

because they provide guidance in areas of inadequate evidence. However, caution should be exercised when recommendations are based on low levels of evidence. The problem lies in the multitude of available systems to grade the evidence and the presence of outdated recommendations. The different methods of grading evidence add to the difficulty in interpreting the guidelines. We agree that the GRADE (Grading of Recommendations Assessment, Development, and Evaluation) system not only helps in the assessment of strength of the recommendations but also critiques the robustness of the underlying evidence.⁵ The GRADE system will also allow transparent judgments in the guideline development process, thereby minimizing potential conflicts of interests.⁵

Clinical practice guidelines from various professional societies have done a great service not only in patient care by developing practice recommendations but also by identifying gaps in the evidence base for further research. Still, much effort is needed to strengthen the evidence base and streamline the process of guideline development.

Abdur Rahman Khan, MD
Faraz Khan Luni, MD
George Victor Moukarbel, MD

University of Toledo
 Toledo, OH

1. Feuerstein JD, Akbari M, Gifford AE, et al. Systematic analysis underlying the quality of the scientific evidence and conflicts of interest in interventional medicine subspecialty guidelines. *Mayo Clin Proc.* 2014;89(1):16-24.
2. Khan AR, Khan S, Zimmerman V, Baddour LM, Tleyjeh IM. Quality and strength of evidence of the Infectious Diseases Society of America clinical practice guidelines. *Clin Infect Dis.* 2010;51(10):1147-1156.
3. Tricoci P, Allen JM, Kramer JM, Califf RM, Smith SC, Jr. Scientific evidence underlying the ACC/AHA clinical practice guidelines [published correction appears in *JAMA*. 2009;301(15):1544]. *JAMA.* 2009;301(8):831-841.
4. Harpole LH, Kelley MJ, Schreiber G, Toloza EM, Kolimaga J, McCrory DC. Assessment of the scope and quality of clinical practice guidelines in lung cancer. *Chest.* 2003;123(1, suppl):7S-20S.
5. GRADE Working Group. Grading the quality of evidence and the strength of recommendations. <http://www.gradeworkinggroup.org/intro.htm>. Accessed January 22, 2014.

www.gradeworkinggroup.org/intro.htm. Accessed January 22, 2014.

<http://dx.doi.org/10.1016/j.mayocp.2014.03.007>

In reply—Clinical Practice Guidelines: Still Miles to Go...

We thank Khan et al for their interest in our article assessing practice guidelines in interventional medical specialties¹ and strongly agree that the issues with guidelines go beyond just those of the interventional subspecialties. In fact, we have already reported the results of other studies citing the limited evidence among gastroenterology² and inflammatory bowel disease³ guidelines, and others have shown similar results for cardiology,⁴ infectious diseases,⁵ and liver diseases.⁶

We believe that considerable improvements can be made in the quality of contemporary guidelines, beginning with the makeup and conduct of guideline development committees, in which much of the guidelines' strengths are rooted.⁷ A key aspect of establishing a guideline is the degree of transparency mandated throughout the development process. How the committee deals with potential conflicts of interest, who is chosen to participate in the committee, how the evidence is researched, and how the recommendations are formulated all must be determined before starting the guideline development process. All of these standards are determined by the guideline development committee.⁷

As we stated in our article,¹ we agree with Khan et al that the GRADE (Grading of Recommendations, Assessment, Development, and Evaluation) system is an easier system for the reader to understand and has the additional benefit of highlighting areas in need of further research. However, although we agree that the professional societies have done a great service in the development of practice guidelines, when statements based on poor evidence are published, there is a potential for

harm. For example, guidelines based only on expert opinion are oftentimes perceived (eg, by insurance companies and in malpractice cases) as an irrefutable standard of care to which clinicians should be held accountable. Instead of relying so heavily on expert opinion guidelines, we suggest, as we have in our previous publications, that a "best practice statement" be used instead of a guideline when quality evidence is not available.^{2,3} A best practice statement would complement the GRADE system, indicating that evidence is lacking and that the recommendations are based on expert opinion. However, it is likely that as research is reported over time, an evidence-based standard of care may be established. Until that time, though, expert opinions should be viewed with circumspection when used as a standard for physicians' actions (eg, in malpractice cases or in quality assessments).

Ultimately, we commend Khan et al for further highlighting the important work that still needs to be done to improve current practice guidelines.

Joseph D. Feuerstein, MD
Daniel A. Leffler, MD, MS
Adam S. Cheifetz, MD

Beth Israel Deaconess Medical Center
 Boston, MA

1. Feuerstein JD, Akbari M, Gifford AE, et al. Systematic analysis underlying the quality of the scientific evidence and conflicts of interest in interventional medicine subspecialty guidelines. *Mayo Clin Proc.* 2014;89(1):16-24.
2. Feuerstein JD, Gifford AE, Akbari M, et al. Systematic analysis underlying the quality of the scientific evidence and conflicts of interest in gastroenterology practice guidelines. *Am J Gastroenterol.* 2013;108(11):1686-1693.
3. Feuerstein JD, Akbari M, Gifford AE, et al. Systematic review: the quality of the scientific evidence and conflicts of interest in international inflammatory bowel disease practice guidelines. *Aliment Pharmacol Ther.* 2013;37(10):937-946.
4. Mendelson TB, Meltzer M, Campbell EG, Caplan AL, Kirkpatrick JN. Conflicts of interest in cardiovascular clinical practice guidelines. *Arch Intern Med.* 2011;171(6):577-584.
5. Lee DH, Vilemeyer O. Analysis of overall level of evidence behind Infectious Diseases Society of America practice guidelines. *Arch Intern Med.* 2011;171(1):18-22.
6. Rowe IA, Parker R, Armstrong MJ, King AL, Houlihan DD, Mutimer D. Assessment of the quality of evidence underlying international guidelines in liver disease. *Am J Gastroenterol.* 2012;107(9):1276-1282.

7. Institute of Medicine (US) Committee on Standards for Developing Trustworthy Clinical Practice Guidelines. In: Graham R, Mancher M, Miller Wolman D, Greenfield S, Steinberg E, eds. *Clinical Practice Guidelines We Can Trust*. Washington, DC: National Academies Press; 2011.

<http://dx.doi.org/10.1016/j.mayocp.2014.03.005>

A Novel Treatment for Subacute Thyroiditis: Administration of a Mixture of Lidocaine and Dexamethasone Using an Insulin Pen

To the Editor: Patients with subacute thyroiditis (SAT) generally have neck pain and fever. No fast-acting therapy has been reported. We hypothesized that intrathyroidal injection using an insulin pen filled with a mixture of lidocaine and dexamethasone could produce therapeutic benefit compared with oral medications.

After ethics board approval, we enrolled 36 patients with SAT in our study. One group of 18 patients received a local thyroid gland injection, and the other 18 patients received prednisone, 5 to 20 mg in a tapering dose.¹

Insulin cartridges were filled with 3.0-mL mixtures that contained 50 mg of lidocaine, 3 mg of dexamethasone, and saline solution. The thyroid isthmus was injected with a 4-mm needle (32G) and the lobe with a 6-mm needle (32G) under ultrasound guidance. The lidocaine dose could be doubled depending on the pain severity. The visits and injections were scheduled and performed by physicians whenever needed to relieve pain. The painful lobe was injected with 20 to 80 U at each administration until the pain abated. Ten units of the combination contained 1.67 mg of lidocaine and 0.1 mg of dexamethasone. For patients who continued to experience severe pain after 3 injections, 600 mg/d oral ibuprofen was added.

Pain was evaluated by a verbally administered numerical rating scale from 0 to 10 (0 = no pain, 10 = worst

possible pain).² The thyroid pain score was assessed at presentation, 30 and 60 seconds after treatment, 30 and 60 minutes after treatment, and once a day.

The therapeutic schedule, efficacy parameters, and clinical outcomes are presented in the Table. Most patients in the injection group reported rapid pain relief and significant neck relaxation within 1 week compared with the oral group ($P < .0001$). In addition, the frequency and duration of treatments were significantly less ($P < .0001$). There were no differences with respect to fever cure between the 2 groups. Complications associated with injection included small subcutaneous hematomas without pain, which

occurred in 2 patients. This complication can be avoided by compression and skilled technique. At the end of the average follow-up of 12 months, none of the patients repeated the cycle of treatment.

Patients with SAT are naturally dissatisfied with oral corticosteroid treatment's slow action, adverse effects, and risk of pain recurrence. The administration of lidocaine and dexamethasone with the insulin pen has the following advantages over conventional oral therapy. First, this method was as simple and easy to perform as an insulin injection, with the microneedle stably inserted into the edge of the thyroid gland. The injection itself was nearly

TABLE. Treatment Protocol and Clinical and Biochemical Characteristics of the Study Patients^{a,b}

Variable	Injection group (n=18)	Oral group (n=18)
Time course		
Week 1	Injection every other day	Prednisone 20 mg/d
Week 2	Ibuprofen 600 mg/d	Prednisone 15 mg/d
Week 3	Ibuprofen 600 mg/d	Prednisone 10 mg/d
Weeks 4-6	Ibuprofen 600 mg/d	Prednisone 5 mg/d and ibuprofen
Sex (F/M)	12/6	15/3
Age (y)	46±10	45±11
Diabetes	2 (11.1)	1 (5.6)
Fever	10 (55.6)	7 (38.9)
Lobe pain	18 (100.0)	18 (100.0)
TSH (mIU/L) ^c	0.062 (0.004-0.822)	0.023 (0.006-2.018)
FT3 (pmol/L)	6.40±1.89	8.25±4.25
FT4 (pmol/L)	22.57±11.82	28.46±16.10
WBCs ($\times 10^3/L$)	7.40±2.42	9.14±2.58
Neutrophils ($\times 10^3/L$)	5.07±1.98	6.24±2.23
Treatment frequency		
1 Time	8 (44.4)	0 ^d
2 Times	9 (50.0)	1 (5.6) ^d
>2 Times	1 (5.6)	17 (94.4) ^d
Pain score of 0-3		
30 seconds	18 (100.0)	0 ^d
1-2 d	15 (83.3)	13 (72.2)
3-6 d	16 (88.9)	13 (72.2)
>6 d	17 (94.4)	18 (100.0)
Fever cure		
1-2 d	4 (22.2)	4 (22.2)
3-6 d	4 (22.2)	1 (5.6)
>6 d	2 (5.56)	2 (11.1)
Treatment duration (d)	4.0 (2.0-10.0)	17.0 ^d (5.0-200.0)

^aFT3 = free triiodothyronine; FT4 = free thyroxine; TSH = thyrotropin; WBC = white blood cell.

^bData are presented as mean ± SD or No. (percentage) of patients unless indicated otherwise.

^cTSH levels and treatment duration are presented as median and range (minimum-maximum).

^dThe mean of FT3 in the oral group is higher than in the injection group but reach no difference; $P=0.243$.