News and Views

CRP: A Potential Biomarker to Predict Risk of Delirium in Stroke Patients

Acute stroke patients with high C-reactive protein (CRP) levels >7.09 mg/L are at greater risk for developing delirium, suggests a study from Poland published in the journal *Acta Psychiatrica Scandinavica*.[1]

For this study, researchers retrospectively analyzed data from 459 patients who had been hospitalized for acute stroke or transient ischemic attack (TIA) within 24 hours with the aim to find out if including CRP with other clinical factors (Models A and B) could enhance prediction of delirium in these patients. The factors in Model A were age and stroke severity, while in Model B, severity of stroke, diabetes, atrial fibrillation, pre-stroke dependency and hemorrhagic stroke were the factors included. They were a part of the PRospective Observational POLIsh Study on delirium (PROPOLIS), which was an observational, prospective single-center study and had recruited patients with ischemic stroke, TIA or intracerebral hemorrhage from May 2014 to March 2016, within 48 hours of symptoms. Patients who had CRP measured at baseline were enrolled for this study. Their median age was 73 years and more than half (52.7%) the study population was comprised of women. Patients were evaluated for neurological deficits (National Institutes of Health Stroke Scale [NIHSS]), cognitive decline, pre-stroke dependency (modified Rankin Scale) and delirium (Brief Confusion Assessment Method for verbal patients and the Confusion Assessment Method for the Intensive Care Unit for nonverbal patients).

Nearly one-third (29.2%) of patients developed delirium with 46.2% experiencing mixed delirium, 39.2% hypoactive delirium and 14.2% hyperactive delirium. The delirious patients also had higher levels (median) of CRP than those who did not have delirium; 13.2 mg/L vs. 4.4 mg/L, respectively.

A cut-off level of 7.09 mg/L was identified as marking the distinction between the two groups. On univariate analysis, CRP and other clinical factors such as age, diabetes, atrial fibrillation, pre-stroke dependency, pre-stroke cognitive decline, NIHSS score on admission. Hemorrhagic stroke were associated with increased risk for delirium. But on multivariate analysis, this association remained significant only for CRP. The risk was threefolds higher in patients with CRP levels >7.09 mg/L with an adjusted odds ratio (aOR) of 2.98. The researchers also noted that addition of CRP to the two clinical models examined, the "area under receiver operator curve increased from 0.77 to 0.80 for Model A and from 0.81 to 0.84 for Model B."

Delirium in stroke patients is indicative of a poor clinical outcome. Identification of a factor that could predict development of delirium enables monitoring of at-risk patients and timely implementation of appropriate management strategies. CRP, a marker of systemic inflammation, is a commonly performed test in clinical practice. Based on their findings, the authors suggest CRP as a potential marker for risk of delirium in post-stroke patients. Acute stroke patients with high CRP levels, above the cut-off level defined in this study, should be closely monitored for delirium.

(*Ref: [1]Klimiec-Moskal E, et al. Serum C-reactive protein adds predictive information for post-stroke delirium: The PROPOLIS study. Acta Psychiatr Scand. 2022 Aug 23. [Epub ahead of print]*)

Strong Immune Response Induced by Monkeypox Vaccine

According to a study published recently in the journal *Viruses*, the vaccines based on the vaccinia virus (VACV) could create a potent immune response against the monkeypox virus that is causing the current outbreak.

The vaccine virus is a large, intricate, enveloped member of the poxvirus family. More than 52,000 cases have been confirmed in more than 90 countries and regions since the new virus was originally discovered in early May.

The study compared and contrasted the genetic makeup of VACV and MPXV-2022, focusing on the regions of the proteins that T cells or antibodies produced as a result of vaccination target. The study more broadly demonstrates that VACV and MPXV-2022 are highly genetically similar in the regions targeted by the immune system through vaccination. Researchers claim to have identified a small number of distinct mutations in MPXV-2022.

Based on the analysis, it is predicted that the immune responses produced by VACV-based vaccinations would continue to perform an excellent job of recognizing and responding to MPXV-2022.

Pre-exposure prophylaxis, commonly known as primary preventive immunization against the novel monkeypox virus, has been advised by the World Health Organization (WHO) for people who are at a high risk of exposure.

The researchers concluded that combining sequencing and immunological data provided evidence to expect a high immune response, but additional clinical studies were needed to precisely assess these vaccines' efficacy against MPXV-2022. (*Source: The Print, Sept. 9, 2022*)

Scientists Identify Two Antibodies which may be Effective against All Known COVID Strains

Israeli researchers have identified two antibodies from the immune systems of coronavirus disease 2019 (COVID-19) patients who have recovered that have a 95% chance of neutralizing all known strains of severe acute respiratory syndrome coromavirus 2 (SARS-CoV-2), including Omicron. The investigation, which was just published in the journal *Communications Biology*, is an extension of initial work done in October 2020 at the height of the COVID-19 crisis.

The researchers found nine antibodies after sequencing all of the B immune system cells from the blood of persons who had recovered from the initial COVID-19 strain in Israel at the time. According to the research, the new coronavirus variants, Delta and Omicron, can be neutralized by some of these antibodies.

The SARS-CoV-2 virus uses the spike protein to invade and enter cells. Researchers demonstrated that the Delta and Omicron variants could be effectively neutralized by two more antibodies, TAU-1109 and TAU-2310, which bind the viral spike protein in a different location than the sites where most antibodies have previously been focused.

According to experts, the first antibody, TAU-1109, is 92% successful at neutralizing the Omicron strain and 90% effective at neutralizing the Delta strain. The second antibody, TAU-2310, is 84% effective at neutralizing the Omicron variation and 97% effective at neutralizing the Delta variant. Thus, these findings may be a helpful alternative for vaccines, especially for high-risk groups and immunocompromised people. (*Source: Finance Express, Sept. 8, 2022*)

NIH Launches Trial of Tecovirimat for Monkeypox

The National Institutes of Health (NIH) has commenced a phase 3 randomized, placebo-controlled, double-blind clinical trial STOMP (Study of Tecovirimat for Human Monkeypox Virus; A5418) investigating the safety and efficacy of the antiviral drug tecovirimat in patients with monkeypox. The recruitment of patients, both adults and children, with monkeypox infection in the United States is now on. A total of 530 volunteers will be enrolled. Tecovirimat is currently available for US patients through an expanded access or "compassionate use" request put in by the clinicians. The multicenter trial is being led by the AIDS Clinical Trials Group (ACTG), which is the largest body engaged in global HIV research.

All patients with severe monkeypox and persons at risk of severe disease including children, pregnant and lactating women, immunocompromised patients or those with active inflammatory skin disease will be administered the drug in the open-label arm of the trial. Other patients would be randomized to receive tecovirimat or placebo orally for 14 days in a 2:1 ratio. Patients who develop severe disease or experience severe pain will have the option to move to the open label arm.

The impact of the drug on pain scores, progression to severe disease and clearance of monkeypox virus will be studied in addition to its safety. Pediatric dosing and safety will also be examined. Optimal dosing for pregnant women will also be a part of the study.

The follow-up period will be 8 weeks during which the participants will be required to maintain a symptom diary, carry out daily self-skin examination for the status of skin lesions and visit the clinic, both virtual and in-person. Blood samples and swabs from skin lesions will be collected.

(*Sources: National Institutes of Health (NIH) Press Release, September 9, 2022. AIDS Clinical Trial Group (ACTG) Press Release, September 9, 2022.*)

Short-term Benefits of Robotic Surgery for Rectal Cancer

The oncological quality of resection was better with robotic surgery in patients with middle and low rectal cancer with fewer positive resection margins compared to the standard laparoscopic surgery, reports a multicenter, randomized trial from China in the *Lancet Gastroenterology & Hepatology*.[1]

Researchers recruited 1,240 patients, aged 18 to 80 years, with low (≤5 cm from the anal verge) and middle (>5 to 10 cm from the anal verge) adenocarcinoma of the rectum, cT1-T3 N0-N1 or ycT1-T3 Nx stage with no sign of distant metastasis. They (620 patients in each group) were randomized 1:1 to undergo robotic or laparoscopic resection from July 2016 to December 2020.

Locoregional (pelvic/perineal) recurrence rate at 3 years was the primary outcome of the study, while a positive circumferential resection margin and complications within 1 month of the surgery were the secondary endpoints. The objective of this multicenter, randomized, controlled, superiority trial was to compare the two procedures in terms of surgical quality and outcomes in the long-term. This trial is ongoing and only the short-term outcomes have been reported at present. The primary endpoint results are expected by the end of next year.

Among the 1,171 patients in the modified intention-to-treat analysis, results showed fewer positive circumferential resection margins in 4% (22/547) patients who underwent robotic surgery versus 7.2% (39/543) among those in the laparoscopic surgery group. The postoperative complication rate within 30 days of surgery was 16.2% with robotic surgery versus 23.1% with laparoscopic surgery. Grossly, the resection was more complete in the robotic surgery group (95.4%; 559/586) compared to the laparoscopic surgery group (91.8%; 537/585). The benefits of robotic surgery were also evident intraoperatively with less estimated blood loss (40 mL vs. 50 mL) and fewer complications (5.5% vs. 8.7%). Ninety-nine (~17%) robotic surgery patients needed abdominoperineal resections for low rectal cancer, while this number was 133 (~23%) in the laparoscopic group.

Postoperatively, robotic surgery patients exhibited better gastrointestinal recovery (shorter time to first flatus and bowel movement); they also had shorter hospitalization (7 days vs. 8 days, respectively [median]). Just 10 patients in this group required conversion of the procedure to open surgery, whereas 23 patients in the laparoscopic group needed open surgery. Although the total costs incurred were higher with the robotic surgery, the costs in the postoperative period were less ($2,768 vs. $3,060).

The short-term results of the secondary endpoints of this study demonstrate better circumferential resection margins indicating "better oncological quality of resection" with robotic surgery compared to laparoscopic surgery with "better postoperative recovery" suggesting that robotic surgery was superior to laparoscopic surgery for patients with mid or low rectal cancer.

(*Ref: [1]Feng Q, et al. Robotic versus laparoscopic surgery for middle and low rectal cancer (REAL): short-term outcomes of a multicentre randomised controlled trial. Lancet Gastroenterol Hepatol. 2022;7(11):991-1004.*)

Bell's Palsy in Children Cured without Medication in 6 Months

A recent study from the Murdoch Children's Research Institute, which was published in *Neurology*, found that most children with Bell's palsy, which temporarily weakens or paralyses the muscles in the face, recovered without medication in less than 6 months. Prednisolone had no discernible impact on a child's Bell's palsy recovery, but it did minimize facial nerve swelling and temporal bone damage in adults.

The randomized controlled study included 187 Bell's palsy patients who visited emergency departments (EDs) between 6 months and 17 years. Within 72 hours of the onset of symptoms, they were enrolled and administered either prednisolone or a placebo for 10 days. The investigation was carried out in 11 EDs using sites provided by Australia and New Zealand's Paediatric Research in Emergency Departments International Collaborative (PREDICT) research network.

The observations found that 57% of those who did not take any medication had their facial function restored after 1 month, 85% had it back after 3 months and 93% had it back after 6 months. Recovery rates in individuals who received prednisolone were 49% after 1 month, 90% after 3 months and 95% after 6 months. During the testing, no adverse events were identified. Brief behavioral changes and an increase in hunger were the most frequent events observed.

Experts stated that the use of steroids in children with Bell's palsy had not been proven. However, knowing that early prednisolone therapy does not speed up recovery may help medical professionals, emergency room physicians and pediatricians to have better conversations with impacted families. (*Source: Hindustan Times, Sept. 10, 2022*)

Chances of Fertilization may be Enhanced by a New Protein MAIA

A large number of beads, each with a unique protein fragment, were used to create artificial eggs by an international team of researchers, enhancing the likelihood of fertilization. According to research results that were published in the journal *Science Advances*, just a small fraction of the beads had sperm attached to them when sperm was incubated with them.

Researchers eventually found that beads corresponded to one specific protein, MAIA, and sperm linked to all of these beads after going through numerous rounds of deleting beads that didn't have sperm bound to them. The novel protein MAIA, which bears the name of the

Greek motherhood goddess, is thought to be responsible for attracting sperm into the egg for fertilization. After inserting the MAIA gene into human culture cells, these cells became receptive towards the sperms precisely in a similar manner as they would in normal fertilization.

The discovery of the MAIA protein not only significantly advances the understanding of the human fertilization process but it also opens up new avenues for the treatment of infertility and will transform the development of future contraceptives. (*Source: The Tribune, Sept. 9, 2022*)

Similar CVD Risk Factors Found among Men and Women

Researchers found that the several risk factors for cardiovascular disease (CVD) are the same for both men and women. The study was published in the journal *The Lancet*. It included individuals from low- and middle-income nations, where the prevalence of CVD is higher, in addition to high-income ones.

The large-scale study evaluated risk variables in around 1,56,000 persons without a history of CVD between the ages of 35 and 70, including metabolic (such as high blood pressure, obesity and diabetes), behavioral (smoking and food) and psychosocial (economic status and depression). They were monitored for an average of 10 years while residing in 21 low-, middle- and high-income nations across five continents.

Similar CVD risk factors for men and women highlight the significance of a similar approach to preventing CVD in both sexes. In general, women had a lower risk of CVD than men, especially when younger. However, women's CVD risk was more strongly correlated with their dietary habits than men's.

Depression and high levels of bad (LDL) cholesterol were more significantly linked to CVD risk in males than in women. High-income, upper-middle-income, low-income and lower-middle-income countries generally showed similar patterns in these findings. (*Source: Hindustan Times, Sept. 09, 2022*)

First Oral Once-a-Day Treatment for Patients with Moderate to Severe Plaque Psoriasis

Deucravacitinib, the first-in-class tyrosinase kinase 2 (TYK2) inhibitor has been approved by the US Food and Drug Administration (FDA) for patients with moderate to severe plaque type psoriasis making it the only approved TYK2 inhibitor. It is indicated only for those patients who need systemic therapy or phototherapy.

This approval is based on the results of the phase III POETYK PSO-1 and PSO-2 clinical trials where deucravacitinib was superior to placebo and apremilast in improving skin clearance.

Dose: 6 mg orally once daily, with or without food.

Contraindication: Hypersensitivity to deucravacitinib or any of its components, severe hepatic impairment.

Side effects: Upper respiratory infection, increased creatine phosphokinase (CPK), herpes simplex, mouth ulcers, folliculitis, acne.

Warnings and precautions

- Avoid co-administration with other immuno-suppressant drugs or live vaccines. All age-appropriate immunizations should be complete prior to starting treatment.
- Avoid deucravacitinib in patients with active or serious/opportunistic infection.
- Monitor the patient for signs and symptoms of infection. Discontinue treatment in case serious infection develops.
- Examine the patient for tuberculosis before starting treatment with deucravacitinib.
- Regularly monitor serum triglycerides and liver enzymes.
- Stop the drug if CPK levels increase significantly.

(*Sources: US FDA Sotyktu prescribing information; Bristol Myers Squibb Press Release, Sept. 9, 2022*)