomarkers in severe COVID-19 patients

A thorough analysis of immune markers would boost early diagnosis for COVID-19 patients with "atypical" ARDS due to the lack of correlation between oxygenation and lung function. NLR is an extremely common laboratory test in which the initial NLR value can be used to identify patients with moderate-serious ARDS with the optimal threshold value.

Total of 11. This biomarker can be useful in assessing respiratory equipment allocation in ICU patients and early ECMO assessment. Further clinical studies are, however, required to assess the benefits of NLR in ARDS.

REFERENCES

Ma A, et al. Neutrophil-to-lymphocyte ratio as a predictive biomarker for moderate-severe ARDS in severe COVID-19 patients. Crit Care. 2020; 24: 288

Interventions supporting long term adherence and decreasing cardiovascular events after myocardial infarction (ISLAND) trial

INTRODUCTION

For nearly all patients with signs of coronary heart damage following a myocardial infarction, recommendations prescribe long-term use of four types of drugs: statins, antiplatelets, β blockers, and angiotensin pathway antagonists (that is, angiotensin binding enzyme antagonists or angiotensin receptor blockers). The medications tend to have an cumulative effect, and exposure to some of them is related to lower death, lower morbidity, and reduced health care costs. Most patients are released with these medications following a myocardial infarction. Nonetheless, suboptimal sensitivity to cardiac medications is normal and almost half of patients discontinue their drug 12 months following myocardial infarction. When addition to medications, experts encourage involvement when cardiac therapy for additional treatment of myocardial infarction. Patients are provided with information to enhance adherence to cardiac drugs and a supervised physical activity plan to reduce cardiovascular mortality and improve the quality of life, whether in a healthcare institution or at home. Sadly, during myocardial infarction most people are not referred and thus do not engage in cardiac recovery programs. Cochrane 's 2014 analysis of strategies to improve drug adherence acknowledged that multiple studies include multifaceted approaches that will be difficult to execute on a scale. Conversely, a new economic study found that informative updates delivered via mail are the most likely to be cost-effective of all the current approaches to increase commitment to opioid therapy following myocardial infarction. Cochrane 's 2019 analysis of strategies to improve commitment to therapy described reasonably low cost approaches, including mailed letters, as being effective if adapted to the limitations of the individual, but stated that more research was required to guide best practice. Here, we present the results of the Interventions Supporting Long term Adherence aNd Decreasing cardiovascular events after myocardial infarction (ISLAND) trial.

ISLAND evaluated the results of a collection of mailed informative updates, with or without the inclusion of telephone calls from an electronic immersive voice response device and a qualified lay health professional, as opposed to the normal commitment to approved secondary preventive procedures.

METHODS

DESIGN: Three arm, pragmatic randomised controlled trial with blinded outcome assessment.

SETTING: Nine cardiac centres in Ontario, Canada.

PARTICIPANTS: 2632 patients with obstructive coronary artery disease after a myocardial infarction, identified from a centralized cardiac registry.

INTERVENTIONS: Participants were randomized 1:1:1 to receive usual care, five mail-outs developed through a user centered design process, or mail-outs plus phone calls. The phone calls were delivered first by an interactive automated system to screen for non-adherence to treatment. Trained lay health workers followed up as necessary. Interventions were coordinated centrally but delivered from each patient's hospital site.

MAIN OUTCOME MEASURES: Co-primary outcomes were completion of cardiac rehabilitation and adherence to recommended medication. Data were collected by blinded assessors through patient report and from administrative health databases at 12 months.

RESULTS

2632 patients (mean age 66, 71% male) were randomised: 878 to the full intervention (mail plus phone calls), 878 to mail only, and 876 to usual care. Of the respondents, 174 (27%) of 643 in the usual care group, 200 (32%) of 628 in the mail only group, and 196 (37%) of 531 allocated to the full intervention completed cardiac rehabilitation (adjusted odds ratio 1.55, 95% confidence interval 1.18 to 2.03). In the mail plus phone group, 11.7%, 6.0%, 14.4%, 32.9%, and 35.0% reported adherence to 0, 1, 2, 3, and 4 drug classes after one year, respectively, in comparison with 12.5%, 6.8%, 13.6%, 30.2%, and 36.8% in the mail only group, and 12.2%, 8.4%, 13.1%, 30.3%, and 36.1% in the usual care group, respectively (mail only v usual care, odds ratio 0.98, 95% confidence interval 0.81 to 1.19; full intervention v usual care, 0.99, 0.82 to 1.20).

CONCLUSIONS

This comprehensive, three-arm, single-blind, multicenter randomized study through provinces found that therapeutic theory-informed approaches and patient feedback provided through both mail and phone would substantially improve the presence and completion of cardiac recovery following myocardial infarction, although not adherence to medicine. Routinely collected data will help service implementation of improving health systems (and vice versa); this research illustrates both the benefits and limitations of utilizing registry data to endorse system-wide quality assurance trials. This research further illustrates how systemic management successfully enabled the introduction of evidence-based care through the utilization of administrative statistics, not just for surveillance, but also for measures to better benefit high-risk individuals. This is therefore seen the viability realistic assessments of these initiatives to educate the programme's scope, size and quality improvement.

REFERENCES

Ivers NM, et al. Interventions supporting long term adherence and decreasing cardiovascular events after myocardial infarction (ISLAND): pragmatic randomised controlled trial. *BMJ* 2020;369:m1731.

