A randomized, double-blind, placebo-controlled, 6-week multicenter study of 171 patients with neurogenic orthostatic hypotension evaluated the efficacy of a 10-mg dose of midodrine or placebo 3 times per day. All patients had weekly visits during which blood pressure was taken supine and standing 1 hour after dosing. Patients reported frequency of lightheadedness using a 10-point scale (0=always, 10=never). Patients in the midodrine group had an average increase in standing systolic blood pressure of 21.8 mmHg, compared with <5 mmHg in the placebo group (P<.001). Treatment group symptom scores increased significantly (indicating fewer symptoms) compared with placebo in the 4th week (5.2 vs 4.4 for placebo, P=.02) and 5th week (5.4 vs 4.7 for placebo, P=.05). The main adverse effects were supine hypertension, pilomotor reactions, and urinary retention. This study was commissioned by the Roberts Pharmaceutical Corporation.3

An article in Evidence-Based Practice reviewed 3 studies of counterpressure maneuvers for the treatment of vasovagal syncope.4 In a case series of 21 patients, leg crossing and tensing for 30 seconds upon the onset of tilt-table-induced symptoms uniformly resolved prodromal symptoms and blocked syncope. A crossover study challenged 19 patients on a tilt table, asking them to use active hand grip versus placebo hand grip. Patients’ systolic blood pressures increased with active hand grip (from 92±10 up to 105±38 mmHg) and decreased in the placebo group (from 91±11 down to 73±21 mmHg); only 5% developed syncope in the active group, compared with 40% in the placebo group (P=.01).4

A third, multicenter RCT of 223 patients with syncope compared counterpressure with conventional care. The patients in the counterpressure group were trained in using a sequence of leg crossing, hand grips, and arm tensing. Training in counterpressure reduced the risk of recurrent syncopal episodes (relative risk reduction 0.36; 95% confidence interval, 0.11–0.53; number needed to treat=5 to prevent 1 patient from having recurrent syncope).4

The European Federation of Neurological Societies (EFNS) recommends increased water and salt ingestion and physical measures, including leg crossing, squatting, elastic abdominal binders and stockings, and careful exercise, prior to initiating pharmacologic therapies. The EFNS recommends fludrocortisone as a valuable first-line treatment (giving it a Level C recommendation), although they note that midodrine has higher-quality evidence supporting its use in mono- or combined therapy (a Level A recommendation). The EFNS also recommends discontinuing medications that can contribute to orthostatic hypotension, gradual staged movements, isotonic exercises, avoiding prolonged recumbence, performing counter maneuvers (eg, leg crossing/squatting), and avoiding activities that induce the Valsalva maneuver.5

Anthony M. Caporaso, MD
Ruchi Chhabra, MD
Hina I. Qureshi, MD
North Shore/LIJ Hospital FMR
Glen Cove, NY
José E. Rodríguez, MD
Florida State University
Tallahassee, FL
Kristin Hitchcock, MSI
Am. Assoc. of Orthopaedic Surgeons
Rosemont, IL

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How accurate is the Spurling maneuver for detection of cervical radiculopathy?

Evidence-Based Answer

The Spurling maneuver has a sensitivity ranging from 26% to 92% and a specificity ranging from 95% to 100%, when computed tomography (CT) myelogram, magnetic resonance imaging (MRI), or surgery are used as reference standards. Consequently, the Spurling maneuver is better for ruling in cervical pathology than ruling it out. (SOR B, based on 4 diagnostic studies with heterogeneous results.)

The Spurling maneuver was designed to distinguish cervical radiculopathy from other sources of neck and upper extremity pain. It is performed by extending and laterally flexing the patient’s neck while axial pressure is
applied to the spine. A positive test results in limb pain or paresthesias.

A prospective cohort study evaluated 43 neurosurgery patients on whom the Spurling maneuver was performed prior to CT myelography. The CT myelogram is considered the gold standard for diagnosis of foraminal compression. However, it is not useful for identifying newly forming osteophytes or noncompressive sources of radiculopathy. The Spurling maneuver had a sensitivity that ranged from 26% to 50% and a specificity of 100% for detecting nerve compression at C6-C8. The study was not able to validate the Spurling maneuver for lesions at the C4-C5 level, as most patients with symptoms from C4-C5 also had signs and symptoms from C6-C8 disease.

In another prospective cohort study, the Spurling maneuver was performed on 50 neurosurgery patients prior to surgery or MRI. Results of both groups were combined and reported as 1 value. When compared with MRI or surgical findings, the Spurling test had 92% sensitivity and 95% specificity for predicting soft-disc prolapse. This study was limited by a small size, homogeneous nonrandomized population, and inadequate data interpretation due to combining results without accounting for differences in reference standards.

A third cohort compared the Spurling maneuver with electromyography (EMG) (N=255) among consecutive patients. Patients were referred for EMG to evaluate upper extremity nerve disorders and received the Spurling maneuver prior to the procedure. The Spurling maneuver had 30% sensitivity and 93% specificity for cervical radiculopathy as diagnosed by EMG. However, the Academy of Electrodagnostic Medicine estimates EMG to have a sensitivity of 50% to 71% when compared with operative findings, and EMG alone is not generally used to diagnose radiculopathy.

The final study was a blinded, prospective randomized investigation of 82 consecutive patients. They were referred for EMG and nerve conduction study (NCS) for evaluation of suspected cervical radiculopathy or carpal tunnel syndrome. Several provocation tests were performed in cluster on participants and compared with EMG and NCS results. The Spurling maneuver was found to have 50% sensitivity and 74% to 86% specificity for assessing the presence of cervical radiculopathy. This study had adequate size and spectrum of patients, but interpretation is limited due to the low sensitivity of EMG and its use as a reference standard.

What is the risk of CHF and CV death associated with the use of pioglitazone?

Evidence-Based Answer

Pioglitazone use may be associated with a small (<2%) increased risk of nonfatal heart failure. (SOR B, based on heterogenous meta-analyses.) There is no adverse effect on cardiovascular death rates. (SOR A, based on consistent meta-analyses.)

A 2008 meta-analysis of 94 randomized controlled trials (RCTs) assessed the effect of pioglitazone on cardiovascular (CV) risk. Data from unpublished trials identified through the US Food and Drug Administration and clinicaltrials.gov were used to supplement data pooled from MEDLINE searches. Patients treated with pioglitazone (total=7,644) were compared with patients treated with placebo, a sulfonlurea, metformin, rosiglitazone, or a glitazar (total patients=6,106). The pooled comparator analysis found no clear effect of pioglitazone on CV death (odds ratio [OR] 0.49; 95% confidence interval [CI], 0.21–1.15) or nonfatal congestive heart failure (CHF; OR 1.38; 95% CI, 0.90–2.12).

This result varies from that of a 2007 meta-analysis of 19 pioglitazone treatment RCTs, which included more than 16,000 patients with type 2 diabetes. The primary outcome was the combination of death, myocardial infarction, or stroke. CHF was a secondary outcome. Death, myocardial infarction, or stroke occurred in 375/8,554 (4.4%) of patients treated with pioglitazone versus 450/7,836 (5.7%) of patients treated with placebo (hazard ratio [HR] 0.82; 95% CI, 0.72–0.94). However, there was no effect on the risk of CV death (OR 0.92; 95% CI, 0.76–1.11). CHF occurred more commonly