ASRA NEWS

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In This Issue

Advancing the Science and Practice of Regional Anesthesia and Pain Medicine

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American Society of Regional Anesthesia and Pain Medicine

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President's Message

A Pillar of Research

Taking over as your president this past April, at our very successful Regional Anesthesiology and Acute Pain Medicine Meeting, I continue to be in awe of what a vibrant organization ASRA is. Just 3 years ago, ASRA had only two staff members working in a tiny office in Pittsburgh, embarking on a new and challenging adventure under self-management. Today, we have six staff supporting a dynamic, flourishing organization with 12 standing committees, 10 special interest groups (SIGs), and more than 4,500 members. As I take the baton from former President Oscar de Leon-Casasola, MD, I look forward to continuing to build on the organization's successes and helping it to grow in impact and influence.

As an anesthesiologist specializing in pain medicine, my activities are divided between research, teaching, and clinical practice at Rush University, and I am involved in clinical and basic research in both acute and chronic pain. Research is truly one of my passions, and it will be a significant theme of emphasis throughout my presidency.

"ASRA's mission is built around the two pillars of education and research."

ASRA's mission is built around the two pillars of education and research. Most ASRA members are aware of our popular annual meetings and weekend courses that continue to draw the highest quality faculty and large audiences who are very much appreciated. However, you may not be as familiar with all of the activities that we do around research.

In 2016, we increased the amount of grant money available through the ASRA research grants to $200,000 annually, and we hope to be able to continue to increase grant amounts as we attract funders and build our investment reserves. This increased funding allows us to provide funding for larger projects addressing both regional anesthesia and chronic pain medicine. We have also identified specific research priorities to help guide grant applicants in their development of projects that support our strategic plan. The Carl Koller Memorial Research Grant was first awarded in 1986 and is now given in even-numbered years. In 2016, we selected the Carl Koller Memorial Research Grant recipient, Harsha Shanthanna, MBBS, MD, MSc, and his team at St. Joseph's Hospital in Hamilton, Ontario, Canada, who are studying postsurgical pain after thoracoscopic surgery.

The Chronic Pain Medicine Research Grant, first given in 2011, is typically awarded in odd-numbered years but was not awarded in 2015. In 2016, we selected Shalini Shah, MD, and her team at UC Irvine for a project that will look at the use of Botox in pediatric migraine patients.

Asokumar Buvanendran, MD
ASRA President

A critical component of these grants is bringing the study findings back to our members following project completion. We require grant recipients to provide updates on their projects after 1 year at the relevant annual meeting, and we publish summaries of those updates on our website. For example, Carl Koller Memorial Research Grant recipient Barys Ihnatsenka, MD, shared an update on his exciting work using a mixed-reality simulator at the 41st Regional Anesthesiology and Acute Pain Medicine Meeting in 2016 in New Orleans.

Grant recipients are encouraged to submit their completed findings to *Regional Anesthesia and Pain Medicine* for publication. To see the published findings of past recipients, please visit www.asra.com/research and click on the links under each grant.

The process of developing and submitting a grant application can sometimes be intimidating. ASRA has looked at some of the challenges of this process and identified a couple of ways to help ease the burden. One tactic will be a transition to a "letter of intent" (LOI) format for research grant applicants. Instead of completing the entire grant proposal for review, applicants will be asked to prepare an LOI describing their research goals. Members of the selection committees can then review and provide direction to support applicants in preparing full proposals.

Furthermore, although these grants are competitive, we intend to provide mentorship to applicants who have not been successful in receiving funds to help them develop their proposals further. I strongly believe that mentoring the next generation of pain medicine researchers is one of ASRA's duties.

Another way that ASRA will be able to aid in developing quality research will be through the recently established Professional Development Committee. Led by Board Member Brian Sites, MD, this committee will provide unique mentoring opportunities such as aiding faculty members with presentation skills, helping new researchers develop hypotheses, and teaching the art of reading and interpreting scientific papers. At this writing, the committee is developing a survey to assess members' interests and needs in these areas.

As a testament to the increasing influence of our organization and our members' research, we received a record number of abstract

submissions to our Regional Anesthesiology and Acute Pain Medicine meeting this spring. The previous record was 350, and we received a whopping 501 submissions for this meeting. We have invited our abstract authors to also submit videos summarizing their work. These videos allow dissemination of findings to our colleagues beyond the meeting as we work to ultimately better serve our patients.

Watching as a project goes from an LOI to a grant proposal to a study, from an abstract to a published paper and, ultimately, to clinical practice, is an inspiring and exciting process. I hope you will join me in supporting ASRA's research efforts—whether it be through direct participation, reading the study findings, or even a donation to one of our funds. Our organization will continue to stand tall through the support of this key pillar.

What else can ASRA do to support the research pillar? If you have suggestions on this or any other aspect of ASRA, please e-mail me at ASRAPresident@asra.com. And, thank you for your support of ASRA!

What Are They Looking for?

I recently had this conversation with one of our senior residents (J) who chose to return for an elective rotation in the ambulatory surgical center to get more exposure to regional anesthesia and to be more acquainted with patients' flow through an efficient surgery center's operating rooms.

After we were done with the morning round of first start blocks, I asked him: Did you find a job yet?

J: I interviewed in four places around the area, and I accepted a job at X hospital.

Me: Are you going to be doing all subspecialties there?

J: Pretty much, they have diverse surgical volume. Dr E [that is me], do you know what was the one question I was asked in all my four interviews?

Me: What was that?

J: "Are you comfortable with blocks and regional anesthesia?" They did not ask me whether I am comfortable doing big vascular or thoracic cases or whether I am comfortable with line placements or invasive monitors. Regional anesthesia was the one thing that they all asked me about.

Me (with a big smile on my face): Well, we are here to help you learn. Is that next patient ready for a block yet?

The practice of regional anesthesia has expanded over the past decade, and most groups (academic and private practices) value having new partners with this skill set. This conversation made me think about the responsibility we have toward our trainees. We need to help them think about regional anesthesia as a means to an end goal. This goal should always be to add value to our patients' surgical experience. The only way to do this is to think and act like an acute pain medicine consultant skilled in regional anesthesia and knowledgeable about all other modalities of treatment for acute pain.

"The only way to add value is to think and act like an acute pain medicine consultant skilled in regional anesthesia and knowledgeable about all other modalities of treatment for acute pain."

The record number of registrants for the ASRA spring meeting in San Francisco and the diversity of the program this year make me look forward to the meeting and all that it will have to offer. It is also a testament to the success of the ASRA programs in supporting education and research.

Nabil Elkassabany, MD MSCE
ASRA News Editor

I would like to thank Dr Melanie Donnelly, the associate editor for regional anesthesia for the *ASRA News,* for her service as her term ends. Melanie has been instrumental in the development of the *ASRA News* to its current form. I also would like to welcome Dr Kristopher Schroeder to the *ASRA News* family as he takes over for Melanie. I am sure he will bring new energy to your *ASRA News*.

In this issue of the newsletter, Dr Asokumar Buvanendran offers an interesting inaugural presidential message. His very first message focuses on research and education as the main pillars of the ASRA mission. Innovations, defining the impact of our practice on patients' outcomes, and new discoveries are the end product of research and the way of the future. We also bring to you in this issue snippets of the practice experience from different institutions around the country. You will read how the University of California at Irvine conforms its care for joint arthroplasty patients to adapt to the bundled payment model. You will also learn about the experience of one institution in using stellate ganglion blockade for treatment of posttraumatic stress disorder in United States veterans. On a lighter (but a very scientific) note, Dr Veena Graff explains her effort to apply music therapy in her previous institution (the University of Vermont) and how she plans to do the same at the University of Pennsylvania. From the same institution, Dr Taras Grosh and colleagues describe their regional anesthesia group's experience with mitigating some of the inherent risks of the sitting position in patients undergoing shoulder arthroscopy by stratifying patients by their comorbidities. As enhanced recovery protocols become more popular for different surgical service lines, the University of Virginia group describes theirits protocol for using intravenous lidocaine as part of their multimodal regimen for postoperative pain management in patients undergoing colorectal surgery.

However, this is not everything we have for you in this issue. You have to read it all to learn it all!

Initial Experience With Bundled Pay for Total Joint Arthroplasty Procedures

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The current healthcare landscape is evolving to yield paradigms that improve patient care and curtail cost.[1] Patient centric and collaborative models that accentuate "value" as opposed to "volume" are gaining impetus.[2–4] This is exemplified by the Bundled Payments for Care Improvement (BPCI) initiative of 2013 that aims to study if holistic episode based payments can diminish Medicare payments for total joint arthroplasty (TJA) procedures while perpetuating quality.[5,6] The purpose of this review is to outline initial experiences with bundled payments for TJA procedures and potential implications on anesthesiology practice.

There is consensus that existing healthcare paradigms in the United States are plagued by unsustainable cost inflation that does not parallel enhanced patient outcomes.[7] The current system has been characterized as a broken model with widespread waste, redundancy, and care fragmentation.[7,8] Rather than accepting the status quo, the Affordable Care Act (ACA) has a multitude of initiatives and incentives that strive to strengthen partnership amongst practitioners.[8–10] A prominent element of the ACA is savings and enhanced care achieved via accountable care organizations (ACO); defined by Epstein et al[10] as models "in which various constellations of providers agree to assume collective responsibility for the care delivered to a defined Medicare population." The Medicare Access and CHIP Reauthorization Act of 2015 further manifests the Centers for Medicare and Medicaid Services (CMS) goal of transitioning to merit based incentive payment systems or advanced alternate payment models (such as Accountable Care Organizations). CMS also instituted the Hospital Readmissions Reduction Program in 2013, which includes explicit provisions for payment reduction after elective TJA procedures for hospitals with 30 day readmission rates above national benchmarks.

Health care delivery redesign is being accelerated by a long needed transition in payment systems towards value based paradigms. Porter et al[11] elucidate, "The clear message is that hospitals, health care centers, and clinicians should no longer be spending time discussing *whether* to participate in bundled payment programs but instead focusing on *how* to do the work necessary to succeed under them." In contrast to a fee for service model, an integral feature of ACOs is a progression toward bundled payments that encompass comprehensive episodes of care.[6] In an ACO, it is incumbent upon hospitals, physicians, and post–acute care providers to collaborate and restrain both the quantity and cost of unnecessary and non–evidence based services.[12,13] Demonstrating patient centric value contribution is paramount in so called "incentive compatible" paradigms that aim to marginalize individual predilections.[14] Value is essentially a global assessment of quality in relation to cost.[3,4,15] In the context of perioperative care, appraisal of quality is linked to longitudinal patient dispositions, such as the haste with which patients return to baseline function.[3]

"As forthcoming payment models are dynamically redefined, it is sensible for anesthesiologists to explore expanding roles that augment both the scope and quality of patient interaction during the surgical course."

While there is timely evidence that has demonstrated both cost savings[16] and improved patient experiences[17] in ACO paradigms, outcomes in the setting of surgical procedures are only recently materializing by analyzing the experience with BPCI for TJA. In 2016, CMS made bundled payments for total hip and knee replacement mandatory in 67 regions under its Comprehensive Care for Joint Replacement model.[18] Within this context, Lee et al[18] reported clinical outcomes were maintained along with an 11% cost decline for TJA procedures. One key step toward enhanced efficiency was modifying physical therapists' schedules so that

Figure 1: *Opportunities for value added care within the context of bundled perioperative care.*

Decreased perioperative morbidity and mortality	Augmented patient experience	Augmented surgeon satisfaction
Enhanced disease monitoring	Optimized multimodal analgesia utilization	Leverage of the opioid epidemic via enhanced risk stratification
Decreased average length of hospital stay	Decreased readmission post-discharge	Diversion of postdischarge care from inpatient facilities
Decreased same day surgery cancellation rates	Prevention of non–evidence based perioperative testing and intervention	Decreased utilization of emergency care resources
Clinical implementation of point of care ultrasound	Enhanced patient education	Perioperative lifestyle modification & preventative care
Quality improvement & research contribution	Leadership & management of perioperative clinical pathways	Optimization of seamless care coordination with perioperative practitioners
Optimization of health information technology infrastructure	Leadership & management of interdisciplinary care teams	Optimized operative throughput and reduced surgical times

virtually all patients were out of bed on the day of surgery. This translated to a 9.5% decrease in average length of stay.[18] An original investigation by Dummitt et al[5] demonstrated that in comparison to nonparticipating hospitals, significant Medicare payment declines are observed for lower extremity joint replacement episodes in BPCI participating hospitals. Notably, these savings are achieved without negotiation of important quality metrics, including unplanned readmissions, postdischarge emergency department visits, and perioperative mortality. Iorio et al[1] are similarly able to exhibit positive fiscal experiences for TJA procedures in a BPCI model. Here, cost savings are primarily attained via decreasing the average length of hospital stay and diversion of postdischarge care from inpatient facilities. A study by Bozic et al[19] revealed that the cost for TJA procedures is highly contingent on postdischarge care, noting that it contributes to upwards of one third of total episode payments. Enabling tailored intervention, Siracuse and Chamberlain[20] validated that a risk stratification scale can effectively identify elevated risk patients scheduled for TJA.

As forthcoming payment models are dynamically redefined, it is sensible for anesthesiologists to explore expanding roles that augment both the scope and quality of patient interaction during the surgical course.[21] The Figure presents several diverse opportunities for anesthesiologists to contribute *value added* (defined as either enhanced quality or decreased cost[3,4,15]) care within the context of bundled care compensation. Notably, many of the prospects outlined in the Figure transcend the immediate operative period and embrace a philosophy of shared accountability for ultimate patient centric outcomes throughout the perioperative continuum. This integration of complete and interdisciplinary care that primarily focuses on the patient—starting from the decision to pursue surgery until full patient recovery—is exemplified by the discipline of perioperative medicine.[4] Within the realm of perioperative medicine, emerging paradigms such as enhanced recovery after surgery (ERAS)[22] and the perioperative surgical home (PSH)[23] aim to unify providers for the collective goal of improved patient care provided in a fiscally responsible manner.[8] The essential foundations of a PSH include patient centeredness, comprehensiveness, coordination, accessibility, and commitment to quality and safety.[24–26] Similarly, the key components of ERAS include collaborative decision making, lifestyle modification before surgery, standardized in hospital perioperative care, achieving full recovery, and using clinical data for quality improvement.[4]

In close partnership with other disciplines, the Department of Anesthesiology and Perioperative Care at University of California, Irvine (UCI) implemented an innovative PSH program for TJA procedures in 2012.[27] Encouraging results included a decreased incidence of major complications, lowered blood transfusions rates, shortened lengths of hospital stay, and reduced postdischarge readmission rates.[27] A subsequent report from UCI indicated that program success was maintained with outcomes further improved.[28] The PSH model has also been implemented in a number of other organizations, including University of Alabama,[29] Kaiser Permanante,[30] and DC Children's.[31]

Specific multimodal and opioid sparing strategies that can be implemented throughout the perioperative course to optimize analgesia after TJA procedures are elucidated.[28,32] Amidst a major public health crisis[33] (often delineated as "the opioid epidemic"), this presents a particularly keen opportunity for value added care after TJA procedures. Raphael et al[34] also demonstrated that direct hospital fiscal burden was substantially below benchmark levels

for patients enrolled in the TJA PSH at UCI Health. The explicit strategies utilized in the program throughout the perioperative continuum to curtail repeat admissions after hospital discharge are outlined in a separate case report.[35]

Using the "burning platform" business lexicon,[36,37] it has been said that the current healthcare landscape is at a crossroads. Paradigms that hasten surgical recovery[3] are gaining much momentum, fulfilling the Institute for Healthcare's proposed triple aim of improving the experience of care, improving the health of populations, and reducing per capita costs.[38] The BPCI initiative is a transparent strategy that is currently being utilized by CMS to clarify if episode based payment can translate to "higher quality, more coordinated care, at a lower cost to Medicare."[1] Early results have demonstrated that there is indeed significant potential for cost savings and improved care quality with the application of collective ("bundled") fiscal models.[1–5] In a dynamic landscape[21] where value added contribution to patient care is anticipated to be financially endorsed, it is prudent to integrate clinical opportunities that parallel favorable patient outcomes. An expansion in scope of practice throughout the perioperative continuum, via paradigms such as ERAS and PSH, is one such means to enhance care quality while also preparing anesthesiologists for bundled pay.

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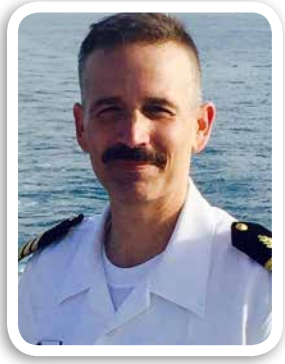
Stellate Ganglion Block for Posttraumatic Stress Disorder: A Call for Clinical Caution and Continued Research



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A 53-year-old man, retired United States Naval Officer with more than five combat deployments in support of special operations suffered from posttraumatic stress disorder (PTSD)–like symptoms for 12 years before entering into the study protocol. Initially, medications enabled him to continue on active duty service; however, upon retiring from the military, he noted that his PTSD symptoms became more apparent. Although he had received standard of care mental health visits' medications and group, family, and individual counseling for PTSD, he ultimately suffered what he called a "nervous breakdown," resulting in self-medication with alcohol and social isolation from his wife and children. He was formally diagnosed with PTSD in 2010. In 2012 he heard about a study for a rapid treatment for PTSD called the stellate ganglion block (SGB) that could be performed in less than a day. He subsequently sought out the treatment and entered into the study protocol.

He described the procedure as very tolerable, especially in light of his decreased symptoms, which he explained as a sense of wellness and a lifting of his anxiety after treatment No. 1 (placebo). He noted that he felt the best he had in over a decade. He continued to feel good about participating in the study after his subsequent procedure (active SGB treatment) and noted similar, but less dramatic, results as compared to the first procedure. In fact, he felt so good that he was able to go on a trip with his family for several weeks. During the trip he suffered a significant relapse of symptoms that he described as rapid onset over the course of a day. The patient notes that he would gladly undergo such a simple procedure multiple times if he could continue to see the same reduction in symptoms that he had with both injections.

It is estimated that 7 to 8 of 10 Americans will suffer from PTSD. Military populations suffer PTSD at rates estimated at 11–15% since Vietnam, Gulf War, and Operations Iraqi Freedom and Enduring Freedom, and it is estimated to occur at up to rates of 35% if the operational tempo seen in the last decade is maintained.[1,2]

Yet, current evidence-based PTSD therapies are not without challenges and have limited reach and impact.[3] Overall, existing evidence-based treatments have a 30–40% success rate.[4,5] However, existing treatment guidelines have often disagreed on first-line therapy. For instance, there is disagreement on the role that pharmacotherapy should play in the treatment of PTSD. While the Institute of Medicine seemingly downplays the role of medications, the Veteran Affairs/Department of Defense emphasizes the use of medications in their clinical practice guidelines.

Regardless of the treatment guideline chosen, there is a sense that patients have to overcome significant obstacles to receive current evidenced-based treatment options. These obstacles include the stigmata of seeking mental health care, profound pharmacological side effects, and perhaps most insurmountable—the time commitment of weeks, months, and even years necessary for effective therapy.

This has led physicians to explore the potential benefits of alternative therapies for improved clinical management of PTSD in order to find more rapid treatments with longer durations of effect.

SGB case reports indicating immediate, dramatic, and sustained benefit have led to widespread lay press endorsement of the treatments, with reports appearing on Fox News, *Time Magazine*, and endorsements by Oprah Winfrey. The idea that a one-time SGB could cure PTSD has become so pervasive in society that the authors' team has been approached by a Congressman and leaders of military units requesting that their patients be flown to the treatment facility in order to receive an SGB.

Although case reports are becoming more common, the block itself has been around for decades and used primarily for indications related to vascular and pain-related conditions. Side effects are rare but can be catastrophic; these include rapid-onset seizures, stroke, respiratory compromise secondary to phrenic and recurrent

laryngeal nerve blocks, inadvertent intrathecal and epidural injections, as well as hematoma-induced respiratory insufficiency and local anesthetic systemic toxicity.

The stellate ganglion is a structure in the sympathetic chain commonly found at the level of the 7th cervical vertebra. In 80% of cases, it is a single ganglion formed by fusion of the inferior cervical sympathetic ganglion and the first thoracic sympathetic ganglion; in the remainder of individuals, it is two ganglia in close proximity. By the 1930s, clinicians recognized that injecting local anesthetic into the stellate ganglion, known as a *stellate ganglion block*, inhibited both efferent sympathetic fibers and visceral pain fibers to the upper extremity and face.[6] SGB is now commonly used for the treatment of hypersympathetic activity influencing the upper extremity, such as Raynaud's phenomenon, or in sympathetically mediated pain as may be present in complex regional pain syndrome.

In 1947, Karnosh and Gardner[7] reported a series of cases in which SGBs were used to treat depression. The technique, however, largely was forgotten as a psychiatric treatment until recent cases and popular press reports of SGBs being used to treat PTSD, alcoholism, and menopause.[8–14] The mechanism of action of an SGB's ability to mitigate symptoms in patients with PTSD is unknown. Proposed mechanisms for the SGB's benefit in patients with a psychiatric condition include downregulation of norepinephrine and/or nerve growth factor. A second theory notes that the SGB procedure should be performed on the right side for patients with PTSD. This proposal is likely because initial case series happened to be performed in patients with right upper extremity pain conditions and PTSD. Correlation with current functional MRI studies has not provided a convincing model to date.

"Current evidence-based PTSD therapies are not without challenges and have limited reach and impact."

Despite the limited understanding of the mechanism of action of right-sided SGBs to mitigate PTSD symptoms, coupled with the possibility of rare, but catastrophic risks, the appeal for a rapidly acting treatment modality with long duration of action is highly desirable in light of the rising tide of PTSD. Equal to that appeal is the need for further research on the topic to ensure efficacy and safety of SGBs for PTSD.

Table 1 summarizes the entire body of published work on SGBs and PTSD at the time the Naval Medical Center San Diego initiated the first randomized controlled trial on this topic.[15] Previous published work was entirely composed of case series, totaling 27 patients. Each of these case series had significant methodologic flaws, the most notable being inconsistent follow-up. However, it should be pointed out that a study by Mulvaney et al[11] on military populations in 2010 was a turning point in the study of SGBs for PTSD, as it was the first study to use standard outcome measures and to collect data prospectively. Randomized controlled trials and large-scale registry data were clearly absent despite widespread clinical use of the procedure.

The first randomized, blinded, sham-controlled study to evaluate the efficacy of SGB on PTSD symptoms in a military population was published in *Regional Anesthesia and Pain Medicine* in 2016.[15] In addition to patient-reported symptom severity scores, such as the PTSD Checklist (PCL), this study was the first to require a diagnosis of PTSD by a psychiatrist and used the Clinician-Administered PTSD Scale (CAPS).

Although previous case series have suggested SGBs offer an effective intervention for PTSD, this study did not demonstrate any appreciable difference between SGB and sham treatment. The results indicated that observed PTSD symptoms (CAPS) improved in participants in both the active and sham groups. This was also true for self-reported scores for depression (Patient Health Questionnaire), and anxiety (Beck Anxiety Inventory), but not for self-reported PTSD scores (PCL) or pain (visual analogue scale). The overall magnitude of improvement was modest, less than previously reported in case series. Moreover, improvement with the SGB was not superior to the sham intervention.

The results of this randomized controlled trial differed significantly from a larger retrospective study previously published in the journal *Military Medicine* in 2014 by Mulvaney et al.[16] Mulvaney and colleagues[16] observed the response that active duty military patients suffering from combat-related PTSD symptoms had to treatment with SGBs. The authors used a well-validated PTSD symptom severity scale (PCL-Military [PCL-M]) and considered a 10-point change as indicative of a clinically significant improvement. The PCL-M was collected at baseline, 1 week, and each month after treatment up to 6 months. If patients had an initial response and PCL scores after 3 months returned to or were near baseline, they were offered another SGB. In this nonrandomized data set, most patients responded within the first week (79%). This phenomenal response rate seemed to persist at each data collection point (82% at 1–2 months, 74% at 3–6 months). Not only was the response rate significant, but the degree of the response was remarkable with a 22-point average reduction observed.

It is interesting to consider why the results from this study differed so significantly from the randomized trial performed in a similar

Table 1: *Summary of published work on stellate ganglion blocks and posttraumatic stress disorder.*

Author/year	Patient population	Study type	n	Conclusions
Lebovits et al, 1990	CRPS and PTSD 15 y/o s/p GSW in RUE. Series of 13 SGB injections for CRPS treatment.	Case report	1	Need to diagnose PTSD in pain patients; unlikely to decrease pain without treating both
Lipov et al, 2008	PTSD	Letter to editor	1	
Lipov et al, 2009	Unifying theory on SGB, CRPS, hot flashes, and PTSD	Hypothesis	n/a	Animal model of central representation of sympathetic nervous system (2001)
Lipov et al, 2010	Pulsed radio frequency to the SGB for PTSD	Case report	1	Symptom diary: 1 week: 10% of anxiety; 50% appetite; 25% sleep
Mulvaney et al, 2010	Panic/anxiety symptoms of PTSD	Case series: prospective	2	PCL: 50% reduction Meds: 100% reduction
Lipov, 2010	PTSD: Can the SGB be the answer?	Editorial	n/a	n/a
Alino, 2011	Misleading conclusion from unifying theory	Hypothesis	n/a	Central projections unknown: previous study based on rabies virus (retrograde)
Lipov et al, 2012	Novel application: preliminary observation of treatment of PTSD	Case series: retro	8	PCL-M pre: 67.8 (55–79) PCL-M post: 35.3 (21–63) * Average follow-up 17.5 days (1–59)
Hickey et al, 2012	PTSD	Case series: letter to editor	9	CAPS score: Baseline/1 week/4–6 weeks Success > 30% reduction: 56%
Lipov et al, 2012	Modulation of NGF and SGB – link between memory and PTSD	Hypothesis	n/a	Same as 2009 article
Lipov et al, 2013	Refractory PTSD and memory	Case report	1	PCL-M: Pre (71)/post (40) RAVLT: Immediate 3 -> 6/15 -> 15 Alcoholism: now a social drinker
Alino et al, 2013	PTSD – military trauma	Case report	4	PCL-M pre procedure (1–3 days): > 50 PCL-M post procedure (1–3 days): < 24* * Post PCL-M not recorded in 25%

CAPS – Clinician-Administered PTSD Scale; CRPS – complex regional pain syndrome; NGF – nerve growth factor; PCL-M - PTSD CheckList – Military version; PTSD - post-traumatic stress disorder; RAVLT - Rey Auditory Verbal Learning Test; SGB – stellate ganglion block

patient population by experienced physicians with nearly identical technique. Indeed, the differences highlight well the problems with drawing significant conclusions from nonrandomized or retrospective trials or from low-powered randomized controlled trials.

Both articles identified potential bias and possible confounders that could explain the widely disparate outcomes.

In the study of Hanling et al,[15] the authors noted that most of their study population had combat-related PTSD. Furthermore, many subjects were in the process of disability evaluation, which in part determines the amount of lifetime disability payments subjects will receive. Both of these factors are associated with a high rate of treatment failures. The fact that all patients showed improvement over time makes this conclusion less plausible, but the possibility still remains given the low number of subjects enrolled in the study.

In the study of Mulvaney et al,[16] the authors noted that most of the study population consisted of Special Forces members, highly motivated to redeploy with their units, and that the data were collected retrospectively with low follow-up rates. However, it should be added that without randomization, there is a significant possibility of observer and confirmation bias. For example, the article points out that many patients inflated their PCL scores in order to receive an SGB, once they heard from some of the early participants that the injections helped with symptoms, indicating that patients may have been actively minimizing their symptoms to avoid being stigmatized with a psychological diagnosis and/or not being allowed to deploy with their units. Likewise, patients may have also underreported post-SGB symptoms in order to ensure their return to full duty. A well-powered, randomized, blinded study design with military and civilian populations would mitigate this type of bias, as it would be evident in both the active and control arms of the study.

Ultimately, large-scale, randomized, controlled trials or the formation of an SGB for PTSD registry to track outcomes and determine if any populations in particular receive benefit or harm from this novel treatment of PTSD are needed. Fortunately, it appears that the United States Army Medical Research Acquisition Activity has funded a more definitive multicentered, well-powered study at Womack Army Medical Center, Tripler Army Medical Center, and Landstuhl Regional Medical Center, facilitated by the nonprofit RTI International research organization.

However, until such time as more conclusive studies can be completed, current evidence does not support widespread clinical use of the SGB procedure for PTSD. If it is used, it should be viewed as a bridging therapy meant to minimize PTSD symptomatology to allow increased engagement in existing evidence-based treatment options. In our current clinical practice, we receive requests to perform SGBs routinely on patients with PTSD; therefore, we have established practice guidelines to ensure we maximize the efficacy of these treatments. First, all patients must carry a diagnosis of PTSD confirmed by a mental health professional. Given the limited evidence, we do not perform SGBs for other mental health conditions such as generalized anxiety disorder. Second, we require that our patients have a therapeutic relationship with a mental health professional, as current evidence indicates the SGB procedure to be, at worst, an effective placebo and, at best, a method of symptom management rather than a cure. Third, each patient must complete a baseline biopsychosocial questionnaire that measures relevant parameters related to PTSD as well as follow-up baseline questionnaires every 4–6 weeks to assess the efficacy of the SGB procedures and their overall progress with their condition. Fourth, per previous protocols described in case reports and prospective studies, we perform all SGB procedures under continuous ultrasound guidance on the right side with a standardized dose and volume of local anesthetic (5 mL of 0.25% bupivacaine with 1:400,000 epinephrine). Finally, we perform a series of three SGBs separated by 1–2 week intervals and reassess each patient's progress via a follow-up visit and follow-up biopsychosocial questionnaire. If the patient is showing substantial progress with PTSD, we continue the SGBs. If the patient has demonstrated minimal or no improvement, we discontinue the SGBs. By following this protocol, we allow patients suffering from PTSD to receive this experimental treatment, while continuously monitoring their progress to ensure optimal outcomes for each patient.

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Shared Decision-Making in Regional Anesthesia

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Consider this all too common scenario: You meet a patient scheduled for a total joint arthroplasty. This is your first time meeting the patient, and he has not spoken with anyone from anesthesia before today. You believe this patient is a perfect candidate for a spinal anesthetic, but the patient is nervous and instead opts for a general anesthetic. He tells you that he is afraid of being paralyzed and/or he knows someone who had a bad experience with a spinal. As an anesthesiologist you wonder if this patients' reluctance could have been avoided with a preoperative meeting on another day, before the day of surgery and separated from the stress of the preoperative holding area. And if so, how might preoperative anesthesia education affect his decision?

Anesthetic choice on the day of surgery can be influenced by multiple factors: patients' comorbidities, coagulation status, body mass index, culture of the institution, surgeon preference, and also the comfort level of the anesthesiologist.[1–4] But how does patient preference factor into this decision? This is an important question, especially in the era of the perioperative surgical home (PSH) where patient satisfaction with surgical care is highlighted. With this in mind, how can we, as anesthesiologists and perioperative physicians, involve patients more concretely in decision-making for their anesthetic in a timely and meaningful way? The first step along this road is making sure the patient is appropriately informed and educated, and that often means preoperative education regarding anesthetic options.

PATIENT EDUCATION AND HOW IT CAN AFFECT ANESTHESIA

Preoperative patient education is certainly not a new concept. In fact, patient education forms the underpinnings of the informed consent process. Ideally, the informed consent process includes enough information for patients to make educated decisions about their health care. When it comes to anesthesia, throughput pressures in the operating room can influence the consenting process when it occurs immediately preoperatively. This situation is especially evident when there are several anesthetic options to choose from, as is the case when offering blocks to patients for pain control or as an anesthetic. Patients are often not sure about the different anesthetic options available to them when presenting for surgery. It is possible that patients may harbor incorrect assumptions regarding anesthetic management that is derived from a previous occasion, a family member's experience, or even information researched online.[5,6] In a practice with a preoperative clinic, a fully informed dialogue about anesthetic options can be conveyed in a calm environment.[7] If a preoperative clinic does not exist, the first interaction that a patient has with an anesthesiologist is often in the preoperative holding area before surgery. This is usually a time when the patient's anxiety level is high, possibly interfering with his or her ability to process new information, and therefore potentially affecting the patient's ability to appropriately weigh the anesthetic options presented.[8] With this in mind, it is worth considering the utility and merit of introducing information to the patient earlier and in more diverse formats.

Researchers at the University of Pennsylvania examined the impact of incorporating anesthetic information into a preoperative education course for patients scheduled to undergo total knee arthroplasty. They found that patients who had this early education on anesthetic options were more likely to choose a regional anesthetic in the form of neuraxial anesthesia than those who did not have that educational experience.[9] This study helps demonstrate that patient education is a crucial step toward fostering an environment for informed decision-making. Brooks et al[10] examined similar principles by using an iPad and providing patients with an informational brochure about regional anesthesia options in the preoperative clinic. They discovered that not only did this intervention lead to a 10% increase in their regional anesthesia acceptance rate, but also it reduced delays to operating room. This reduction in delays to the OR reflects a decreased need to exhaust preoperative time discussing the various anesthetic options with patients who are undecided. Groves et al[11] also demonstrated a similar principle. They were able to establish that by providing patients with "relevant websites" of anesthesia information and education, the utilization of neuraxial anesthesia increased.

These studies demonstrate that there are a number of ways to educate patients before the day of surgery. These improvements can be further reinforced by creating a service whereby an anesthesiologist is available for questions and concerns that a patient may have by way of telephone calls or e-mails. By introducing this information to patients and educating them before the day of their surgery, we give them the tools necessary to successfully take part and share in the decision regarding their anesthesia.

Figure 1: *The SHARE Approach to shared decision-making. Reprinted from Agency for Healthcare Research and Quality, 2016.*[12]

THE CONCEPT OF SHARED DECISION-MAKING

Shared Decision-Making is the model of including patients and their family in the decision-making process (Figure 1). The Agency for Healthcare Research and Quality has published the "SHARE" Approach to this type of process, which includes the following five steps: (1) Seek your patient's participation, (2) Help your patient explore and compare treatment options, (3) Assess your patient's values and preferences, (4) Reach a decision with your patient, and (5) Evaluate your patient's decision.[12] The conventional informed consent discussion typically includes a description of the treatment. However, a full explanation of alternatives and an assessment of how this treatment choice fits within the patient's values and preferences are often lacking. According to Posner et al,[13] 70% of the informed consent litigation complaints revolve around the risks of treatment. To avoid the pitfalls of using incorrect data, using terms not comprehensible to patients, and avoiding the dissatisfaction that patients express is associated with the paternalistic approach to the consent processes, providers may choose to rely more on the SHARE principles for consent and consider the creation and use of decisions aids.[14] This would allow the patient and family, who may have strong beliefs and views, to communicate with the physicians about their medical management and for both to come together to craft a unique and specific plan: a true ideal of patient-centered care.

Shared decision-making has become popular within many specialties across medicine.[15–19] These discussions are now starting to populate the field of anesthesia and chronic pain.[20] One impact of this process is improved patient satisfaction. Flierler et al[14] showed that 94% of patients wanted to be involved in their anesthetic decision-making and that to be involved increased patient satisfaction. Hwang et al[21] similarly demonstrated that 88% of patients wanted to be involved in their choice of anesthetic, resulting in patients feeling satisfied and respected.

The field of regional anesthesia is rapidly growing and can help serve as the face of this movement toward patient education and shared decision-making, owing to the frequent existence of

multiple analgesic or anesthetic options and the nuanced decision-making that accompanies these options.

BRINGING IT ALL BACK HOME: HOW PATIENT INVOLVEMENT IS PART OF THE PSH

The evolving medical landscape is being guided by the "Triple Aim" set out by the Institute of Healthcare Improvement. These aims include improving the individual experience of care, improving the health of populations, and reducing per capita costs.[22] These goals require a collaborative effort for success, and anesthesiologists are counting on the PSH to be that collaborative effort.[23] The principles of the PSH lend themselves to the use of shared decision-making tools as part of the perioperative process, as well as anesthetic discussions taking place before the day of surgery. This allows patients to have their values and preferences regarding their anesthetic choices taken into consideration with ample time before the day of surgery. Brooks et al[10] found that by moving the patient consent process to the preoperative assessment clinic, their practices were more consistent with the triple aim of health care improvement.

As our care evolves to meet the triple aim and to accomplish patient-centered care, we need to also upgrade the tools we use to accomplish this care. Our processes for preoperative evaluation need to grow to allow for patient participation in decisions about their anesthetic. This may result in the creation and use of shared decision-making tools, as well as improved preoperative patient education in using multiple modalities. By leading the charge to educate our patients preoperatively and involve them in their care, we are leading the perioperative field into the future. And bringing them into our home: the PSH.

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Genotyping and Phenotyping in Pain Management

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According to the American Academy of Pain Medicine, chronic pain is an epidemic affecting approximately 1.5 billion people worldwide. With age comes more pain related problems. Cross sectional studies of patients with neuropathic pain have shown that even with pharmacological treatment, moderate or severe pain continues. Part of the difficulty is the heterogeneity of causes and symptoms that vary from individual to individual. Physicians who treat patients with pain note a marked variability in pain responses among patients. Physicians often treat these patients with the same arsenal of medications on a trial and error basis. This method may be time consuming and even potentially harmful to patients. Response to pain and medications may be partially but significantly influenced by genetic and phenotypic makeup. In the 1890s, Wilhelm Johannsen was the first to introduce the terms *genotype* and *phenotype*.[1] *Genotype* refers to the genetic components of an individual. *Phenotype* refers to the set of observable characteristics of an individual from the interaction of its genotype with the environment.

Under or overdosing is possible when patients respond differently to medications. Without knowledge of a patient's genetic makeup, treatment plans cannot be tailored to individual patient's needs. Pain is influenced by many factors, including genetic predisposition, prior experiences, physiological status, mood, coping skills, and sociocultural background.[2] The extent to which each of these factors has on the pain experience is unclear.

Several genes likely affect the pain experience and analgesic response. Two hereditary disorders are known to make individuals insensitive to pain: hereditary insensitivity to pain with anhydrosis and familial dysautonomia. As our knowledge grows, so may our ability to understand why pain persists in some patients but not others—despite identical traumas—or why some people have a low tolerance to pain while others have a much higher tolerance.

A recent study presented by Dr. Onojjighofia at the American Academy of Neurology's 66th Annual Meeting suggests that four genes may be involved in pain tolerance. His study examined 2,721 people diagnosed with chronic pain. The genes involved were catechol O methyltransferase (*COMT*), dopamine receptor D2 (*DRD2*), dopamine receptor D1 (*DRD1*), and opioid receptor kappa 1 (*OPRK1*). These four genes help to determine the pain threshold in individuals. Participants were taking opioid pain medications and rated pain from a 0 to 10. Patients with 0 pain were excluded from the study. Patients were divided into three groups according to pain perception: (1) low pain, a score of 1–3; (2) moderate pain, a score of 4–6; and (3) severe pain, a score of 7–10. The *DRD1* gene variant was 33% more prevalent in the low pain group than in the severe pain group. *COMT* and *OPRK* variants were 25% and 19% more prevalent, respectively, in the moderate pain group compared to the severe pain group. The *DRD2* variant was 25% more common among those with severe pain than those with moderate pain.[3]

"Pain is influenced by many factors, including genetic predisposition, prior experiences, physiological status, mood, coping skills, and sociocultural background."

While these sequence variations in DNA (SNPs) may help predict the likelihood of individual pain sensitivity, DNA testing should not be used to diagnose pain according to the Medical Treatment Utilization Schedule (MTUS) guidelines.[4] Although we may not use genetic testing to diagnose pain, genetic testing may affect the selection of medications used to treat it.

There are several reasons to consider genetic testing. Medications may be metabolized slowly in individuals with a genetic polymorphism that eliminates or decreases enzyme activity. Such patients may be at risk of an adverse drug reaction (ADR) or therapeutic failure. In addition, drug therapy may be ineffective if a drug is metabolized too quickly because of genetic polymorphism. Knowledge of these polymorphisms before initiating drug therapy could help in choosing the most efficacious agent and in decreasing the risk of ADRs.

Patients can be classified by how effectively they metabolize a medication according to how many copies of normal versus abnormal alleles they have inherited (Table 1).

Table 1: *Metabolism and alleles*

Metabolism level	Alleles	Activity level
Extensive metabolizer (EM)	2 normal alleles	Normal
Intermediate metabolizer (IM)	1 normal allele and 1 reduced allele or 2 partially deficient alleles	Intermediate activity
Poor metabolizer (PM)	2 mutant alleles	Very limited or complete loss of activity
Ultra rapid metabolizer (UM)	Multiple copies of functional alleles	Excess activity

Approximately 7–10% of Caucasians are *CYP2D6* deficient (poor metabolizers [PM]); only 1–2% of Asians and 2–4% of African Americans are PMs. Among Asians and African Americans, 30% are intermediate metabolizers of *CYP2D6*. Why are these variations important? Many of the medications we use to treat chronic pain are affected by these polymorphisms.

CYP INFLUENCE ON OPIOIDS

Various medications are pro drugs, inactive compounds that are metabolized to their active forms by CYP enzymes. Other medications are metabolized by P450 into clinically active metabolites. Table 2 shows common P450 substrates. Codeine, a pro drug, is metabolized by *CYP2D6* into its active form, morphine. Therefore, if a patient is a poor metabolizer of *CYP2D6*, he or she will not convert codeine into its active form and will get no analgesic benefit from the drug. On the other hand, a patient who is an ultra-rapid metabolizer of *CYP2D6* may experience dangerously high levels of morphine in his or her system. Two other commonly used opioids that are metabolized by *CYP2D6* to stronger, more potent forms are hydrocodone (metabolized into hydromorphone)

Table 2: *Commonly used substrates*[5,6]

1A2	2B6	2C19	2D6	3A4	2C9
Amitriptyline	Buproprion	Barbiturates	Codeine	Alprazolam	Valproic Acid
Nabumetone	Methadone	Topirimate	Tramadol	Midazolam	Piroxicam
Desipramine	Ketamine	Diazepam	Merperidine	Cyclosporine	Celecoxib
Tizanidine	Testosterone	Amitriptyline	Oxycodone	Dildenafil	Ibuprofen
Imipramine		Imipramine	Hydrocodone	Indinavir	Warfarin
Acetaminophen		Clomipramine	Dextromethorphan	Verapamil	
Cyclobenzaprine		Sertraline	Amitriptyline	Atorvastatin	
Clozapine		Citalopram	Nortriptyline	Lovastatin	
Fluvoxamine		Phenytoin	Doxepin	Digoxin	
Theophylline		Carisoprodol	Tamoxifen	Amiodarone	
Melatonin		Clopidogrel	Amphetamines	Methadone	
Duloxetine			Duloxetine	Erythromycin	
Caffeine			Metoclopramide	Trazadone	
Lidocaine			Propranolol	Fentanyl	
Warfarin			Venlafaxine	Buprenorphine	
Methadone					

Modified from Indiana University and Genelex websites.

Table 3. Clinical Consequences of Opioid Cytochrome P450 Drug Interactions

Opioid	CYP2D6 Inhibition or Patient is PM	Patient is CYP2D6 UM (enzyme not inducible by other drugs)	CYP3A4 Inhibition	CYP3A4 Induction	CYP2B6 Inhibition or PM
Codeine	Decreased analgesia (less morphine produced); UDS may show no metabolite present	Increased analgesia and toxicity (more morphine produced)	Increased analgesia and toxicity (more codeine and possibly more morphine)	Decreased analgesia (decreased codeine and morphine)	N/A
Hydrocodone	Possible decreased analgesia and/or increased toxicity (more hydrocodone and less hydromorphone produced); UDS may show fewer or absent metabolite present	Possible increased analgesia and toxicity (more hydromorphone produced); UDS may show fewer or no parent molecules present	Increased analgesia and toxicity (more hydrocodone and possibly more hydromorphone)	Decreased analgesia (decreased hydrocodone and hydromorphone)	N/A
Methadone	Increased analgesia and toxicity risk	Decreased analgesia risk	Increased analgesia and toxicity risk	Decreased analgesia risk	Increased toxicity (QTc prolongation risk)
Oxycodone	Possible decreased analgesia and/or increased toxicity (more oxycodone and less oxymorphone produced); UDS may show fewer or absent metabolite present	Possible increased analgesia and toxicity (more oxymorphone produced);UDS may show fewer or no parent molecules present	Increased analgesia and toxicity (more oxycodone and possibly more oxymorphone)	Decreased analgesia (decreased oxycodone and oxymorphone)	N/A
Tramadol	Decreased analgesia and increased risk of pro-serotonergic side effects, including a decrease in seizure threshold	Increased analgesia and toxicity	Slight increased analgesia and risk of toxicity	Possible decreased analgesia	Slight increased analgesia and risk of toxicity
Hydromorphone	N/A	N/A	N/A	N/A	N/A
Morphine	N/A	N/A	N/A	N/A	N/A
Oxymorphone	N/A	N/A	N/A	N/A	N/A
Tapentadol	N/A	N/A	N/A	N/A	N/A

NA, not applicable, PM, poor metabolizer; UDS, urine drug screen; UM, ultra rapid metabolizer

and tramadol. Oxycodone has an active metabolite, oxymorphone, with significant analgesic effects. Because oxycodone depends on *CYP2D6* for clearance, patients deficient in *CYP2D6* alleles could be prone to overdose.

CYP3A4 is also involved in opioid metabolism. Patients taking fentanyl or buprenorphine who are poor metabolizers of *CYP3A4* would have higher than usual blood levels of these mediations. Methadone, metabolized by *CYP34A*, is also metabolized by *CYP3B6*6*. Lower doses should be given to patients who are deficient in these alleles. Table 3 provides examples of clinical consequences of opioid cytochrome P450 interactions.

URINE DRUG SCREENING

Genetic polymorphism affects urine drug screening. A patient may state that he or she is not getting benefit from oxycodone. A quantitative urine drug screen may show the results listed below in Examples 1 and 2. In Example 1, the level of oxycodone is high, and a small amount of oxymorphone appears in the urine. This patient, who is a poor metabolizer of *CYP2D6*, may benefit from a change to a different opioid. In Example 2, the level of oxycodone is high, but there is no evidence of metabolite in the urine, which may be consistent with adulteration.

Genetic testing, available through several companies, is generally economically feasible. The test is often performed from a buccal swab. Common available SNPs that can be tested include CYP 2D6, 2C9, 2C19, and 3A4. The test is easy to perform, and the results are often received quickly.

The pain phenotype is a window to determine underlying pathophysiological mechanisms and a guide for individualized treatment options. Phenotyping can classify patients into smaller subsets from one large disease group. It can introduce a new standard of healthcare and help clinicians select the most advantageous treatments to improve medical outcomes. It will eliminate the one size fits all model that has been widely accepted today. Phenotyping is a tool for clinical purposes that may help us

Example 1: *Patient prescribed oxycodone who is poor metabolizer of CYP2D6.*

Test	Flag results	Measured results	Unit	Reference value
Confirmation opioids	positive		ng/ml	<100
Codeine	negative		ng/ml	<100
Hydrocodone	negative		ng/ml	<100
Hydromorphone	negative		ng/ml	<100
Morphine	negative		ng/ml	<100
Oxycodone	positive	20,240	ng/ml	<100
Oxymorphone	**positive**	**964**	**ng/ml**	**<100**

Example 2: *Urine drug screen consistent with adulteration.*

Test	Flag results	Measured results	Unit	Reference value
Confirmation opioids	positive		ng/ml	<100
Codeine	negative		ng/ml	<100
Hydrocodone	negative		ng/ml	<100
Hydromorphone	negative		ng/ml	**<100**
Morphine	negative		ng/ml	<100
Oxycodone	positive	63,267	ng/ml	<100
Oxymorphone	negative	0	ng/ml	<100

improve pain management. We can classify patients with similar pain etiology based on pain related sensory abnormalities—otherwise known as "sensory profiling"—and then direct management based on this classification. It is difficult and costly to genotype a large number of patients, but phenotyping with large patient cohorts is possible. Obtaining the sensory profile of a patient may reflect an underlying mechanism or combination of mechanisms influencing pain. Once determined, medication trials would follow. Responses based on sensory profile and certain pain descriptors would lead to targeted treatment options. Detailed phenotypic data gathering is necessary to understand the factors that ultimately define a phenotype. It is something we do every day in clinical practice while gathering information on demographics, pain history, physical examination, and investigations.

An example of clinical phenotyping is the UPOINT (Urinary, Psychosocial, Organ Specific, Infection, Neurologic, and Tenderness of Skeletal Muscles) system for a patient with urological chronic pelvic pain.[8] Instead of including all patients under one diagnosis, patients are classified into subtypes and managed according to the classification system. Based on the best available evidence, clinical phenotyping of patients directs management of individual phenotypes based on best available evidence. Multimodal therapy can then be selected as indicated by phenotype domains in the individual patient.

Another example of clinical phenotyping is a study conducted in patients with diabetic peripheral neuropathy (DPN), postherpetic neuralgia (PHN), radicular (neuropathic), or axial (nonradicular) low back pain (LBP). The investigators conducted 16 interview questions and 23 bedside examinations. They assessed symptoms and signs of 130 patients and performed a cluster analysis that revealed association patterns that characterized six subgroups with neuropathic pain and two subgroups with non neuropathic pain. There were eight subgroups of patients (clusters C1 to C8). Patients with DPN, PHN, and radicular LBP were distributed across the clusters C1 to C6, patients with axial LBP formed the clusters C7 and C8. When the investigators used classification tree analysis to determine the minimum number of interview questions and physical tests that would assign patients to clusters, interview questions were narrowed down to 6 and physical tests to 10. They then evaluated the diagnostic usefulness for LBP. Sensitivity and

specificity in distinguishing neuropathic versus nociceptive LBP was more than 90%. They demonstrated a pain assessment tool independent of disease etiology based on symptoms and signs.[9]

Careful phenotyping of cases can identify subgroups of patients with the same etiology. Personalized pain treatment is in its infancy, but we are advancing. Phenotyping is a clinical tool that can identify underlying pathophysiological mechanisms and guide individualized treatment options. Although genetic testing currently cannot be used to predict and diagnose chronic pain, we can use this information to better treat patients with painful conditions and reduce the process of trial and error that is often frustrating for both physicians and patients. The hope for the future is that genotyping, along with phenotyping, can personalize and individualize pain therapy and improve patient care.

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Clinical Implications of IV Lidocaine Infusion in Preoperative/ Acute Pain Settings


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INTRODUCTION

Lidocaine (xylocaine) was first introduced by Torsten Gordh in the 1940s and, since then, the clinical application of lidocaine has expanded beyond that of local anesthesia, making use of its systemic analgesic, anti-inflammatory, and anti-hyperalgesic effects.[1,2] Systemic lidocaine infusion has been used as an analgesic adjunct for the management of acute perioperative pain in many clinical settings. An ever-growing body of evidence supporting enhanced recovery after surgery (ERAS) protocols has led to a trend toward opioid-sparing multimodal analgesia, which may include intravenous (IV) lidocaine.

MECHANISM OF ACTION

Postoperative pain is due to a combination of inflammatory and neuropathic processes. The systemic inflammatory response to surgical trauma leads to neuroinflammation, decreasing the firing threshold of A-δ and C-fibers and acute postoperative pain. This increases the release of glutamate, which in turn increases N-methyl-D-aspartate (NMDA) receptor activation, leading to hyperalgesia and allodynia. In the chronic setting, this leads to activation of microglia and astrocytes in the dorsal horn of the spinal cord; in turn, this enhances the persistent release of proinflammatory cytokines and algesic mediators.[3,4]

The observed clinical benefits of lidocaine exceed its half-life by greater than 5.5 times (8.5–24 hours) after discontinuation of the infusion.[2] This is long after lidocaine has been metabolized to its nonbiologically active byproducts, pointing to alternative mechanisms beyond its local anesthetic properties. In vitro studies have demonstrated the modulatory effect of lidocaine on potassium channels, calcium channels, G-coupled protein receptors, NMDA receptors, and the glycinergic system. Systemic administration of lidocaine tends to decrease IL-1δ, TNF-α, ICAM-1, mucosal COX-2, and plasma prostaglandin E2. Such mechanisms are thought to contribute to the anti-neuroinflammatory effects of lidocaine and may explain its clinical benefits in the management of acute and chronic pain.[3]

Polymorphonuclear granulocytes (PMNs) have a pivotal role in the release of proinflammatory cytokines and reactive oxygen species (ROS) ramping up the migration of neutrophils through a feed-forward loop. Lidocaine inhibits the priming of PMNs by lysophosphatidic acid (LPA) and platelet-activating factor (PAF).[3,5] Schmidt et al described the inhibitory effect of lidocaine on PMN adhesion and migration.[6] This may contribute to the modulatory effect of lidocaine on the "sterile inflammation" seen in trauma and surgery.[2,3,5,6]

"The growing interest in the ERAS concept has inspired a wave of various investigational endeavors in pharmacology and pathophysiology of acute and perioperative pain."

Some animal studies demonstrate suppression of polysynaptic C-fibers and wide dynamic range (WDR) neurons, which also may play a role in the anti-neuropathic pain properties of lidocaine.[3]

CLINICAL APPLICATION

According to the 2016 review in the *British Journal of Anaesthesia,* perioperative lidocaine infusion correlated with decreased visual analogue scale (VAS) pain scores at 1 to 4 hours and 24 hours postoperatively.[2] Other benefits mentioned by several systematic reviews include decreased opioid requirements, reduced nausea, decreased time to first flatus, and decreased length of hospital stay.[2,7,8] The greatest benefit of perioperative lidocaine infusion was seen in patients undergoing laparoscopic and open abdominal surgery.[2] Similar benefits have been observed

Figure 1: *Colorectal ERAS protocol.*

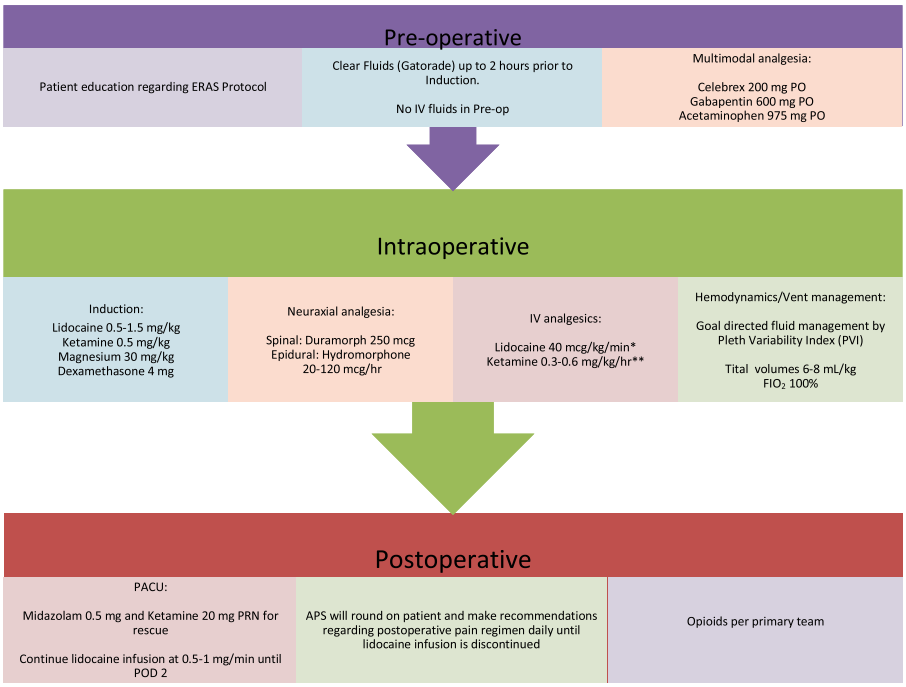

Table 1) UVA Colorectal ERAS protocol. Courtesy of department of anesthesiology and acute pain medicine. University of Virginia.

* Turn to 0.5-1 mg/min 45 min prior to waking and continue into PACU
** Stop 45 min prior to

in genitourinary, breast surgery, thoracic surgery, and spine surgery.[4,8–10] We do not recommend perioperative lidocaine infusion for cardiac surgery, obstetrics, or hip surgery. This conclusion is based on the inability of the corresponding studies to demonstrate significantly different outcome measures when compared to non-lidocaine groups.[11–13]

There are few studies published regarding *postoperative* lidocaine infusion. At our institution, we retrospectively compared postoperative lidocaine infusion to epidural analgesia with bupivacaine and hydromorphone up to postoperative day (POD) 6 in 216 patients (108 in each group) undergoing major abdominal surgery. Lidocaine was associated with fewer episodes of postoperative hypotension, nausea, vomiting, pruritus, and urinary retention and earlier removal of the urinary catheter after surgery.[14] Interestingly, the lidocaine group had higher IV and PO opioid consumption (determined by equianalgesic doses of IV morphine). We did not observe a significant difference in pain scores after POD 2. Another retrospective study in our institution compared 52 patients receiving IV lidocaine as part of the colorectal ERAS protocol (Figure 1) to 52 patients who received standard intraoperative and postoperative lidocaine infusion (see below for dosing) undergoing colorectal surgery (B. Naik, personal communication, October 19, 2016). The ERAS group had lower opioid consumption on POD 1; however, the analysis of POD 1 pain scores was inconclusive. On POD 2 and beyond, lidocaine alone was non-inferior to lidocaine given as part of the ERAS protocol in terms of postoperative pain. The ERAS group demonstrated decreased time to ambulation and discharge, as well as urinary catheter removal.

SAFETY/SIDE EFFECTS

The safety profile of IV lidocaine has been previously described.[2–4,7,15] Mild side effects, including dizziness and visual disturbances, have been described in some meta-analyses.[5,10] Serious side effects, such as neurologic changes and cardiac toxicity, are exceedingly rare.[2,5,15] Anecdotally, some practitioners report delayed emergence among patients receiving lidocaine infusion. However, to date, no association has been demonstrated between perioperative lidocaine infusion and delayed postoperative care unit (PACU) discharges.[16] Blunting of airway reactivity to the endotracheal tube might be an explanation for the perceived delayed emergence.

DOSING

Evidence regarding the optimal dose for IV lidocaine is lacking. Doses that produce serum lidocaine concentrations equivalent to epidural lidocaine infusion (approximately 1 micromolar) have been associated with decreased pain, nausea, opioid requirement, and shorter duration of ileus and length of stay after abdominal surgery.[5,17] Bolus doses of 0.5 to 1.5 mg/kg followed by 1.5 to 3 mg/kg/hr infusion resulted in decreased postoperative VAS pain

Figure 2: *Indications and contraindications of lidocaine infusion.*

INDICATIONS	CONTRAINDICATIONS

• May be utilized on acute, intermediate, and critical care units
• Require APS consult
• Target population
  ○ Inflammatory bowel disease suffering from pain not responding to traditional treatment
  ○ Perioperative patients with history of high opioid use
  ○ Patients with concerns of opioid abuse
  ○ Patients with concerns for using opioids (ie. OSA, opioid sensitivity)
  ○ Chronic pain patients (not necessarily on large doses of opioids preoperatively)
	• Abnormal liver function
	• Abnormal kidney function
	• Cardiac abnormalities (2nd or 3rd degree heart block).
	• Sensitivity or allergy to lidocaine

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scores and cumulative opioid consumption in several clinical trials. Infusion rates of 2 mg/kg/hr or higher are associated with lower pain scores and opioid consumption when compared to lower doses.[2,3,8] In our institution, an infusion rate of 40 mcg/kg/min after 1–1.5 mg/kg bolus is used perioperatively as part of our ERAS protocols. The infusion rate is decreased to 5–10 mcg/kg/min at the end of the surgery and continues at the same rate until POD 2. Our acute pain management lidocaine infusion protocol uses a 0.5 mg/min starting dose with a maximum of 1 mg/min for adults, and doses between 15 to 25 mcg/kg/min for pediatric patients <40 kg.

APPROVAL AND DEVELOPMENT OF THE ACUTE PAIN MANAGEMENT LIDOCAINE INFUSION PROTOCOL AT THE UNIVERSITY OF VIRGINIA

It is well known that factors such as postoperative pain, ileus, nausea, and vomiting contribute to prolonged hospital stay and increased cost.[2,8] These realities have allowed our anesthesiology and acute pain attendings to present IV lidocaine as a relatively safe intervention aimed to improve such outcomes. IV lidocaine is now routinely used for analgesia in acute pain management and ERAS protocols at our institution. This protocol was established through the interdisciplinary efforts of members of the anesthesia, surgery, and nursing staff. Since the approval of the protocol, several quality improvement projects and publications by our department have strengthened the advocacy for the use of lidocaine in the perioperative/acute pain settings.

In our institution, intraoperative lidocaine infusion is routinely used in open and laparoscopic abdominal surgery, urology, GYN, spine, orthopedic, and thoracic surgery in both ERAS and non-ERAS patients. The decision regarding continuing lidocaine infusion postoperatively for non-ERAS patients is made after discussions with the surgical team and the Acute Pain Service (APS). APS is routinely consulted for the start of and management of lidocaine infusions for postoperative and nonsurgical patients (trauma, chronic pain, etc.). Lidocaine infusion can be and is often used in conjunction with lumbar and thoracic epidurals in both ERAS and non-ERAS patients, as long as the epidural infusion does not contain local anesthetic. Figure 2 presents the indications and contraindications for IV lidocaine. APS rounds daily on these patients, and patients are monitored for signs of lidocaine toxicity (Figure 3). Recommendations regarding dosing of the lidocaine infusion, as well as the multimodal pain regimen, are made during rounds. There are specific instructions for nurses to monitor for signs of toxicity while caring for patients receiving lidocaine infusions. Other than mentioned, we do not require additional physiologic monitoring other than unit protocol (ie, patients do not require a monitored bed to be on lidocaine infusion). A member of the APS team is available for nursing staff to contact with any questions or concerns. We have had no adverse events related to lidocaine infusion at the doses recommended in our protocol.

Our APS team takes an active role in nursing engagement (see "Acknowledgement") by including nurses in the daily rounds on patients receiving IV lidocaine. This allows communication between APS and the nursing staff, which has been important to the successful launch of the University of Virginia's acute pain lidocaine infusion protocol as well as its implementation in our ERAS protocols.

FINAL WORD

There are several limitations to the studies supporting the use of perioperative lidocaine infusion. These include a lack of large double-blinded placebo-controlled trials, as well as limited data regarding the optimal dosing and duration of treatment. According to ClinicalTrails.gov, at this time, there are 48 open clinical

Figure 3: *Lidocaine toxicity: signs and symptoms.*

MILD TO MODERATE - Usually seen with serum blood levels 3-5 mcg/ml

- Lightheadedness, dizziness
- Visual disturbance
- Headache
- Peri-oral tingling, numbness or tingling of tongue
- Muscular twitching, tremors
- Sedation
- Impaired concentration
- Dysarthria
- Tinnitus
- Metallic taste

SEVERE side effects/adverse effects – Usually seen with serum blood levels > 5 mcg/ml

- CNS- Tonic-clonic seizures and, eventually, unconsciousness and coma
- Cardiac- Sinus tachycardia, sinus arrest, and partial or complete atrial- ventricular dissociation, cardiac arrest

trials regarding various analgesic applications of IV lidocaine infusion. The growing interest in the ERAS concept has inspired a wave of various investigational endeavors in pharmacology and pathophysiology of acute and perioperative pain. This has enhanced the role of the anesthesiologists as expert consultants and forerunners of research in this field. The future holds the key to the Pandora's box of new interventions aimed at improving the perioperative experience of patients.

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Approval and initiation of the lidocaine infusion protocol within our institution are the results of the valiant efforts of our APS nurse coordinator, Steve Morton, RN.

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Role of Music in the Perioperative Setting

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Patients often feel anxious during their planned surgical procedure and anesthetic with apprehensions about their overall outcome and postoperative pain control.[1,2] These feelings can adversely affect their perioperative experience, elevate their stress markers, cause various fluctuations in their hemodynamics, and could negatively impact their postoperative recovery.[3] Pharmacologic agents, such as short-acting benzodiazepines and opioids, are commonly used to ease patients' anxiety and pain perioperatively. However, patients can have significant side effects, which may limit the use of these medications and, in some instances, prevent their use. Therefore, music can be a very desirable nonpharmacologic alternative that is relatively cheap, with virtually no side effects.

MUSIC MEDICINE VERSUS MUSIC THERAPY

There is a distinction between two terms that are commonly misused: "music medicine" and "music therapy." *Music medicine* is defined as the passive listening to prerecorded music that may be offered by medical personnel. Headphones are commonly used when listening to music, and it may involve patient choice when selecting the type of music. In contrast, *music therapy* involves the "clinical and evidence-based use of music interventions to accomplish individualized goals within a therapeutic relationship by a credentialed professional who has completed an approved music therapy program."[4,5] Therefore, when referring to patients listening to music via headphones in the perioperative period, music medicine is the correct terminology to be used. It is also important to clarify that when referring to music medicine in the perioperative setting, this does not refer to music being played out loud in the operating room theater.

WHAT ROLE CAN MUSIC PLAY IN THE PERIOPERATIVE SETTING?

Music is a safe, noninvasive adjuvant that can positively complement the overall perioperative experience for a patient during one of the most important, sometimes life-changing, stressful periods in his or her life. In the last few decades, numerous studies have been conducted to show that passively listening to music via headphones can be beneficial throughout each phase of the perioperative setting.

In the preoperative setting, it can be used either as an adjuvant or replace anxiolytics.[3,6–8] This can be especially beneficial in patients who may be very sensitive to intravenous anxiolytics and for patients who do not report a significant amount of anxiety.

In the intraoperative setting, it can be highly desirable while undergoing conscious sedation and/or regional anesthesia by reducing a patient's overall medication consumption for sedation and/or analgesia and improving a patient's comfort and satisfaction.[9–14] For example, a common reason that patients may refuse regional anesthetics is simply because they do not want to "hear" their surroundings.[15,16] Therefore, the anesthesia provider may administer deep sedation in conjunction with the regional anesthetic or the patient may refuse regional anesthetics entirely, which is listed as one of the absolute contraindications. As a result, these decisions may unfortunately lead to unnecessary use of deep sedation or general anesthetics when regional anesthetics are suitable or safer to conduct. In scenarios like this, a simple solution to minimize a patient's fear of hearing their surroundings would be to place a pair of headphones and allow the patient to listen to music during the intraoperative setting.

During general anesthesia, limited studies have shown any reduction or changes in inhalational or IV anesthetics when listening to music.[17–20] Both explicit and implicit memory of auditory stimuli is highly unlikely especially when minimum alveolar concentration levels exceed 0.5, which could explain why the anesthetic depth may not change. However, auditory signals are quite resistant to both intravenous and inhalational anesthetics; therefore, there is a potential that auditory stimuli can alter the neurocognitive responses to surgery.[20] Nevertheless, music can still be beneficial during the induction and emergence periods by keeping the patient relaxed and preventing him or her from listening to ambient noise and conversations that may be recalled due to these lighter states of anesthetic periods.

"Music can be a very desirable nonpharmacologic alternative that is relatively cheap, with virtually no side effects."

Finally, listening to music in the postoperative period can reduce acute medication consumption, help relax patients, and improve overall satisfaction. It can be beneficial in the immediate postoperative period and in subsequent days (Figure 1).[21–24]

WHAT TYPE OF MUSIC SHOULD PATIENTS LISTEN TO?

Patients can choose their musical preference when music medicine is involved. However, there are certain genres of music and

Figure 1: *Listening to music in the postoperative period can reduce acute medication consumption, help relax patients, and improve overall satisfaction.*

characteristics within music that are known to be relaxing. These genres include classical, smooth jazz, and music with soothing sounds. The characteristics that are common to relaxing music are nonlyrical, tempo ranges of 60–80 beats per minute, and nonpercussive sounds without too many fluctuations in the melody. Binaural beat-infused music is another recommended style of music that is known to be soothing and relaxing.[4,25]

What are binaural beats? Binaural beats are developed when two different tones are played at the same time through both ears. The difference in the frequencies from these tones form a rhythm produced within the brain and can produce a particular electroencephalography (EEG)-associated state.[25] For example, if there is a tone playing at 410 Hz in the right ear and another tone playing at 400 Hz in the left ear, the difference of the two tones are 10 Hz and can simulate an alpha-wave EEG pattern, a waveform known to occur in the relaxed state. There are numerous styles of binaural beat-infused music options that can simulate the alpha, theta, and delta EEG waveforms and can be found on common music applications.

HOW CAN YOU INCORPORATE MUSIC INTO YOUR PERIOPERATIVE PRACTICE?

With the advancement in technology today, an individual can easily listen to music and access a variety of musical genres. As of 2015, approximately 89% of adult users in the United States use the Internet at least occasionally, and 72% report owning a smartphone.[26] Of those who own smartphones, approximately 67% report listening to an online radio or music service; 87% of these individuals are 18–29 years of age, 74% are 30–49 years of age, and 41% are ≥50 years of age.[27] Therefore, the implementation of allowing patients to listen to music throughout the perioperative period could potentially be easier to adopt in a hospital setting by allowing patients to bring in their own media devices and headphones to listen to music. This project was implemented in 2015 at the University of Vermont Medical Center. To learn more about this project, see an interview conducted by Vermont's WCAX TV here: http://www.wcax.com/story/30719516/using-songs-to-help-surgery-patients-relax.

A news article from the University of Vermont Robert Larner College of Medicine is posted here: http://www.uvm.edu/medicine/?Page=news&storyID=21920&category=spot1.

Another alternative is to offer Wi-Fi capable media player devices with headphones during the perioperative period. This can be an option for patients who do not own smartphone devices, media players, or headphones and for institutions with strict policies that do not allow patients to bring in their personal belongings into the perioperative area.

SUMMARY

Music is a safe, nonpharmacologic option to enhance a patient's perioperative experience. It can be used as an adjunct to minimize or replace medications in certain points of the perioperative period. Allowing patients to listen to music via headphones throughout the perioperative setting gives them a sense of autonomy in a vulnerable period in their life and can be a simple, relatively cheap solution to incorporate in a perioperative practice.

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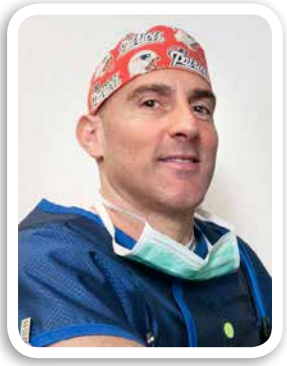
Review of Advances in Spinal Cord Stimulation Waveform Technology: A Neuromodulation Special Interest Group Article

INTRODUCTION

Advances in spinal cord stimulation (SCS) have resulted in new stimulation platforms. Historically, creation of electrical fields resulting in paresthesia was fundamental to SCS analgesia.[1] However, paresthesia-free therapy is now available, as are other platforms. This article will provide a brief overview of neuromodulation platforms.



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CURRENT VERSUS VOLTAGE

The internal pulse generator (IPG) uses either a constant current (CC) or a constant voltage (CV) power source. A CC source supplies current to tissue by adjusting voltage in response to impedance, resulting from lead positioning, fibrous encapsulation, and scar tissue.[2] A CV source adjusts current in response to impedance, maintaining constant voltage. Changes in impedance affect strength of stimulation during a stimulus pulse and efficacy of stimulation over time.[3]

Although both systems produce paresthesia and effectively treat chronic pain, limited studies reveal that some patients prefer CC stimulation, describing more comfortable and better pain relief.[4] Why patients prefer CC over CV stimulation is unknown but may reflect differences in pulse shape. CV generates spike-shaped pulses, which steepen with rise of impedance at the beginning of each pulse. CC generates rectangular-shaped smooth pulses, created in response to increased impedance, which may be perceived as more comfortable.

"Pain specialists should stay informed of advances in neuromodulation to help more patients and to enhance generalizability of therapy."

TONIC STIMULATION

Paresthesia is created by manipulating three basic elements of SCS: frequency, amplitude, and pulse width. Frequency is how often the device delivers charge and depolarization. Amplitude is the relative strength of charge delivered. Pulse width is the duration of charge delivery.[5] Traditionally, tonic stimulation involves low frequencies, typically in the 20–120 Hz range. Amplitude is adjusted until the patient feels stimulation. Perception threshold is the amplitude first detected by the patient. Discomfort threshold is the amplitude when the patient feels paresthesia transitioning from pleasant to noxious.[5] The difference between perception and discomfort threshold comprises the therapeutic window of stimulation amplitude for an individual patient.

Because pulse width is adjustable to widen or narrow the electrical field, amplitude and pulse width have been the primary parameters adjusted during trialing and maintenance of SCS. Frequency is adjusted to alter the "smoothness" of perceived stimulation.

HIGH-FREQUENCY STIMULATION

Low frequencies (20–120 Hz) result in patients feeling individual pulses. At higher frequencies, pulses start to blend, resulting in a tingling sensation without detection of individual pulses.[6] Recently, investigators examined the effect of altering the frequency rate. In preliminary work, application of higher frequency rates in SCS has shown promise for low back pain, while maintaining efficacy for neuropathic pain syndromes. Two-year data shows maintenance of such effect.[7]

Because of these advances, neuromodulation nomenclature has changed.[8–11] Traditional methods of tonic SCS programming are called "conventional" stimulation, whereas platforms between 500 to 10,000 Hz—platforms with higher frequency bursts of stimulation—are now called "high-frequency" (HF) stimulation.[8–11] The 10 kHz setting is an energy-demanding form of stimulation, requiring frequent charging of the device.

BURST STIMULATION

Pulse shape is one factor determining nerve fiber response to SCS. Another factor is the frequency of pulses used to activate large fibers in dorsal column. Frequencies of SCS impulses vary between 30 and 120 Hz but are usually in the range of 50 Hz. Burst stimulation is an alternative paradigm created to combine elements of high-frequency stimulation with less energy-demanding requirements of tonic stimulation. As such, it offers concise signal transmission, allowing for passive discharge during the recovery phase between each pulse within the burst pulse train and between each group of burst pulse trains. This differs from cycling, as cycling requires an active discharge in the recovery phase. The de Ridder[12] burst waveform uses pulse trains of five high-frequency spike pulses at 500 Hz, occurring 40 times per second.

Burst stimulation mirrors neuronal firing patterns in the spinal cord. These neurons fire in groups of action potentials, followed by periods of quiescence, akin to the burst program generated by the IPG. Other neurons, at the same stage of sensory processing, fire in

a tonic or continuous manner. Neuronal languages are transmitted as firing patterns and allow communication from spinal cord to brain. To intervene effectively, a SCS device should speak the same language.

Experimental data extracted from laboratory and clinical studies suggest both bursting and tonically firing neurons efficiently transmit information to thalamus.[13,14] Laboratory animal studies suggest that burst firing is more powerful than tonic firing in activating the cerebral cortex.[15] Results have been interpreted as showing that burst activation requires less temporal integration and may activate dormant neurons not otherwise activated by tonic stimulation.[16]

HIGH-DENSITY STIMULATION

As HF platforms were being trialed abroad and reported in the United States, American investigators began researching additional capabilities of existing stimulation technology to assess if frequencies in the upper ranges would benefit patients.[17] Although most programming in the United States falls in the 20–120 Hz range, existing technology can increase the frequency of then-available systems to >1000 Hz. This option enhanced opportunities to deliver more charge per second to the spinal cord, often in a subperception threshold amplitude, resulting in a greater charge delivered per second than with conventional stimulation. This is without the higher frequencies of 10K stimulation or burst patterns described by DeRidder.[7,8,17] Thus, SCS pulses are the equivalent of a charge dose delivered to the spinal cord, consistent with medication daily dose in intrathecal drug delivery.[18] Specifically, the dose would be consistent with charge (dose) per second. As such, delivery of maximum frequency achievable by a conventional SCS, with manipulation of amplitude and pulse width as needed, would increase time within any given second that charge (dose) is delivered. Compared to conventional SCS, a higher density of charge delivered would be created. This concept became known as "high-density SCS [or] HD" stimulation.[19]

CONCLUSION

Evolution of waveform technologies has been impressive. Pain specialists should stay informed of advances in neuromodulation to help more patients and to enhance generalizability of therapy. The ASRA Neuromodulation Special Interest Group (SIG) (link to www.asra.com/neurosig) was founded in 2014 and is an important resource for members interested in learning more about this therapy. The goals of the ASRA Neuromodulation SIG are to promote the advancement of neuromodulation in the treatment of chronic pain, provide leadership in the responsible and safe use of neuromodulation therapies, and encourage scholarship and research to support neuromodulation strategies in a patient-centric fashion.

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Bring Out Your Beach Chairs

The beach-chair position accounts for two thirds of shoulder surgeries performed in the United States. Traditionally, patients receive general anesthesia (GA) to facilitate positioning, provide analgesia, and offer an adequate surgical field. For the surgeon, it awards numerous advantages whereas anesthesiologists are tasked with rectifying additional physiological derangements. Nationally, only 2% of shoulder arthroscopies are reported to be performed solely under regional anesthesia (RA).

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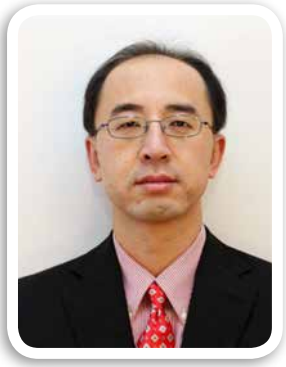

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ANESTHESIA FOR SHOULDER SURGERY: PERSPECTIVE FROM THE LITERATURE

The first joint arthroscopy was performed by Dr Severin Nordentoft of Denmark in 1912.[1] However, the ubiquity of arthroscopic surgery took off only after the 1970s with the help of Drs Masaki Watanabe and Richard O'Connor. Initially solely a diagnostic modality, arthroscopy has blossomed as one of the most frequently performed interventions thanks in large part to advances in techniques and technology making outcomes comparable to open procedures.[2–5] According to the 2006 National Survey of Ambulatory Surgery, ambulatory surgery procedures increased from 380,000 to 57.1 million between 1983 to 2006; of those, 530,000 were shoulder arthroscopies with or without rotator cuff repair.[6]

For select patients, arthroscopy has hastened the diagnosis, treatment, and recovery from surgical interventions of both major and minor joints.[7] Despite being more technically challenging, arthroscopic surgery versus traditional arthrotomy offers lower cost, quicker discharge,[8] more patients reporting improved pain control,[9] and higher satisfaction scores.[10] Moreover, when polled, patients refuse to have surgery unless it will use an arthroscopic approach.[11]

Traditionally, arthroscopic shoulder surgery is performed under GA in either the lateral decubitus or beach chair position. The beach chair position came into vogue in the 1980s. The position maintains anatomic orientation; provides the surgeon with rotational control of the upper extremity; offers excellent visualization of surrounding anterior, inferior, and superior glenohumeral structures, and subacromial space; reduces injuries to the brachial plexus; and presents ease of setup when compared with the lateral decubitus positioning. In the United States, two-thirds of the 530,000 shoulder surgeries are performed in the beach chair position.[6]

However, concerns were raised about developing devastating neurologic complications including stroke, spinal cord ischemia, and transient vision loss while in the beach chair position.[11–13] Although the exact mechanism is not known, many speculate that it relates to loss of cerebral autoregulation, leading to cerebral hypoperfusion and ischemia during general anesthesia (GA). In patients anesthetized with volatile anesthetics, the autoregulatory response is blunted in a dose-dependent manner, with the exception with sevoflurane at relevant doses.[14] By measuring regional cerebral oxygenation, multiple studies demonstrated a correlation relating diminished cerebral autoregulation during

"A team approach and communication between perioperative care management team members are the key elements to success."

GA; nevertheless, there was little to no evidence of causation of neurologic injury.[13,15–17] Despite the fact that the transient intraoperative cerebral desaturation events (CDE) have not been shown to be associated with either postoperative cognitive dysfunction or levels of biomarkers of neuronal injury, and the degree and duration of cerebral ischemia required to produce neurocognitive dysfunction in this patient population remain undefined; there is a need for strict hemodynamic management with higher blood pressure in the upright position during general anesthesia.[16]

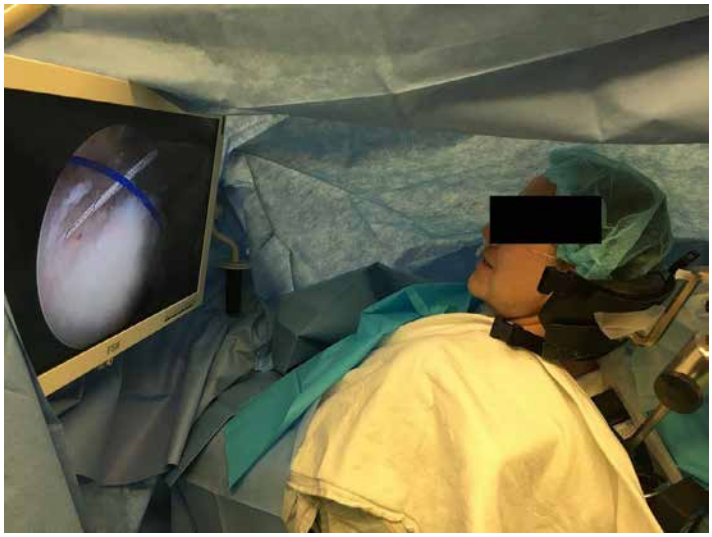
Although GA with or without regional anesthesia (RA) has been the popular practice for shoulder arthroscopy, well-placed RA alone might be sufficient to provide surgical anesthesia. RA has numerous advantages to GA for arthroscopic procedures, including intraoperative analgesia and muscle relaxation without systemic paralysis, avoiding airway manipulation, less hemodynamic variation, preservation of cerebral autoregulation, decreased postoperative nausea and vomiting by reducing systemic opioid administration, superior pain control in the postanethesia care unit (PACU), shorter operating room times, expedited time to discharge, reduced admission rates, and reduction of overall cost.[18,19] Recently, Ende et al analyzed 169,878 shoulder arthroscopy records from January 2010 to December 2014 documented in National Anesthesia Clinical Outcomes Registry and discovered that 105,666 cases (62%) were performed under GA, 60,765 (36 %) with GA+RA, and only 3447 (2.0 %) under RA alone.[20] This suggests that RA alone is still underutilized despite the advantages mentioned above.

APPLICATION OF RA AT OUR INSTITUTION

In our institution, we hypothesized that the frequency of CDE can be significantly reduced by risk stratification and implementation of an anesthesia protocol based on patients' risk category. In 2014, we tested the rate of the CDE in patients undergoing shoulder arthroscopy in the sitting position in 100 consecutive patients. CDE were more frequent in patients who received GA when compared with those who received RA only despite strict hemodynamic control in the GA group. However, this difference was not statistically significant. The result of this quality improvement project was a proposal that patients with the highest risk for cerebral desaturation events (Framingham criteria >10 or previous cerebrovascular accident) should be offered RA with or without sedation for shoulder surgery in the beach chair position as the first option. If GA is chosen, invasive monitors and a strict hemodynamic management protocol should be deployed.

We believe the underutilization of RA for shoulder arthroscopy procedure is likely due to concerns over sufficient intraoperative sensory coverage and airway management. We worked closely with our shoulder surgeons to implement a pilot project aiming to use RA as an alternative to GA in select high-risk patients.

Figure 1: *Setup for the awake shoulder arthroscopy.*



Initially, RA was reserved for patients who were at risk for stroke or compromised cerebral perfusion. As our group (anesthesiologists and surgeons) became more comfortable with RA for intraoperative anesthesia, we started to offer this technique to healthy patients.

We created patient educational material to teach patients about RA options for shoulder surgery. These educational brochures were made available at the surgeon's office and were part of the surgery packet when the patient is scheduled for surgery. An online version of the education material was made available to patients in the waiting room during their clinic visits as well.

During the preoperative visit, surgeons would address expectations of the surgery, provide an overview of the anesthetic options, and direct patients to the Penn Medicine website, which outlines the two techniques: general as well as RA for orthopedic surgery. On the day of surgery, the anesthesia team approaches well-informed patients to confirm their choice and answer any last-minute questions. All patients scheduled for a arthroscopic shoulder surgery expect to have RA but are also given the choice between being "awake" or "sleepy with sedation" for their surgery. An ultrasound-guided interscalene nerve block is performed in the holding area, 20 to 30 minutes before the scheduled surgery. Intraoperatively, the awake and cooperative patient is easily seated in the beach chair position, absolving problems such as postural hypotension and improperly padded pressure points. A separate monitor is placed under the drape for the patient to view the surgery (Figure 1). Once the surgical field is draped, the surgeon assesses the adequacy of the block. In our practice, placement of the posterior (viewing) portal between the inferior edge of the infraspinatus and teres minor may be spared after interscalene block. A separate axillary

nerve block typically addresses this area of discomfort if performed preoperatively or can simply be infiltrated by the surgeon prior to portal placement. Placement of the anterior superior portal (working portal) is generally well tolerated.

In patients who opt to stay awake during surgery, the surgeon evaluates the shoulder and discusses findings with the patient, diagnoses and treats the existing abnormalities, and alludes to postoperative expectations (rehabilitation, recovery, and use). Patients actively participating in their surgery express higher levels of satisfaction, report a better understanding of their procedure, and rarely complain of discomfort.

Patients make a seamless transition from the operating room to the PACU with minimal to no cognitive impairment often bypassing phase I recovery. Moreover, most are ready for discharge upon arrival into the PACU as they have already discussed the goals of care, have adequate pain control, and have negligible residual anesthetic or nausea, all of which are deterrents to discharge. The overwhelming majority of patients who undergo shoulder arthroscopy with minimal sedation and interscalene nerve block report high levels of satisfaction and would repeat the procedure in a similar fashion.

Two and half years ago, we instituted a multimodal perioperative pain protocol for patients undergoing ambulatory shoulder surgery. The main elements of the protocol (in addition to RA) are acetaminophen, gabapentin, short course of nonsteroidal anti-inflammatory drugs, and opioids as needed. Implementation of this protocol resulted in overall reduction in opioid consumption over the first 3 days after surgery, better quality of recovery, and higher patient satisfaction with their pain management. The results of this work were presented at the ASRA spring meeting in San Francisco, 2017.[21]

Continuous ambulatory perineural catheters are offered to select patients. This portion of our practice represents only 20% of our ambulatory surgical volume. Selection criteria include, but are not limited to: patients with chronic pain syndromes or increased analgesic requirements, patients scheduled for arthroscopic capsular release for adhesive capsulitis, and patients who are very sensitive to oral opioids. Patients who are discharged home with an ambulatory catheters should have adequate home support, be reliable, be accessible, and be able to understand and follow instructions.

We believe that a team approach and communication between perioperative care management team members are the key elements to success for implementation of any new care protocols.

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Letter to the Graduating Pain Fellow: Why I Do My Own Implants

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It was not long ago that I was starting my fellowship. Pain medicine fellowship is competitive, and I wanted to make sure I was accepted into a comprehensive program that performed surgical implants. Personally, as a resident, I was specifically interested in a fellowship that fostered a curriculum where I would learn how to treat pain from start to finish—one spanning appropriate use of medications, injections, trials (spinal cord stimulators and intrathecal drug delivery systems), and implants. During my fellowship, I loved being in the operating room, and the truth of the matter is, so did each of my co-fellows. It felt good to scrub in, operate, and enjoy the comradery of the operating room.

When I finished my fellowship, I was fully committed to apply the knowledge gained, but I was quickly discouraged. Many of my former colleagues and experienced practicing pain physicians elected not to implant their own stimulators and pumps. So, I wonder, why is it that many pain practitioners, some of them my very esteemed and surgically talented fellowship colleagues, don't do their own implants after fellowship? I didn't understand the answer myself until I started in private practice. But I realized quickly that outside of the academic world, the reason why many private practice pain doctors don't do their own implants is often financial.

As pain practitioners, reimbursements per amount of time spent are often higher when we see and do injections on patients in clinic versus taking patients into the operating room for surgical implants. The private practice market is flooded with this model. When graduating fellows join these groups, a dominant culture exists with the understanding that the physician sees patients and performs injections in clinic.

Peer and institutional pressure rise, and then what would you, my dear fellow, freshly out of an esteemed academic center, versed in surgical procedures, do? Align with all, stick up as a sore thumb among your group colleagues, or compromise? And many do just that . . . compromise. When indicated, pain physicians will typically do a spinal cord stimulator trial in their office and then refer placement of the permanent implant out to an orthopedic surgeon or neurosurgeon. Many private practice doctors told me they didn't want to deal with the "headache" or "responsibility" of implantation. After fellowship, some physicians feel intimidated by the operating room or nervous about doing their own implants independently.

So, is it bad that I decided to stick out and do my own implants? Why did I decide to do that? This was an easy decision for me, and I am presenting it hoping that it will help you decide how would you want to manage your practice upon graduation. For me, I entered a saturated pain market, which is typical of most geographic regions. Most physicians practiced with the model above, a spinal cord stimulator trial in the clinic followed by surgical implant by neurosurgeon. I decided to do my own implants because (1) it was what I actually enjoyed, and (2) I came out of my fellowship with this notion that I would like to treat pain conditions from start to finish. Doing so, I also end up differentiating myself from other pain practitioners in the area. I feel that when a patient walks into my clinic, I can look him or her in the eye and say that if a spinal cord stimulator or intrathecal pump is indicated, I can do the entire process myself. The patient doesn't need to be referred out to a surgeon halfway through treatment. My operating room day provides a different environment and perspective than being in clinic or in the procedure room doing injections. I was able to grow my practice and became busier in a saturated pain market. I did what made me happy, using and expanding all the skills I achieved in fellowship. I got to know several of my surgical colleagues personally just by being around them in the breakroom between cases. They became my friends and my professional collaborators in the hospital and became more apt to refer patients to me. So, even though I may lose revenue by missing a clinic day to do my own implants directly in the operating room, my revenue increased indirectly because my clinic schedule got busier.

"The best you can do is remember your training, take your time, and do the best you can."

My dear graduating fellow, let me tell you a secret from my personal experience: Every surgeon is nervous during their first surgery, and you will be too. The best you can do is remember your training, take your time, and do the best you can. It's okay to see patients postoperatively, it's okay to be on call for your surgical patients, it's okay to do what you were trained to do. After all the years in training—medical school, residency, and fellowship—you will provide the best patient care. There are plenty of resources at your disposal, including advice from other physicians, former attendings, medical literature, and the device industry. We as doctors cannot be afraid of treating our patients from start to finish. Pain physicians should be careful not to

become just “injectionists,” as a former attending of mine would say. The insurance landscape is changing; no longer can we just inject patients without showing adequate improvement. You need to have another tool in your tool belt. Most of us receive implant training during residency and fellowship. For further knowledge and practice, most device manufacturers provide training outside of fellowship. They offer cadaver courses and on-site visits where you can observe a practicing pain physician placing a permanent implant. Our society meetings provide training courses. You just have to get the motivation, ask for help if needed, and often take a leap of faith to do it. Doing your own implants may provide you with the personal satisfaction that you are able to provide the best care possible for your patients and probably keep you wanting to practice medicine.

So, my dear pain fellows, when the time comes to apply all of the excellent training and knowledge you acquire during your esteemed pain fellowships across the country, I can only say: JUST DO IT!

Platelet-Rich Plasma Injections for Knee Osteoarthritis: How Long Do the Benefits Last?

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THE CHALLENGING PROBLEM OF KNEE OSTEOARTHRITIS

Osteoarthritis (OA) is a common condition, typically discovered in middle age. The prevalence of symptomatic knee OA is as high as 13% in women and 10% in men older than 60 years.[1] It is significantly higher in the population 65 years and older and is one of the top five causes of disability.[1] Direct healthcare costs of knee OA are significant. For example, estimated hospital expenditures for total knee joint replacements are around $10 billion a year in the United States alone.[2] However, this figure likely represents only a small portion of the economic impact of this condition: Likely to increase this cost estimate substantially are the global economic impact of knee OA on work performance, absenteeism, required assistance within households, and the negative impact of decreased physical activity on mental health as well as cardiovascular, endocrine, and other organ systems.[3]

Current evidence suggests that managing pain and other problems associated with knee OA via physical rehabilitation, manipulation therapy, and pharmacotherapy remain unsatisfactory.[4] Corticosteroids and hyaluronic acid are the most commonly used agents for intra-articular knee injections.[4] Despite their widespread use, corticosteroid injections appear to be appropriate predominantly for knee OA with synovitis.[4] The duration of clinical effects for corticosteroid injections is usually only a few weeks, according to the majority of studies.[4] Viscosupplementation with hyaluronic acid has been considered a safe and useful treatment for symptomatic knee OA in many studies, including a recent systematic review of high-quality, placebo-controlled trials.[5] However, other systematic reviews have reported contradictory conclusions, including that viscosupplementation has no or minimal benefit, any benefits that occur last for less than 6 months after injection, and the therapy is associated with adverse effects.[6]

"Regenerative medicine agents are used with the intention of shifting the balance toward reparative processes in the knee joint affected by the degenerative process or injury."

Analgesic outcomes of arthroscopic surgery for knee OA are unclear and, even if present, last less than 2 years.[7] The definitive treatment for knee OA remains knee replacement, which is not without its own adverse effects and limitations.[4] The current published causes of death secondary to knee OA do not include the complications of treatment with opioids, nonsteroidal anti-inflammatory drugs (NSAIDs), or other drugs used to treat knee OA.[4]

A SEARCH FOR NOVEL MANAGEMENT TOOLS

Disappointing treatment outcomes have prompted a rigorous search for agents that will result in restorative reactions in the knee while maintaining a balance between degenerative and regenerative processes in the joint tissues.[4,7,8]

Platelet-rich plasma (PRP) therapy involves the use of a patient's own growth factors contained in platelet alpha-granules in supraphysiologic concentrations.[9] Experimental studies have suggested that PRP injections may stimulate regeneration of the bone, cartilage, and synovia. Initial clinical studies assessing the feasibility of using PRP injections for knee pathology, published more than 7 years ago, showed that PRP might be a viable treatment option to address the pain and functional disability accompanying knee OA.[10] The number of publications in this area has grown significantly since the initial investigations. Various reviews have assessed pain, function, and quality of life for knee OA patients treated with PRP. More recent studies and reviews of the clinical evidence suggest that PRP could be a reasonable management option for temporarily alleviating pain and improving function as well as improving quality of life. However, the current literature does not systematically assess the *duration* of clinical benefit of PRP and recounted autologous products. We have recently reviewed these studies with our colleagues, Dr. Samer Narouze and Dr. Aaron Calodney, in an attempt to answer this important question.[10]

PLATELET-RICH PLASMA INJECTIONS FOR KNEE OSTEOARTHRITIS: DURATION OF CLINICAL EFFECT

Using a systematic review approach, we analyzed published clinical reports on the duration of therapeutic effect of PRP in patients with knee OA. We searched primarily for randomized controlled

Table 1: *Duration of therapeutic effect of platelet-rich plasma and recounted autologous preparations for patients with knee osteoarthritis and knee chondropathy.*

Investigator	Type of study	Number of patients
Studies that reported 9–12 months of therapeutic effect		
Al-Ajlouni J, et al. (2014)	Prospective open-label study	*n* = 160
Filardo G, et al. (2011)	Prospective observational study	*n* = 90
Filardo G, et al. (2012)	Randomized controlled trial	*n* = 144
Gobbi A, et al. (2012)	Observational study	*n* = 50
Gobbi A, et al. (2015)	Randomized, controlled trial	*n* = 93
Jang SJ, et al. (2013)	Prospective observational study	*n* = 65
Raeissadat SA, et al. (2015)	Randomized, controlled trial	*n* = 160
Hart R, et al. (2013)	Observational study	*n* = 50
Sampson S, et al. (2010)	Prospective observational study	*n* = 14
Studies that reported at least 6 months of therapeutic effect		
Cerza F, et al. (2012)	Randomized controlled trial	*n* = 120
Forogh B, et al. (2015)	Randomized controlled trial	*n* = 44
Gormeli G, et al. (2015)	Randomized controlled trial	*n* = 162
Guler O, et al. (2015)	Observational study	*n* = 132
Kon E, et al. (2010)	Prospective observational study	*n* = 100
Kon E, et al. (2011)	Prospective comparative study	*n* = 150
Li M, et al. (2011)	Randomized controlled trial	*n* = 30
Mangone G, et al. (2014)	Observational study	*n* = 72
Patel S, et al. (2013)	Randomized controlled trial	*n* = 78
Raeissadat SA, et al. (2013)	Observational study	*n* = 60
Say F, et al. (2013)	Observational prospective	*n* = 90
Spakova T, et al. (2012)	Prospective observational study	*n* = 120
Torrero JI, et al. (2012)	Observational study	*n* = 30

studies (RCTs). If high-quality RCTs were not available, we included retrospective studies and other clinical reports. The gathered literature focused on PRP and related autologous products for treatment of knee OA and chondropathy.

A total of 24 relevant studies encompassing 2,315 patients were included in the analysis. The investigations addressed the duration of clinical effects of injected PRP or recounted autologous products for knee OA. The outcome measurements in the studies employed conventional pain and function scales. The methodology for PRP preparation, volume of patient's blood obtained, type of anticoagulant, number and timing of knee injections, and other options varied significantly between studies. However, there was a consistent and clinically significant improvement in pain scores and functional indexes for at least 6 months in all included studies (Table 1).

Nine of the studies reported decreased therapeutic effect at 12 months after the start of injection therapy; however, in most of the studies, the pain and functional status scores increased but not to

baseline levels before PRP treatment. Authors of one of the recent RCTs stated that the outcomes were further improved at 18 months by annual repetition of the PRP treatment.[11] Variables possibly affecting the duration of clinical effects are related to the variety of study designs and variability of autologous agent preparations (eg, methods of PRP preparation, white blood cell count in the injectate, volume of blood used for PRP preparations, type of anticoagulant used). Substantial variability in treatment strategies was also noted (number of PRP injections; timing of injections; patients' use of opioids, NSAIDs, or other pharmacologic agents; and concomitant use of physical rehabilitation or other treatment modalities). The duration of clinical benefit depended on variabilities in patient selection, including age, sex, and comorbidities (eg, obesity, depression, disability, worker compensation status) that were not routinely presented in the reports.

SUMMARY

Dissatisfaction with the results of available injectable agents for management of pain and dysfunction associated with knee OA has led to explorations of newer options, including PRP, platelet lysates, conditioned serum, alpha-2-macroglobulin, isolated growth factors, and mesenchymal stem cells. Regenerative medicine agents are used with the intention of shifting the balance toward reparative processes in the knee joint affected by the degenerative process or injury. Results of robust experimental studies, widespread use in sports medicine, and simplicity of preparation of PRP have contributed to its popularity for the treatment of symptoms associated with knee OA. Analysis of existing clinical studies suggests that the duration of therapeutic benefits of PRP or recounted autologous products injection—including decreased pain and improved functional status—for patients with knee OA and chondropathy lasted up to 6 months from the time of injection. Pain and functional scores decreased after 12 months of follow-up but were still superior to pre-injection scores in most of the publications. The analysis is limited by the significant variability of the studies.

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