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In Vivo Diagnosis of Synucleinopathies

A Comparative Study of Skin Biopsy and RT-QuIC

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Study Question

Do immunofluorescence (IF) and real-time quaking-induced conversion (RT-QuIC) analyses of skin and CSF samples achieve similar levels of accuracy at distinguishing synucleinopathies (SOPs) from non-SOPs?

What Is Known and What This Paper Adds

IF and RT-QuIC are both laboratory testing modalities that permit the detection of pathologic α-synuclein, but they focus on different aspects of pathologic α-synuclein. This investigation's results confirm that IF and RT-QuIC both accurately differentiate SOPs from non-SOPs.

Methods

For this diagnostic test study, the investigators prospectively screened skin and CSF samples sent to a diagnostic laboratory in Bologna between 2018 and 2020. The dataset included 40 patients with SOPs, such as Parkinson disease and multiple system atrophy; 50 patients with non-SOPs, such as Alzheimer disease and progressive supranuclear palsy; and 24 controls with neurologic disorders (mainly peripheral neuropathies) but no evidence of neurodegeneration. The patients in the SOP and non-SOP groups met the current clinical and instrumental criteria for their respective diagnoses. The investigators tested the reproducibility of IF findings with samples from 9 patients with SOPs and 12 patients with non-SOPs, and they used samples from the controls and the other 69 patients to compare the diagnostic accuracies of IF and RT-QuIC. Skin samples were available for all patients, but CSF samples were available for a subset of patients. The personnel who performed IF and RT-QuIC testing were unaware of reference diagnoses. The primary outcomes were the comparative diagnostic utilities of IF and RT-QuIC.

Table Diagnostic Performance of IF and RT-QuIC

Test	Sensitivity	Specificity
Skin IF	90%	100%
Skin RT-QuIC	86%	80%
CSF RT-QuIC	78%	100%

Sensitivities and specificities of IF and RT-QuIC given different samples to analyze.

Results and Study Limitations

IF achieved a high degree of reproducibility between pairs of neighboring skin samples. Furthermore, both IF and RT-QuIC achieved high sensitivity and specificity in differentiating SOP cases from non-SOP cases and control cases, but IF achieved the higher degree of diagnostic accuracy. These findings are Class III evidence that both IF and RT-QuIC can accurately discriminate between SOPs and non-SOPs. The present study's limitations include the lack of autopsy confirmation of reference diagnoses, reliance on skin biopsy samples from single skin sites, and a lack of MRI evidence for reference diagnoses.

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