Biomarkers for Neural Injury and Infection in Small Animals

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KEYWORDS

• Biomarker • Diagnosis • Infectious disease testing • Neural injury • Prognosis • Small animals

KEY POINTS

- Biomarkers can assist in understanding the cause, diagnosis, severity, and prognosis for neural injury.
- Integration of conventional testing and new diagnostic techniques will overcome current shortcomings in understanding CNS infectious diseases.
- Diagnostic tests may be limited because of poor positive and negative predictive values, which must be recognized when interpreting test results.

NEURAL INJURY MARKERS

Introduction

Cross-sectional imaging techniques such as computed tomography (CT) and magnetic resonance imaging (MRI) have become more widely available to veterinarians during the past quarter of a century and have facilitated diagnosis of central nervous system (CNS) diseases. However, there is still frequently a lack of definition of the cause of neurologic lesions, because tissue sampling from the pathologic site is often difficult and there are few clinical diagnostic tools to assist diagnosis. A biomarker is a potential option to improve current shortcomings.

A biomarker is a characteristic that can be objectively measured as an indicator of a physiologic or pathologic process or a response to a therapeutic intervention.[1] Biomarkers can be associated with each step of gene-to-protein processing or metabolites that are produced during subsequent intracellular reactions and can be expected to aid in understanding the cause, diagnosis, severity, prediction, or outcome of treatments. Molecular biological techniques have advanced rapidly in

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recent years allowing emergence of the so-called omics technologies of genomics, proteomics, and metabolomics, which has increased the opportunities for developing efficient biomarkers. The omics techniques allow the simultaneous analysis of many candidate molecules and allow selection of disease-specific biomarkers through comparison between groups of healthy and disease-affected animals. Candidates can subsequently be further investigated to determine whether they are clinically useful.

Blood, urine, cerebrospinal fluid (CSF), and tissue samples from the pathologic site have been the main source of biomarkers for CNS disease. Blood and urine are easily collected but CNS tissues and CSF sampling are more difficult and can incur the risk of significant morbidity. However, the blood-brain barrier (BBB) presents a highly selective barrier, which means that pathologic processes in the CNS are not necessarily reflected in the blood, unless its permeability is increased.

Diagnostic Testing

Diagnostic accuracy depends on 2 parameters (**Fig. 1**): sensitivity and specificity. Sensitivity is the identification of true-positives, and specificity indicates true-negatives; both are conventionally expressed as proportions or percentages. The relationship between sensitivity and specificity can be shown using the receiver-operating characteristic (ROC) curve. Poor to fair biomarkers have area under the curve (AUC) values ranging between 0.5 and 0.8, good markers have AUC values between 0.8 and 0.9, and excellent markers have AUC values between 0.9 and 1.0. Positive predictive value (PPV) is the percentage of patients with a positive test that have the disease and negative predictive value (NPV) is the percentage of patients with a negative test that do not have the disease (**Box 1**).

Limitations of Biomarkers

An ideal biomarker specifically and sensitively reflects a disease state and can be used for diagnosing, determining prognosis, and monitoring disease progression during therapy. Although a large number of studies have reported new biomarkers for predicting prognosis with spinal cord injury (SCI) and brain tumors, none are ideal in terms of accuracy and availability. The transfer of biomarkers from discovery to clinical practice encounters many obstacles.

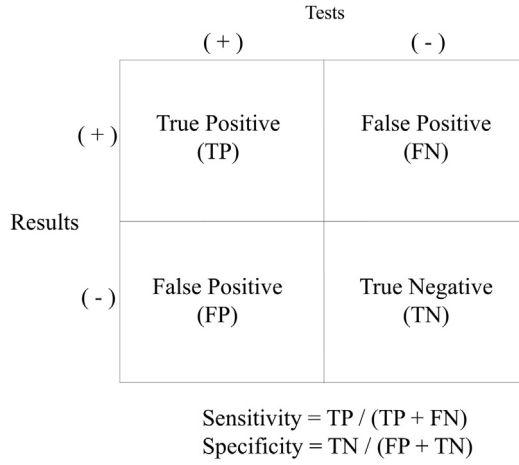

Fig. 1. Diagnostic accuracy depends on 2 parameters: sensitivity and specificity.