IgG lambda paraprotein, although no such paraprotein has been seen in our patients. The pathological findings in our patients are different from those seen in morphea and scleroderma, and in its toxic variants caused by contaminated rapeseed oil and L-tryptophan ingestion. In these diseases, the number of spindle cells in the dermis is decreased, and collagen bundles are thickened, with decreased spaces between them. In patients with scleromyxoedema, as in our patients, we saw the opposite of each of these features. A diagnosis of scleromyxoedema in our patients is the closest match among the range of cutaneous fibrosing diseases. Nevertheless, the absence of both monoclonal protein and systemic signs of the disease, such as mucin deposition in other organ systems, makes us hesitant to unequivocally diagnose scleromyxoedema. Additionally, although scleromyxoedema commonly affects the head and neck, producing sclerosis and linear papules on the face, the pathological changes in all our patients were limited to the limbs and trunk.

To better clarify this disorder, a collaborative multicentre clinicopathological study is currently underway to determine what renal-dialysis-associated features might be responsible for its recent emergence.


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**Screening older adults at risk of falling with the Tinetti balance scale**

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In a prospective study of 225 community dwelling people 75 years and older, we tested the validity of the Tinetti balance scale to predict individuals who will fall at least once during the following year. A score of 36 or less identified 7 of 10 fallers with 70% sensitivity and 52% specificity. With this cut-off score, 53% of the individuals were screened positive and presented a two-fold risk of falling. These characteristics support the use of this test to screen older people at risk of falling in order to include them in a preventive intervention.

Although many balance characteristics are associated with an individual’s risk of falling, a standardised and valid screening instrument to identify people at risk of falling is still unavailable. There is no evidence to include screening for falls in periodic health examinations of older people since there is no valid instrument to do so. The Tinetti balance scale (score of one to 40) is a simple clinical balance which measures characteristics associated with falls. This test assesses balance with 14 items (score out of 24) and gait with ten items (score out of 16) for a total score out of 40, where the higher the score, the better the performance. It is easy to administer in a clinic or at home by health professionals. The Tinetti balance scale has shown good performance on interrater reliability and concurrent validity. The cut-off score to distinguish those at risk of falling from those not at risk has never been determined. In order to determine this score, we assessed the predictive validity of the Tinetti balance scale to prospectively identify those at risk.

Individuals chosen for this study were participants in the control group of a randomised controlled trial examining the efficacy of a multidimensional preventive programme for older adults. From a random sample drawn from the electoral list of the Sherbrooke urban area, 225 individuals who were 75 years and older were selected, gave informed consent, and were followed prospectively for 1 year. The Tinetti balance test was carried out at the home of the participant at the beginning of the study by trained research nurses. A calendar was then given to the individuals with instructions to record the date of any falls. A monthly phone call by the nurse collected the data about the falls. The sensitivity and specificity of each score on the Tinetti balance scale for predicting at least one fall during the year following its administration were calculated. A receiver operating characteristics (ROC) curve was constructed with these results.

The mean age of the individuals was 80·0 (SD 4·4) years and the mean score on the Tinetti balance scale was 33·8 (SD 7·2). During 1 year, 53 individuals fell at least once (23·6%). As shown on the figure, the two points closest to the upper left corner of the ROC curve are the score ≤33 with 51% sensitivity and 74% specificity and the score ≤36 with 70% sensitivity and 52% specificity.

Using this screening test for preventing falls, the cut-off score of ≤36 is preferred since the test has a higher
The sensitivity (70%). The 52% specificity is moderate but the test is cheap to administer and the false positives will be identified subsequently by a multifactorial assessment. With this cut-off score, the test identifies seven of ten individuals at risk of falling. Since 120 of 225 individuals in the sample scored 36 or less, it reduces by almost half the number of people to be assessed with a more complex protocol. People identified as positive had a 30-8% rate of falls (positive predictive value) compared with a 15-2% rate in negative individuals for a relative risk of 2·02 (95% CI 1·20–3·42). Such a predictive value is comparable to the Pap smear for screening cervical cancer.1

Although the Tinetti balance scale showed acceptable characteristics to recommend it as a screening test for falls, research should be done into improving performance. The rapid drop in sensitivity on the ROC curve shows that even with high scores on the Tinetti balance scale (37–40 out of 40), there were still individuals who fell. There could be a ceiling effect of the scale that makes it impossible to identify individuals with very few balance problems. Or it may just be a sign of the multifactorial aspect of the risk of falls, with some important factor (vision, environment) not being captured by the test. These issues could be offset by including more challenging balance items to avoid the ceiling effect and adding items related to other factors associated with falls. Nevertheless, the screening characteristics shown by the Tinetti balance test support its inclusion in periodic health examination of older community-dwellers.


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In-situ immuno-PCR to detect antigens

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In-situ immunoassays do not allow the detection of the minute numbers of target molecules accessible with in-situ PCR. We developed a highly sensitive method, termed in-situ immuno-PCR, in which the DNA marker was linked to target molecules through an antibody-biotin-avidin bridge and amplified by in-situ PCR. Amplified DNA sequences were detected in situ by hybridisation. This technique may be the only one available to detect minute quantities of biological macromolecules such as proteins, carbohydrates, and lipids in intact cells or tissue sections.

Immunohistochemistry and in-situ hybridisation, the in-situ staining approaches for detection of antigens, DNA, or RNA in intact cells and tissue sections, are common and powerful tools for biological and biomedical research and clinical diagnostics. By combining the exponential amplification power of the PCR with in-situ hybridisation, in-situ PCR allows the detection of low copy numbers of nucleic acids in situ. However, with routine immunohistochemistry, detection of the minute numbers of target molecules accessible with in-situ PCR is difficult.

Imuno-PCR, which uses amplification of PCR to increase the signal of immunoassays, exhibits high sensitivity and permits the detection of proteins at concentrations of a few hundred molecules.2 By combining the high sensitivity of PCR amplification with the versatility and high specificity of immunoassays, we have developed a method, termed in-situ immuno-PCR, to detect antigens at low levels in intact cells or tissue sections.

We examined paraffin sections of 17 explanted livers from patients with hepatitis B virus (HBV) infection for HBsAg expression by in-situ immuno-PCR. Two donor livers served as negative controls. All the samples were obtained from the surgical department of Heidelberg University, Germany. In-situ immuno-PCR was done as follows. The sections were treated with avidin-biotin blocking kit (Vector Laboratories), non-specific binding sites were inhibited with normal goat serum, and intrinsic DNA and RNA were destroyed by deoxyribonuclease and ribonuclease. The DNA marker was linked to target molecules through an antibody-biotin-avidin bridge by successively incubating the sections with reagents and thoroughly washing them after each incubation step. Reagents were anti-HBsAg monoclonal antibody,