AMA Journal of Ethics®
August 2020, Volume 22, Number 8: E695-701

POLICY FORUM: PEER-REVIEWED ARTICLE

Revisiting the WHO Analgesic Ladder for Surgical Management of Pain

Laura Stone McGuire, MD and Konstantin Slavin, MD

Abstract

The opioid epidemic challenges current attitudes toward pain management and necessitates the reexamination of the World Health Organization (WHO) 3-step analgesic ladder, introduced in 1986 for cancer pain management. Surgical treatment of pain is a logical extension of the original guideline, which is often absent in conversations with patients about treatment options for their pain and consequentially underutilized. However, with concerns growing regarding opioid use, a shift in the stepwise approach of the WHO analgesic ladder in an age of developing technology and surgical offerings could have profound implications for patients and public health. Surgical interventions potentially provide a long-term, cost-effective management strategy to reduce opioid use. This review canvasses surgical options, highlights literature on failed back surgery syndrome and spinal cord stimulation and reconsiders the current ladder approach to pain management.

To claim one AMA PRA Category 1 Credit™ *for the CME activity associated with this article, you must do the following: (1) read this article in its entirety, (2) answer at least 80 percent of the quiz questions correctly, and (3) complete an evaluation. The quiz, evaluation, and form for claiming* AMA PRA Category 1 Credit™ *are available through the* AMA Ed Hub™.

Introduction

Presented in 1986, the World Health Organization (WHO) analgesic ladder provided a framework for the stepwise medical management of cancer-related pain.[1] This 3-step ladder begins with nonopioid analgesics with or without nonpharmacological approaches for mild pain, continues with weak opioid medications (eg, codeine) with or without nonopioid analgesics and adjuvants for mild-to-moderate pain, and progresses to strong opioids (eg, oxycodone) with or without nonopioid analgesics and adjuvants for moderate-to-severe pain.[1] The American Pain Society's identification of pain as the "fifth vital sign" in 1995 portended the increased importance of not only adequate treatment of pain in patients but also education of health care professionals.[2,3] Eventually, a modified version of the 3-step ladder placed interventional pain management as a fourth step.[4,5] Development of this algorithmic approach aimed to control refractory or

intractable pain in both an efficient and a safe manner, providing a rational and balanced method to maximize pain relief while minimizing side effects and risks.

However, the opioid epidemic challenges current attitudes toward pain management and necessitates the reexamination of the WHO analgesic ladder. One issue relates to the perceived priority of medical as opposed to surgical intervention for pain relief due to high risk of surgery and low risk of medications. Within the current interpretation of the ladder, it would be inappropriate to bypass a step and to use pain-relieving interventions, such as surgery, without trying opioids first.[4] Although initially designed for cancer-related pain, the analgesic ladder now serves many pain types, including neuropathic pain, which often proves refractory to opioid-based management.[6] Thus, in the experience of the authors, most patients initially presenting to a neurosurgeon for evaluation for possible surgical intervention have been managed with opioid medications for extended periods.

Practical Considerations in Surgical Management of Pain

Surgery for pain differs from many conventional operations, neurosurgical and others, aimed at elimination of the source of pain—such as, for example, appendectomy, spinal decompression, carpal tunnel release, or joint replacement. Instead, it is aimed at the pain-processing (nociceptive) system and includes destructive procedures (open or percutaneous ablations and transections), electrical neuromodulation (via cortical, deep-brain, spinal, and peripheral neurostimulation), and chemical neuromodulation (with implantable drug delivery systems). Neurodestruction interrupts the pain-transmitting pathways by removing a peripheral nerve (neurectomy) or dorsal root ganglion (ganglionectomy), removing a sympathetic ganglion or cutting a nerve chain (sympathectomy), severing spinal or cranial nerve roots (rhizotomy), lesioning spinothalamic tracts or the dorsal root entry zone (DREZ) within the spinal cord (cordotomy, DREZ myelotomy), or severing nerve tracts in the pain-processing centers of the brain (tractotomy, thalamotomy, cingulotomy). Electrical neuromodulation relieves pain either by directly suppressing pain transmission (with a complete but reversible conductance block, as in cases of high-frequency peripheral nerve stimulation) or by activating inhibitory mechanisms (through production of paresthesias or through paresthesia-free paradigms, as in cases of spinal cord stimulation) via electrical stimulation of the peripheral nerves, dorsal root ganglia, dorsal columns of the spinal cord, deep cerebral structures (thalamic nuclei and periaqueductal and periventricular gray matter) or via electrical stimulation of the motor cortex using implantable electrodes that are usually connected to internal pulse generators or externally powered receivers. Chemical neuromodulation is based on continuous delivery of various medications (analgesics, local anesthetics, ion channel blockers, adrenergic agonists, or various combinations thereof) via implanted catheters, pumps, and ports.

Each modality has advantages and disadvantages. Neuromodulation, both chemical and electrical, tends to be reversible, adjustable, testable, and nondestructive. It also provides patients with real or perceived ability to control the treatment using dedicated remote controllers. Benefits might not be immediate, however, and expensive implantable hardware and multiple adjustments are usually required for long-term success.[7] Neurodestruction, on the other hand, tends to bear more risk, as the procedural results are neither reversible nor adjustable. However, the advantages include immediate pain relief and relatively low cost in comparison to neuromodulation techniques, as there is no requirement for expensive implants and no subsequent adjustments. Due to the inherent plasticity of the nervous system, some of the

destructive interventions are associated with a higher rate of pain relapse in the long-term and have been traditionally reserved for patients with shorter life expectancy.[8,9,10]

Each of these interventions has been used for decades. Due to cumulative surgical experience and advances in imaging techniques, the safety of surgery for pain has significantly improved. Percutaneous cordotomy with computed tomography (CT) guidance is safer than the open cordotomy of the 1950s.[10,11,12,13,14] Magnetic resonance imaging (MRI) guidance, together with intraoperative neurophysiological testing, increases accuracy of deep-brain stimulation targeting to a fraction of a millimeter.[15] Advancement from a single-contact electrode to 32-contact electrodes provides countless options for stimulation paradigms in cases of spinal cord stimulation. Thus, the prior argument that risk of surgery outweighed risk of opioid prescription, which previously predominated in the avoidance of surgical intervention for pain, no longer holds completely true, at least for neuromodulation.

Impact of Surgical Management of Pain

Given the scope of the opioid crisis, the potential impact of surgical intervention for pain is far-reaching, extending from patient-level to systems-level outcomes. Of the pain interventions available, perhaps the most studied to date is spinal cord stimulation (SCS), particularly in patients with chronic low-back pain or failed back surgery syndrome (FBSS). The long-term success rate following conventional SCS is as high as 74%,[16] and, in a retrospective study, 69% of the 130 patients with FBSS who were treated and continued with SCS during an average 6-year follow-up reported substantial improvement of symptoms.[17] Additional prospective studies have shown that traditional and 10-kHz SCS also can reduce reliance on opioids for management of pain,[18,19] and systematic reviews and meta-analyses have similarly reported stable or reduced medication use in patients treated with SCS.[20,21,22] For example, a recent meta-analysis of 63 studies found a 58% average level of pain relief at 24 months postoperatively.[23] Importantly, retrospective studies have found patient outcomes following SCS to be time dependent, with earlier intervention linked to better symptom relief.[16,24,25] These findings suggest that the stepwise approach of the analgesic ladder could play a role in delaying referral to neurosurgical evaluation.

From a public health perspective, the use of SCS in the treatment of FBSS is cost effective, as it is one of the conditions most commonly treated with surgical intervention for pain management. FBSS may occur in 5% to 40% of all patients who undergo lumbosacral spine surgery for back pain,[26,27] contributing to the estimated $19.8 billion in indirect costs of back pain.[28] Despite evidence of the clinical efficacy and low complication rates of SCS,[29] SCS remains largely underused: an analysis of 16 455 patients with FBSS found that only 2.4% underwent SCS implantation,[30] and a later study of 122 827 FBSS patients identified 4.3% who underwent SCS.[31] The same study found that SCS implantation results in a short-term increase in costs at 1 year but significantly decreased annual cumulative costs at 9-year follow-up.[31] Furthermore, SCS for patients with FBSS has been shown to be cost-effective for all payers (commercial insurance, Medicare, and Medicaid) beginning at 2 years and extending through 9 years.[32] Additional studies have demonstrated the cost effectiveness of SCS not only in FBSS[30,33] but also in other indicated pathologies, such as chronic back and limb pain, complex regional pain syndrome, peripheral arterial disease, and refractory angina pectoris.[34,35,36] In a value-based health care economy, using interventions to provide the most value and benefit to the patient while incurring the least expense over time is essential.

Ethical Considerations and Paradigm Shift

Despite advances, surgical treatments remain a final step in pain management, typically after all other approaches fail.[37] With concerns growing regarding complications of opioid use in an age of developing technology and surgical offerings, a paradigm shift in pain management away from the WHO analgesic ladder toward earlier surgical intervention could have profound implications for patients and public health. Over time, surgical procedures have become more precise, less invasive, and better understood and recognized by both patients and their physicians. The ethical dilemma of beneficence vs nonmaleficence is not limited to weighing the advantages and risks of surgery alone. The risks of surgery *avoidance* should also be considered, given that medical ("conservative") treatments can cause tolerance, dependence, or clinical side effects, as seen with most analgesic regimens, opioid or otherwise. The possibility of long-term pain relief and associated increase in functionality and improvement in quality of life justifies surgery as an earlier treatment option, perhaps before opioids are introduced.

Paramount to good pain management, however, is a discussion with the patient about operative management of pain as part of a spectrum of available treatments and a multimodal approach to pain control. Establishing an institutional multidisciplinary team, which could include interested primary care practitioners, pain specialists, neurosurgeons, and ethicists, with regular conferences on the comprehensive management plans of patients with pain syndromes could facilitate reliance on a multimodal approach rather than on the standard stepwise ladder. In a broader sense, it would be important to have clinical ethicists provide input on (1) the value and consequences of choosing surgery vs nonsurgical options for pain management, (2) the risk of delay in offering surgery due to concerns about surgical complications vs the risk of initiating or continuing medical treatment, and (3) the value of introducing various alternative management strategies early with the patient's involvement in decision-making process. Ultimately, providing an individualized treatment plan for patients and their pain control is critical,[38] and, in adherence to Beauchamp and Childress' concept of respect for patient autonomy,[39] patients have a right to choose their treatments and should be presented with objective pros and cons of each treatment approach, including surgery for pain, especially when considering the initiation of opioid medications.

References

1. World Health Organization. Cancer pain relief: with a guide to opioid availability. 2nd ed. Geneva, Switzerland: World Health Organization; 1996. http://apps.who.int/iris/bitstream/10665/37896/1/9241544821.pdf. Accessed April 23, 2020.
2. Campbell JN. APS 1995 Presidential address. *Pain Forum*. 1996;5(1):85-88.
3. Morone NE, Weiner DK. Pain as the fifth vital sign: exposing the vital need for pain education. *Clin Ther*. 2013;35(11):1728-1732.
4. Vargas-Schaffer G. Is the WHO analgesic ladder still valid? Twenty-four years of experience. *Can Fam Physician*. 2010;56(6):514-517.
5. Pergolizzi JV Jr, Raffa RB. The WHO pain ladder: do we need another step? *Pract Pain Manag*. 2014;14(1):42-52.
6. Dworkin RH, O'Connor AB, Backonja M, et al. Pharmacologic management of neuropathic pain: evidence-based recommendations. *Pain*. 2007;132(3):237-251.

7. Slavin KV. Epidural spinal cord stimulation: indications and technique. In: Schulder M, ed. *Handbook of Functional and Stereotactic Surgery*. New York, NY: Marcel Dekker; 2002:417-430.
8. Crul BJ, Blok LM, van Egmond J, van Dongen RT. The present role of percutaneous cervical cordotomy for the treatment of cancer pain. *J Headache Pain*. 2005;6(1):24-29.
9. Berger A, Hochberg U, Zegerman A, Tellem R, Strauss I. Neurosurgical ablative procedures for intractable cancer pain [published online ahead of print, May 10, 2019]. *J Neurosurg*.
10. Teoli D, An J. Cordotomy. In: StatPearls [internet]. Treasure Island, FL: StatPearls Publishing; 2020. https://www.ncbi.nlm.nih.gov/books/NBK535446/. Updated April 5, 2020. Accessed June 9, 2020.
11. Bekar A, Taskapilioğlu MO, Eser P, Bilgin H. CT-guided high-level percutaneous cervical cordotomy for intractable cancer pain. *Turk Neurosurg*. 2017;27(1):133-137.
12. Kanpolat Y, Ozdemir M, Al-Beyati E. CT-guided percutaneous cordotomy for intractable pain in what is more than a disease: lung malignancies. *Turk Neurosurg*. 2013;23(1):81-87.
13. Sanders M, Zuurmond W. Safety of unilateral and bilateral percutaneous cervical cordotomy in 80 terminally ill cancer patients. *J Clin Oncol*. 1995;13(6):1509-1512.
14. Shepherd TM, Hoch MJ, Cohen BA, et al. Palliative CT-guided cordotomy for medically intractable pain in patients with cancer. *AJNR Am J Neuroradiol*. 2017;38(2):387-390.
15. Lee PS, Richardson RM. Interventional MRI-guided deep brain stimulation lead implantation. *Neurosurg Clin N Am*. 2017;28(4):535-544.
16. Kumar K, Hunter G, Demeria D. Spinal cord stimulation in treatment of chronic benign pain: challenges in treatment planning and present status, a 22-year experience. *Neurosurgery*. 2006;58(3):481-496.
17. Nissen M, Ikäheimo TM, Huttunen J, Leinonen V, von Und Zu Fraunberg M. Long-term outcome of spinal cord stimulation in failed back surgery syndrome: 20 years of experience with 224 consecutive patients. *Neurosurgery*. 2019;84(5):1011-1018.
18. Al-Kaisy A, Van Buyten JP, Carganillo R, et al. 10 kHz SCS therapy for chronic pain, effects on opioid usage: post hoc analysis of data from two prospective studies. *Sci Rep*. 2019;9(1):11441.
19. North RB, Kidd DH, Farrokhi F, Piantadosi SA. Spinal cord stimulation versus repeated lumbosacral spine surgery for chronic pain: a randomized, controlled trial. *Neurosurgery*. 2005;56(1):98-106.
20. Cameron T. Safety and efficacy of spinal cord stimulation for the treatment of chronic pain: a 20-year literature review. *J Neurosurg*. 2004;100(*Spine* 3):254-267.
21. Taylor RS, Van Buyten JP, Buchser E. Spinal cord stimulation for chronic back and leg pain and failed back surgery syndrome: a systematic review and analysis of prognostic factors. *Spine*. 2005;30(1):152-160.
22. Pollard EM, Lamer TJ, Moeschler SM, et al. The effect of spinal cord stimulation on pain medication reduction in intractable spine and limb pain: a systematic review of randomized controlled trials and meta-analysis. *J Pain Res*. 2019;12:1311-1324.
23. Taylor RS, Desai MJ, Rigoard P, Taylor RJ. Predictors of pain relief following spinal cord stimulation in chronic back and leg pain and failed back surgery

syndrome: a systematic review and meta-regression analysis. *Pain Pract*. 2014;14(6):489-505.
24. Kumar K, Rizvi S, Nguyen R, Abbas M, Bishop S, Murthy V. Impact of wait times on spinal cord stimulation therapy outcomes. *Pain Pract*. 2014;14(8):709-720.
25. Kumar K, Wilson JR. Factors affecting spinal cord stimulation outcome in chronic benign pain with suggestions to improve success rate. *Acta Neurochir Suppl*. 2007;97(pt 1):91-99.
26. Fritsch EW, Heisel J, Rupp S. The failed back surgery syndrome: reasons, intraoperative findings, and long-term results: a report of 182 operative treatments. *Spine*. 1996;21(5):626-633.
27. North RB, Campbell JN, James CS, et al. Failed back surgery syndrome: 5-year follow-up in 102 patients undergoing repeated operation. *Neurosurgery*. 1991;28(5):685-690.
28. Stewart WF, Ricci JA, Chee E, Morganstein D, Lipton R. Lost productive time and cost due to common pain conditions in the US workforce. *JAMA*. 2003;290(18):2443-2454.
29. Lad SP, Babu R, Bagley JH, et al. Utilization of spinal cord stimulation in patients with failed back surgery syndrome. *Spine*. 2014;39(12):e719-e727.
30. Zucco F, Ciampichini R, Lavano A, et al. Cost-effectiveness and cost-utility analysis of spinal cord stimulation in patients with failed back surgery syndrome: results from the PRECISE Study. *Neuromodulation*. 2015;18(4):266-276.
31. Farber SH, Han JL, Elsamadicy AA, et al. Long-term cost utility of spinal cord stimulation in patients with failed back surgery syndrome. *Pain Physician*. 2017;20(6):e797-e805.
32. Elsamadicy AA, Farber SH, Yang S, et al. Impact of insurance provider on overall costs in failed back surgery syndrome: a cost study of 122,827 patients. *Neuromodulation*. 2017;20(4):354-360.
33. Taylor RS, Ryan J, O'Donnell R, Eldabe S, Kumar K, North RB. The cost-effectiveness of spinal cord stimulation in the treatment of failed back surgery syndrome. *Clin J Pain*. 2010;26(6):463-469.
34. Hoelscher C, Riley J, Wu C, Sharan A. Cost-effectiveness data regarding spinal cord stimulation for low back pain. *Spine*. 2017;42(suppl 14):S72-S79.
35. Kumar K, Rizvi S. Cost-effectiveness of spinal cord stimulation therapy in management of chronic pain. *Pain Med*. 2013;14(11):1631-1649.
36. Kemler MA, Raphael JH, Bentley A, Taylor RS. The cost-effectiveness of spinal cord stimulation for complex regional pain syndrome. *Value Health*. 2010;13(6):735-742.
37. Rosenow JM, Slavin KV. Destructive neurosurgical procedures for treatment of chronic pain. In: Bajwa ZH, Wootton RJ, Warfield CA, eds. *Principles and Practice of Pain Medicine*. 3rd ed. New York, NY: McGraw-Hill; 2017:840-847.
38. Mercadante S. Management of cancer pain. *Intern Emerg Med*. 2010;5(suppl 1):S31-S35.
39. Beauchamp TL, Childress JF. *Principles of Biomedical Ethics*. 5th ed. New York, NY: Oxford University Press; 2001.

Laura Stone McGuire, MD is a resident physician within the Department of Neurosurgery at the University of Illinois at Chicago in Chicago, Illinois.

Konstantin Slavin, MD is a neurosurgeon and professor at the University of Illinois College of Medicine at Chicago in Chicago, Illinois, who specializes in functional neurosurgery. He is a past president of the American Society for Stereotactic and

Functional Neurosurgery, the secretary of the International Neuromodulation Society, and the vice president of the World Society for Stereotactic and Functional Neurosurgery.

Citation
AMA J Ethics. 2020;22(8):E695-701.

DOI
10.1001/amajethics.2020.695.

Conflict of Interest Disclosure
The author(s) had no relevant conflicts of interest to disclose.

The viewpoints expressed in this article are those of the author(s) and do not necessarily reflect the views and policies of the AMA.

ISSN 2376-6980