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Using Biomarkers for Traumatic Brain Injury: Are There Lessons That Can Be Learned from Implementing Cardiac Troponin?

Article:
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Guest: Dr. Alan Wu is a Professor of Laboratory Medicine at the University of California, San Francisco and is Co-Core Lab Director at Zuckerberg San Francisco General Hospital.

Bob Barrett: This is a podcast from *Clinical Chemistry*, a production of the American Association for Clinical Chemistry. I'm Bob Barrett.

Every year in the United States, approximately five million people seek care at a hospital emergency department for the evaluation of traumatic brain injury. One task for the medical team is to diagnose or rule out acute traumatic encephalopathy, and serum biomarkers are under consideration as a diagnostic tool to complement clinical evaluation and imaging studies. A negative test result essentially excludes traumatic encephalopathy but a positive result is harder to interpret as these biomarkers are released in other neurologic conditions.

While initial studies have generated promising results, a concerted effort by laboratorians and test manufacturers will be needed to avoid pitfalls encountered during the implementation of other clinical laboratory tests. A perspective article appearing in the June 2023 issue of *Clinical Chemistry* draws parallels between the development of traumatic brain injury biomarkers and the evolution of cardiac troponin assays for the assessment of myocardial injury.

A clinical laboratorian with expertise in both fields explains how lessons learned from cardiac troponin can help maximize the positive impact of TBI biomarker assays on patient care. In this podcast, we're excited to talk with the author of the perspective article. Dr. Alan Wu is a Professor of Laboratory Medicine at the University of California San Francisco and is Co-Core Lab Director at Zuckerberg San Francisco General Hospital.

Dr. Wu, let's get basic first. What are the causes of mild traumatic brain injury?

Alan Wu: Well, there are many causes. Probably the most common are falls that we see, certainly with an elderly population, but there can also be contact sports injuries. You think of football, hockey, soccer, perhaps judo or wrestling. There can be traffic accidents, which probably occur more often in the young adult ages, whether it be motorcycle or car accidents.

Bob Barrett: What are the current blood-based biomarkers for mild traumatic brain injury?

Alan Wu: Well, there are a few. There's only one set that is FDA-approved but all the others are in varied stages of research investigation. S100 beta, there is neurofilament protein, there is probably a dozen that are thrown about in the literature today.

Bob Barrett: So, how is mTBI currently diagnosed?

Alan Wu: Concurrently, it's diagnosed by medical history and physical exam. The obvious cases of TBI, where you have bruising or bleeding or memory loss or severe concussions; we don't need a biomarker for that. Those are pretty evident. It's the mild cases, where you're not sure if there were any actual cerebral damage or not, that are difficult to do by just physical exam and taking a history and therefore, the need for a blood test.

Bob Barrett: Earlier, you mentioned that there was an FDA-approved mTBI test. What is that test and what is its medical indications?

Alan Wu: So, every laboratory has an FDA clearance for their TBI tests. This includes a combination of testing for ubiquitin C-terminal hydrolase L1 and glial fibrillary acidic protein. When negative, this indicates that a traumatic brain injury, a mild traumatic brain injury, has been ruled out and it obviates the need to do a head CT scan. Head CT scans are invasive, they expose the individual to radiation, there is an expense involved, there is a time involved, there's expertise. All of these things consume resources but if we have a blood test, that can obviate the need for that test and so much the better.

Right now, we don't have any FDA-approved laboratory blood tests that diagnose TBI and that's something I think that we're hoping to see in the near future.

Bob Barrett: Well, finally Dr. Wu, why are biological variation studies an important consideration for the diagnosis of mild traumatic brain injury?

Alan Wu: So, biologic variation studies determine the within-individual change in biomarker levels during health and the differences between biomarker levels during health between individuals. For some tests, like glial fibrillary acidic protein, there is tight within-individual variation but between individuals, the differences could be great, and again we're talking in healthy subjects.

So, this sets the stage for using the test and comparing results, not against a population-based reference interval but

instead against a value that has been predetermined during health. So, we're not going to probably have everybody do baseline levels of adults for these TBI biomarkers but there are certain higher risk occupations where that could make more sense, and that could increase the utility and fidelity of this test. And I'm speaking of people who work in the defense industry or soldiers. They could be professional athletes in sports that are associated with contact, such as football or hockey. And it could even be an elderly population, where the risk for falls are much higher than in an adult population.

So, in that scenario, it's not something that we're doing today but because these tests appear to have low biologic variability, that this could be an increased utilization.

Bob Barrett: That was Dr. Alan Wu from the University of California San Francisco. He shared his thoughts on the development of traumatic brain injury biomarker assays in the June 2023 issue of *Clinical Chemistry* and he's been our guest in this podcast on that topic. I'm Bob Barrett. Thanks for listening.