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“Evidence-Based Interventional Pain Medicine According to Clinical Diagnoses”: Update 2018

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Abstract

Introduction: Between 2009 and 2011 a series of 26 articles on evidence-based medicine for interventional pain medicine according to clinical diagnoses were published. The high number of publications since the last literature search justified an update.

Methods: For the update an independent 3rd party, specialized in systematic reviews was asked in 2015 to perform the literature search and summarize relevant evidence using Cochrane and GRADE methodology to compile guidelines on interventional pain management. The guideline committee reviewed the information and made a last update on March 1st 2018. The information from new studies published after the research performed by the 3th party and additional observational studies was used to incorporate other factors such as side effects and complications, invasiveness, costs and ethical factors, which influence the ultimate recommendations.

Results: For the different indications a total of 113 interventions were evaluated. Twenty-seven (24%) interventions were new compared to the previous guidelines and the recommendation changed for only 3 (2.6%) of the interventions.

Discussion: This article summarizes the evolution of the quality of evidence and the strength of recommendations for the interventional pain treatment options for 28 clinical pain diagnoses.

Key Words: interventional pain management, evidence-based medicine, systematic review, GRADE, recommendations

INTRODUCTION

Clinical practice guidelines are statements that include recommendations intended to optimize patient care that
are established by a systematic review of evidence and an assessment of the benefits and harms of alternative care options. For guidelines to reflect the best available evidence, it is important that they be based on a comprehensive systematic review of all available evidence. Guidelines, though much appreciated by clinicians, may rapidly become outdated. Between 2009 and 2011, a series of articles were published on recommendations for diagnosis and treatment of 26 diagnoses. In particular, the evidence on interventional pain management techniques was analyzed and used as the basis for the recommendations. The recommendations were formulated according to a system adapted from Guyatt by van Kleef et al. For a detailed description of this scoring system, we refer the reader to van Kleef et al. The guidelines were published in Pain Practice. The large number of publications since the previous literature search justifies an update.

Method of Reviewing the Literature
An independent company, Kleijnen Systematic Reviews (KSR), was asked to review the literature.

This review aimed to identify and summarize relevant evidence using Cochrane and Grading of Recommendations Assessment, Development and Evaluation (GRADE) methodology to inform guidelines on interventional pain management. This objective was achieved by conducting a review of existing systematic reviews (SRs) and randomized controlled trials (RCTs) for the conditions outlined in the research question.

RESEARCH QUESTION
What is the place for interventional pain management techniques in the treatment algorithm of the following conditions?

1. Trigeminal neuralgia
2. Cluster headache
3. Persistent idiopathic facial pain
4. Cervical radicular pain
5. Cervical facet pain
6. Cervicogenic headache
7. Whiplash-associated disorders
8. Occipital neuralgia
9. Thoracic radicular pain
10. Thoracic facet joint pain
11. Lumbosacral radicular pain
12. Failed back surgery syndrome
13. Pain due to spinal canal stenosis
14. Pain originating from the lumbar facet joints
15. Sacroiliac joint pain
16. Discogenic low back pain
17. Complex regional pain syndrome
18. Herpes zoster and postherpetic neuralgia
19. Painful diabetic polyneuropathy
20. Carpal tunnel syndrome
21. Meralgia paresthetica
22. Phantom pain
23. Traumatic plexus lesion
24. Chronic refractory angina pectoris
25. Ischemic pain in the extremities and Raynaud’s phenomenon
26. Pain in chronic pancreatitis
27. Pain in patients with cancer

METHODS

Selection of the Literature
The search by the independent research company (KSR) was performed in 2015. The search covered the period 2010 to 2015.

Inclusion Criteria
Studies that met the following criteria were eligible for inclusion.

Participants. Patients (adults or children) had any of the conditions under research.

Interventions. Interventional treatments were defined as procedures targeting the source of the patient’s pain. The interventions discussed in the previous guideline were included, except for shoulder pain. Additionally, 2 new topics were added: failed back surgery syndrome and spinal canal stenosis. A list of treatments categorized by clinical diagnosis is presented in Appendix 1. When we identified RCTs of interventional treatments that were not listed in the protocol, the members of the guideline committee decided on inclusion in the review.

Outcome. Inclusion was not restricted based on outcome; any outcome was considered. The primary outcome, which is also most often used in SRs and RCTs, is pain reduction; improvement in function and quality of life were included as well. There is little information regarding medication use, but when available it was included.

Study design. SRs and RCTs were eligible for inclusion. If no relevant RCTs were identified for any prespecified
interventional technique of interest, then case-control or cohort studies were included.

Literature Searches

Literature searches were conducted to identify relevant studies for each of the conditions of interest. The searches were carried out using a stepwise approach according to study design:

- SRs
- RCTs
- Observational studies (case-control or cohort studies)

SRs were identified by screening the in-house KSR pain database of SRs. This database consists of SRs identified by regular literature searches of a range of bibliographic databases. Additionally, a search for recent guidelines was undertaken.

The search strategies used to identify RCTs combined relevant search terms comprising indexed keywords (e.g., medical subject headings [MeSH]) and text terms appearing in the titles and/or abstracts of database records for each of the target conditions. When searching for RCTs where the quantity of literature is likely to be large, the search strategies included an additional facet of search terms for the interventional treatments of interest for those particular conditions, for example, cancer pain, thoracic pain, and angina pectoris.

Search methods met best practice standards in SRs. The search strategies were developed specifically for each database and the keywords adapted according to the configuration of each database. Where appropriate, searches were limited to remove animal studies. Searches were not limited by language or publication status.

1. SRs and guidelines

The following databases were searched for the KSR pain database of SRs:
- Cochrane Database of Systematic Reviews (Wiley Online Library)
- Database of Abstracts of Reviews of Effects (Wiley Online Library)
- Medline In-Process Citations, Medline Daily Update (OvidSP)
- Embase (OvidSP)
- Cumulative Index to Nursing and Allied Health Literature (CINAHL; EBSCO)
- PsycINFO (OvidSP)

2. RCTs

The following databases were searched for RCTs and, where appropriate, included a search filter designed to identify RCTs:
- Medline (OvidSP)
- Medline In-Process Citations, Medline Daily Update (OvidSP)
- PubMed (National Library of Medicine [NLM])
- Embase (OvidSP)
- Cochrane Central Register of Controlled Trials (CENTRAL) (Wiley Online Library)

3. Observational studies

If no evidence from SRs and RCTs was identified, the following databases were searched and included a search filter designed to identify observational studies:
- Medline (OvidSP)
- Medline In-Process Citations, Medline Daily Update (OvidSP)
- PubMed (NLM)
- Embase (OvidSP)

Reference Checking. The bibliographies of identified research and review articles were checked for relevant studies.

Handling of Citations. Identified references were downloaded into Endnote reference management software Thomson Reuter (Scientific) LLCC, London, UK for further assessment and handling. Individual records within the Endnote reference libraries were tagged with search information, such as searcher, date searched, database host, database searched, strategy name and iteration, theme, or search question. To save time removing duplicate records, as well as reviewer screening time, the results of searches for all chapters were combined into one Endnote library.

Quality Assurance Within the Search Process. The main Embase strategy for each search was independently peer reviewed by a second information specialist.
using the Canadian Agency for Drugs and Technologies in Health Peer Review checklist. 13

Methods of Study Selection, Quality Assessment, and Data Extraction

Study Selection. Two KSR reviewers independently screened the titles and abstracts of all reports identified by the searches; any discrepancies were discussed and resolved by consensus. Full copies of all studies deemed potentially relevant were obtained. One reviewer assessed full text papers for inclusion, and a second reviewer checked the decision; any disagreements were resolved by consensus.

Data Extraction. Structured data extraction was performed using a Microsoft Access (Microsoft Corporation, Redmond, WA, U.S.A.) database that was developed specifically for the project. For interventional studies, details on the following parameters were extracted: participant characteristics, study design, brief inclusion and exclusion criteria, brief intervention details, details of outcomes assessed, and results. Data for pain and available functionality and quality of life were extracted by one KSR reviewer and checked by a second; any disagreement was resolved by consensus.

Quality Assessment. SRs were assessed for methodological quality using the ROBIS tool. 36 This tool aims to assess the risk of bias in SRs and includes domains covering study eligibility criteria, identification and selection of studies, data collection and study appraisal, synthesis and findings, and interpretation. Trials were assessed for methodological quality using the Cochrane Risk of Bias tool. 31 This includes items covering selection bias (random sequence generation and allocation concealment), performance bias (participant blinding), detection bias (blinding of outcome assessors), attrition bias (incomplete outcome data), and reporting bias (selective reporting). There was also an additional field for other sources of bias. For all tools, if at least 1 of the domains was rated as “high,” the study was considered at high risk of bias; if all domains were judged as “low,” the trial was considered at low risk of bias; otherwise the trial was considered to be at “unclear” risk of bias.

Data Synthesis. If sufficient studies assessing similar populations, interventions, comparators, and outcomes were found, a formal meta-analysis was used to estimate summary measures of effect. GRADE methods were used to define the levels of evidence.

Integration of the Evidence Before 2010 and New Publications Retrieved After 2015

The studies used in the previous 2010 guidelines were usually included in SRs that were identified. When studies were included in the previous guideline, but were not included in the most recent SR, the panel retrieved the publications used in the previous guideline. A member of the guidelines committee who was an epidemiologist judged the quality of studies that were withheld from the previous guideline.

Last Update

Since the KSR search included studies published up to 2015, a new search of the abstracts was performed to identify more recent publications (until March 1, 2018) using the terms “diagnosis” and “intervention” for each diagnosis and for the different interventional pain management techniques.

When an SR was found, it was compared with the review reported up to 2015. If no new information was listed in the new SR, it was discarded. When new RCTs or important observational studies were found, they were discussed and included in the considerations paragraph, and a judgment was made to what extent this new information would influence (the strength of) the recommendations.

The quality of the evidence found by KSR was maintained.

The strength of recommendation could be adapted based on the following factors:

- Studies published after 2015 providing relevant information
- Risk–benefit balance
- Values and preferences such as:
  - Clinical relevance
  - Invasiveness
  - Technical requirements needed to perform the interventional pain management technique (degree of specialization, need for special equipment)
  - The need for shared decision making.

Table 1 shows the classification of the quality of evidence, strength of recommendation, and description of the recommendations.
Validation

The chapters were placed on a closed website. Members of the Dutch Society of Anesthesiologists; Flemish Association of Anesthesiological Pain Management; World Institute of Pain, Benelux section; and the educational committee of the World Institute of Pain were invited to give comments and feedback. All remarks from the Netherlands and Belgium were discussed in a plenary session. The comments from the educational committee were reviewed by the guideline committee. Where necessary, corrections were made.

RESULTS

The search strategy resulted in a large number of references; for example, for the indications lumbar facet joint pain, sacroiliac joint pain, and discogenic pain, 10,333 records after deduplication were screened for inclusion in the study and 38 studies were finally included in our review (22 for lumbar facet pain, 6 for sacroiliac pain, and 10 for discogenic pain).

Table 2 summarizes the evolution of the evidence/recommendation for the different diagnoses and the relevant interventional pain management techniques. The studies included in the quality assessment and those used in the considerations, which may influence the strength of recommendation, are described in the individual chapters, which can be retrieved from https://www.anesthesiologie.nl/publicaties/#filter=pijngeneeskunde.

For the different indications, a total of 113 interventions were evaluated. Twenty-seven interventions (24%) were new compared to the 2010 guidelines, and the recommendation changed for only 3 (2.6%) of the interventions.

The scientific justification of the rating of the quality of evidence and the strength of recommendations can be retrieved from https://www.anesthesiologie.nl/publicaties/#filter=pijngeneeskunde.

DISCUSSION

Quality of Evidence

The large number of publications retrieved for this guideline project indicates the interest in the appropriate use of interventional pain management techniques. The quality of evidence may seem rather low and the strength of the recommendations weak. However, this must be viewed in the context of guideline methodology. GRADE rates evidence based on RCTs as high quality, but the confidence in evidence may be decreased for several reasons, such as:

- Study limitations
- Inconsistency of results
- Indirectness of evidence
- Imprecision
- Reporting bias

The quality of observational studies (eg, cohort and case-control studies) starts with a “low quality” rating; grading upwards may be warranted if the magnitude of the treatment effect is very large, if there is evidence of a dose-response relationship, or if all plausible biases would decrease the magnitude of apparent treatment.37

The fact that the quality of the evidence is rather low does not mean that the effect of the treatment is minimal; it indicates the need for clinical research. However, performing RCTs for (interventional) pain management techniques is hampered by several factors, such as difficulty in blinding the patient and interventionalist, patient refusal to enter a study with a risk of receiving a noneffective treatment, and ethical concern of withholding potential effective treatment from patients who suffer from chronic intolerable pain. This results in few selected RCTs, and when they are available they are downgraded because of risks of bias such as blinding and low number of participants.

The meaning of the GRADE rating is described in Table 3.

Strength of recommendation, quality of evidence, and size of the effect are not synonymous. When the quality of the evidence is low, this does not mean that the intervention is not effective. And the quality of the evidence may be high, indicating that the intervention is not effective.

The rating of the quality of evidence has a direct impact on the strength of recommendation. The members of the guideline committee considered factors such as risk for complications, degree of invasiveness, and
| Treatment | Recommendations in 2010† | GRADE Level of Evidence in 2015 | Recommendations in 2018 |
|-----------|--------------------------|---------------------------------|------------------------|
| Trigeminal neuralgia | Microvascular decompression | Very low | Very weak |
| Stereotactic radiosurgery | Radiofrequency treatment of the ganglion Gasseri | 2 B+ | Low | Weak |
| Pulsed radiofrequency | | 2 B– | Very low | Very weak |
| Cluster headache | Uni- or bilateral injection of nervus occipitalis | Not graded | Very weak |
| Radiofrequency treatment of ganglion pterygopalatinum | 2 C+ | Very low | Weak |
| Stimulation of ganglion pterygopalatinum | Occipital nerve stimulation | 2 C+ | Low | Very weak |
| Persistent idiopathic facial pain | Pulsed radiofrequency of ganglion pterygopalatinum | 2 C+ | Very low | Very weak |
| Radiofrequency of ganglion pterygopalatinum | | | Very low | Very weak |
| Cervical radicular pain | Interlaminar epidural corticosteroid administration | 2 B+ | Moderate | Weak |
| Transforaminal epidural preservative-free dexamethasone | Pulsed radiofrequency treatment adjacent to de DRG | 1 B+ | Moderate | Moderate |
| Radiofrequency treatment adjacent to de DRG | Spinal cord stimulation | 2 B+ | Moderate | Weak |
| Cervical facet joint pain | Intra-articular corticosteroid administration | 0 | Low | Weak against |
| Therapeutic (repetitive) cervical medial branch injections of local anesthetic with or without corticosteroid | Radiofrequency treatment of ramus medialis of the ramus dorsalis | 2 C+ | Low | Weak |
| Cervicogenic headache | Injection of the nervus occipitalis major with local anesthetic with or without steroid | 1 B+ | Moderate | Weak |
| Injection of atlanto-axial joint with local anesthetic with or without steroid | Radiofrequency treatment of cervical ramus medialis | 2 B+/– | Very low | Very weak |
| Pulsed radiofrequency treatment of nervus occipitalis major | Pulsed radiofrequency treatment of atlanto-axial joint | Not graded | Not graded | Very weak |
| Pulsed radiofrequency of cervical DRG (C2–C3) | | | | |
| Whiplash-associated disorder | Botulinum toxin injections | 2 B– | Moderate | Moderate against |
| Radiofrequency treatment of cervical ramus medialis of the ramus dorsalis | Intra-articular corticosteroid injections | 2 B+ | Moderate | Weak |
| Occipital neuralgia | A single infiltration of the nervi occipitales with local anesthetic and corticosteroids | 2 C+ | Very low | Very weak |
| Pulsed radiofrequency of the nervi occipitales | Pulsed radiofrequency adjacent to the DRG | 0 | Very low | Very weak |
| Peripheral nerve stimulation | Botulinum toxin injections | 2 C+/– | Very low | Very weak |
| Stimulation of the nervi occipitales | | 2 C+ | Very low | Very weak |
| Thoracic radicular pain syndrome | Intercostal nerve blocks | 0 | Not graded | Not applicable |
| (Pulsed) radiofrequency of thoracic DRG | | 2 C+ | Low | Weak |
| Pain originating from the thoracic facet joint | Addition of corticosteroids to local anesthetic for thoracic medial branch blocks | | | High | Moderate against |
| Lumbosacral radicular pain | Epidural corticosteroid administration (interlaminar, transforaminal contained herniation, and transforaminal extruded herniation) | Moderate | Weak |
| Epidural TNF-α inhibitors | Radiofrequency treatment adjacent to lumbar DRG | 2 A– | Moderate | Moderate against |
| Pulsed radiofrequency treatment adjacent to lumbar DRG | Failed back surgery syndrome | 2 C+ | Moderate | Moderate |
| Adhesiolysis | | 2 B+/– | Very low | Very weak |
| Epiduroscopy | | 2 B+/– | Moderate | Weak |
| Spinal cord stimulation (tonic) | | 2 A+ | Moderate | Moderate |
| Spinal cord stimulation (HF-10) | Subcutaneous stimulation as add-on to spinal cord stimulation | Not graded | Not graded | Moderate |
| Pain originating from the lumbar facet joints | Intra-articular injection of local anesthetic with or without corticosteroid | 2 B+/– | Low | Very weak |
| Radiofrequency treatment of the ramus medialis of the ramus dorsalis | Pulsed radiofrequency treatment of ramus medialis of the ramus dorsalis | 1 B+ | Low | Weak |
| Pulsed radiofrequency treatment of ramus medialis of the ramus dorsalis | | Low | Very weak |
| Treatment                                      | Recommendations in 2010† | GRADE Level of Evidence in 2015 | Recommendations in 2018 |
|------------------------------------------------|------------------------|---------------------------------|------------------------|
| Spinal canal stenosis                          |                        |                                 |                        |
| Spinal cord stimulation                        |                        |                                 |                        |
| Pulsed radiofrequency treatment adjacent to DRG|                        | Very low                        | Very weak              |
| Epidural local injections (without steroids)    |                        | Low                             | Weak                   |
| Epidural corticosteroid injections             |                        | High                            | Moderate against       |
| Sacroiliac joint pain                          |                        |                                 |                        |
| Intra-articular corticosteroid injections      | 1 B+                   | Low                             | Weak                   |
| Radiofrequency treatment of rami dorsalis and lateralis (palisade) | 2 C+                   | Very low                        | Very weak              |
| Radiofrequency treatment of rami dorsalis and lateralis (palisade) | Moderate against ankylosing spondylitis | Moderate against ankylosing spondylitis | Moderate against ankylosing spondylitis |
| Radiofrequency treatment of rami dorsalis and lateralis (simplicity) | Not graded             | Moderate against                |
| Pulsed radiofrequency treatment of rami dorsalis and lateralis | 2 C+                   | Not graded                      | Very weak              |
| Radiofrequency treatment of rami dorsalis at L4–L5 and cooled radiofrequency of the ramus lateralis | 2 B+                   | Low                             | Weak                   |
| Discogenic pain                                |                        |                                 |                        |
| Intradiscal methylene blue injection          |                        | Moderate                         | Weak                   |
| Intradiscal corticosteroid injection          | 2 B−                   | Low                             | Weak against           |
| Intradiscal radiofrequency treatment         | 2 B+ /−                | Low                             | Weak against           |
| Intradiscal electrothermal therapy            |                        | Low                             | Weak                   |
| Intradiscal pulsed radiofrequency treatment  | 2 B+/−                 | Very low                        | Very weak              |
| Intradiscal biacluaplasty                     | 0                      | Moderate                        | Moderate               |
| Distrode                                       | 0                      | Moderate                        | Weak                   |
| Radiofrequency treatment of ramus communicans | 2 B+                   | Very low                        | Very weak              |
| Complex regional pain syndrome                 |                        |                                 |                        |
| Sympathetic blocks with local anesthetics     | 2 B+                   | Moderate                        | Moderate against       |
| Thoracic block (T2–T3) with ropivacaine and triamcinolone |                        | Low                             | Weak                   |
| IV regional blocks with guanethidine          | 2 A−                   | Moderate                        | Moderate against       |
| Spinal cord stimulation                       | 2 B+                   | Moderate                        | Moderate               |
| DRG stimulation (for lower extremity CRPS)    |                        | Moderate                        | Moderate               |
| Peripheral nerve stimulation                  | 2 C+                   | Very low                        | Very weak              |
| Low-dose IV ketamine                          |                        | Moderate                        | Weak                   |
| Herpes zoster and postherpetic neuralgia      |                        |                                 |                        |
| Acute phase: epidural injection of corticosteroid with local anesthetics | 2 B+                   | Moderate                        | Moderate               |
| Acute phase: paravertebral injections of corticosteroids with local anesthetics |                    | Moderate                        | Moderate               |
| Acute phase: repeated epidural injections of corticosteroid with local anesthetics and epinephrine |                        | Moderate                        | Weak                   |
| Acute phase: stellate ganglion block          | 2 C+                   | Low                             | Weak                   |
| Treatment of postherpetic neuralgia: epidural corticosteroid injections or combined therapy with intrathecal midazolam | 0                     | Low                             | Weak                   |
| Treatment of postherpetic neuralgia: sympathetic nerve block | 2 C+                   | Very low                        | Very weak              |
| Treatment of postherpetic neuralgia: spinal cord stimulation | 2 C+                   | Very low                        | Very weak              |
| Treatment of postherpetic neuralgia: pulsed radiofrequency on intercostal nerve |                        | Moderate                        | Moderate               |
| Treatment of postherpetic neuralgia: pulsed radiofrequency adjacent to DRG |                        | Very weak                       | Moderate               |
| Treatment of postherpetic neuralgia: intrathecal administration of corticosteroid |                        | Low                             | Strong against         |
| Treatment of postherpetic neuralgia: lumbar sympathetic block |                        | Very low                        | Very weak              |
| Painful diabetic polyneuropathy                |                        |                                 |                        |
| Spinal cord stimulation                       | 2 C+                   | Moderate                        | Moderate               |
| Lumbar sympathetic block                      |                        | Very low                        | Very weak              |
| Meralgia paresthetica                         |                        |                                 |                        |
| Infiltration of LFCB with local anesthetic with or without corticosteroid | 2 C+                   | Very low                        | Very weak              |
| Pulsed radiofrequency of LFCB                | 0                      | Very low                        | Very weak              |
| Spinal cord stimulation                       | 0                      | Not graded                      | Very weak              |
| Carpal tunnel syndrome                        | 1 B+                   | Moderate                        | Moderate               |
| Intracarpal corticosteroid injection(s)       |                        | Moderate                        | Moderate               |
| Pulsed radiofrequency treatment of median nerve |                        | Very low                        | Very weak              |
| Phantom pain                                   |                        |                                 |                        |
| Pulsed radiofrequency treatment of the most tender part of the neuroma | 0                     | Very low                        | Very weak              |
| Spinal cord stimulation                       | 0                      | Very low                        | Very weak              |
| DRG stimulation                               | 0                      | Very low                        | Very weak              |
| Traumatic plexus lesion                       | 0                      | Not graded                      | Very weak              |
| Spinal cord and DRG stimulation               |                        |                                 |                        |
| Chronic refractory angina pectoris            |                        |                                 |                        |
| Spinal cord stimulation                       | 2 B+                   | Low                             | Weak                   |
technical requirements to formulate a strength of recommendation. A treatment option with low-quality evidence and a weak recommendation may be preferred over a treatment with high-quality evidence when the former has fewer risks for complications and/or is less invasive.

For example, in the judgment of epidural corticosteroid injections for the treatment of spinal canal stenosis, high-quality evidence based on several SRs of 13 studies showed no significant difference in pain reduction between the groups treated with corticosteroids compared to the group treated with local anesthetics. This observation, together with considerations on the potential side effects and complications of corticosteroids, led to the recommendation against the use of corticosteroids. The epidural administration of local anesthetics alone is recommended.

Another example is in the treatment of postherpetic neuralgia. Pulsed radiofrequency treatment of the dorsal root ganglion has a very weak quality of evidence, but this treatment is documented to be rather easy to perform and safe; therefore, the strength of the recommendation is upgraded to moderate.

**Further Research**

When the recommendation is very low, there is a high need for more research.

Each intervention that received a very weak recommendation should be performed in the context of a study, which means at least the systematic recording of:

- Patient characteristics
- Diagnostic process
- Treatment, including the details of the technique concerned
- Evaluation of the result (preferably VAS, Euro-Qol, and a complaint-specific scale over 3, 6, and 12 months)
- Recording of side effects and complications
- Systematic reporting of the results.

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**Table 2. (Continued)**

| Treatment | Recommendations in 2010† | GRADE Level of Evidence in 2015 | Recommendations in 2018 |
|-----------|--------------------------|---------------------------------|-------------------------|
| Raynaud's phenomenon | | | |
| Radiofrequency of T2-T3 and T2 thermolesion with a local application of phenol | 2 C+ | Very low | Very weak |
| Spinal cord stimulation | | | |
| Ischemic pain of the extremities | | | |
| Sympathectomy | 2 B +/- | Not graded | Very weak |
| Spinal cord stimulation | 2 B +/- | High | Moderate |
| Chronic pancreatitis | | | |
| Plexus coeliacus block with local anesthetic and corticosteroid | 2 C+ (radiofrequency) | Low | Weak against |
| Splanchnic nerve block | 2 C+ | Very low | Very weak |
| Spinal cord stimulation | 2 C+ | Very low | Very weak |
| Pain in patients with cancer | | | |
| Intrathecal drug administration | 2 B+ | Moderate | Weak |
| Epidural drug administration | 2 C+ | Very low | Very weak |
| Spinal cord stimulation | 2 C+ | Very low | Very weak |
| Cervical percutaneous cordotomy | 2 C+ | Very low | Very weak |
| Neurolytic plexus coeliacus block | 2 A+ | High | Strong |
| Neurolytic plexus hypogastricus block | 2 C+ | Low | Weak |
| Intrathecal phenolization of lower sacral roots of cauda equina (lower end block) | 0 | Very low | Very weak |
| Kyphoplasty | 2 B+ | Not graded | Very weak |
| Vertebroplasty | 2 B+ | Very low | Very weak |

*2010 recommendations as reported in the previous guideline; the level of evidence in 2015 as identified by independent evaluation using GRADE; and the strength of recommendation as updated by the Guideline Committee in 2018, taking into consideration newer publications and potential risks for side effects and complications.

†A is the highest level of evidence (various RCTs of good quality), B stands for RCTs with methodological limitations or large observational studies and C stands for observational studies or case series.

CRPS, chronic regional pain syndrome; DRG, dorsal root ganglion; GRADE, Grading of Recommendations Assessment, Development and Evaluation; HF-10, High frequency 10-kHz stimulation; LFCB, lateral femoral cutaneous nerve; SIJ, sacroiliac joint; TNF-α, tumor necrosis factor-α.

**Table 3. Interpretation of the Quality of Evidence**

| Level    | Interpretation                                                                 |
|----------|--------------------------------------------------------------------------------|
| High     | Much confidence that real effect is close to observed effect                  |
| Moderate | Moderate confidence that real effect is close to observed effect, but there is a possibility that it is substantially different |
| Low      | Restricted confidence that real effect is close to observed effect, the real effect can be substantially different than the observed effect |
| Very low | Little confidence that real effect is close to observed effect; the real effect is probably substantially different from the observed effect |
The aim is thus to accumulate information that enables estimation of the value of the technique when it has been applied to a larger number of patients. If these results are positive, they may then lead to the justification for a prospective randomized study.3

Critical Look at Guidelines

Guidelines have gained in popularity because clinicians have easy access to the recommendations that may facilitate their daily work. These guidelines may have an immense impact, because they act as a standard of care and may be used to devise national and local protocols, measure physician performance, and evaluate adherence to standards. They can also be used as expert testimony in cases of litigation and malpractice.38 There are, however, some points that deserve attention.

The recommendations formulated in guidelines are valid for a specific patient population; however, they may not be valid for the individual patient with comorbidities. This stresses the role of the clinician to select a treatment based on the complete medical picture of the patient.

Furthermore, there is an increasing number of guidelines that are not performed according to the rigorous methodology advocated by scientific groups such as the Cochrane collaboration. A recent article in the European Journal of Anaesthesiology described the different factors that may influence the interpretation of the literature.38 The authors listed a methodological shortage in many published SRs, the apparent ignorance among reviewers and editors of scientific journals to methodological issues and shortcomings of SRs, the influence of sponsors on research outcome, financial links of principal investigators of clinical trials that are strongly associated with a positive clinical trial outcome, conflicts of interest and lack of methodological knowledge of peer reviewers, scientific fraud promoted by the financial incentives of scientific publications, and the poor quality of published clinical trials.38

Towards an Integrated Treatment Plan

Pain is a complex physical, psychosocial, ethnocultural, affective-cognitive, and environmental phenomenon. No single treatment can influence all these aspects and, therefore, a multidisciplinary and multimodal approach has been advocated. For the management of chronic pain discussed in this guideline, a stepwise approach is indicated. Firstly, conservative treatment options should be used to their full extent. Secondly, interventional treatment can be used. In the design of a treatment algorithm, the first parameter to consider is the efficacy of the treatment, but secondarily the grade of invasiveness of the intervention should be taken into consideration. As stated earlier, quality of evidence is not synonymous with effectiveness and use of healthcare resources.

The correct application of interventional pain management techniques requires an excellent knowledge of the neuroanatomy, experience in the interpretation of the images obtained during the procedure, and adequate training. It is obvious that a more complicated intervention can only be performed by a well-trained and experienced physician. Therefore, it is preferred that such interventions be performed in specialized centers.39

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CONFLICTS OF INTEREST

The authors have no conflicts of interest to declare.

REFERENCES

1. Institute of Medicine Committee on Standards for Developing Trustworthy Clinical Practice Guidelines. Clinical
## APPENDIX 1

### Eligible Populations and Interventions

| Population                        | Interventional treatments                                                                                                                                 |
|-----------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------|
| Trigeminal neuralgia              | Surgical microvascular decompression  
                                    | Stereotactic radiation therapy, gamma knife  
                                    | Percutaneous balloon microcompression  
                                    | Radiofrequency treatment of the Gasserian ganglion  
                                    | Pulsed RF treatment of the Gasserian ganglion |
| Cluster headache                  | RF treatment of the pterygopalatine ganglion (sphenopalatinum)  
                                    | Occipital nerve stimulation |
| Persistent idiopathic facial pain | Pulsed RF treatment of the ganglion pterygopalatinum (sphenopalatinum)  
                                    |                                                                 |
| Cervical radicular pain           | Interlaminar epidural corticosteroid administration  
                                    | Transforaminal epidural corticosteroid administration  
                                    | RF treatment adjacent to the cervical ganglion spinale (DRG)  
                                    | Pulsed RF treatment adjacent to the cervical ganglion spinale (DRG)  
                                    | Spinal cord stimulation |
| Cervical facet pain               | Intra-articular injections  
                                    | Therapeutic (repetitive) cervical ramus medialis (medial branch) of the ramus dorsalis block (local anesthetic with or without corticosteroid)  
                                    | RF treatment of the cervical ramus medialis (medial branch) of the ramus dorsalis  
                                    | Injection of nervus occipitalis major with corticosteroid + local anesthetic  
                                    | Injection of atlanto-axial joint with corticosteroid + local anesthetic  
                                    | RF treatment of the cervical ramus medialis (medial branch) of the ramus dorsalis  
                                    | Pulsed RF treatment of the cervical ganglion spinale (DRG) (C2 to C3) |
| Whiplash-associated disorders     | Botulinum toxin type A  
                                    | Intra-articular corticosteroid injection  
                                    | RF treatment of the cervical ramus medialis (medial branch) of the ramus dorsalis  
                                    | Pulsed RF treatment of the cervicale occipitales Pulsed  
                                    | RF treatment of the cervical ganglion spinale (DRG)  
                                    | Subcutaneous stimulation of the nervi occipitales  
                                    | Botulinum toxin A injection |
| Occipital neuralgia               | Single infiltration of the nervi occipitales with local anesthetic and corticosteroids  
                                    | Pulsed RF treatment of the nervi occipitales Pulsed  
                                    | RF treatment of the cervical ganglion spinale (DRG) |
| Thoracic pain                     | Intercostal block  
                                    | RF treatment of thoracic ganglion spinale (DRG)  
                                    | Pulsed RF treatment of thoracic ganglion spinale (DRG) |
| Lumbosacral radicular pain        | Interlaminar epidural corticosteroid administration  
                                    | Transforaminal epidural corticosteroid administration in “contained herniation”  
                                    | Transforaminal epidural corticosteroid administration in “extruded herniation”  
                                    | RF lesioning adjacent to the lumbar ganglion spinale (DRG)  
                                    | Pulsed RF treatment adjacent to the lumbar ganglion spinale (DRG)  
                                    | Spinal cord stimulation (FBSS only)  
                                    | Adhesiolysis-epiduroscopy |
| Pain originating from the lumbar  | Intra-articular corticosteroid injections  
                                    | RF treatment of the lumbar rami mediales (medial branches) of the dorsal ramus |
| facet joints                      | Therapeutic intra-articular injections with corticosteroids and local anesthetic  
                                    | RF treatment of rami dorsales and rami laterals  
                                    | Pulsed RF treatment of rami dorsales and rami laterals  
                                    | Cooled/RF treatment of the rami laterales  
                                    |  
| Sacroiliac joint pain             | Intradiscal corticosteroid injections, ganglion impar block, RF ganglion impar, caudal block Neurostimulation |
| Coccycodynia                      | Local injections corticosteroids/local anesthetic  
                                    | Intradiscal corticosteroid administration  
                                    | RF treatment of the discus intervertebralis  
                                    | Intradiscal electropherotheral therapy  
                                    | Biacuplasty  
                                    | Discrode  
                                    | RF of the ramus communicans |
| Discogenic low back pain          | Intravenous regional block guanethidine  
                                    | Ganglion stellatum (stellate ganglion) block  
                                    | Lumbar sympathetic block  
                                    | Plexus brachialis block  
                                    | Epidural infusion analgesia Spinal cord stimulation  
                                    | Peripheral nerve stimulation  
                                    | Intervenotional pain treatment of acute herpes zoster  
                                    | Epidural corticosteroid injections  
                                    | Herpes zoster and post-herpetic neuralgia |
Appendix A. (Continued)

| Population                              | Interventional treatments                                                                 |
|-----------------------------------------|------------------------------------------------------------------------------------------|
| Sympathetic nerve block                 |                                                                                          |
| One-time epidural corticosteroid injection |                                                                                          |
| Repeated paravertebral injections       |                                                                                          |
| Sympathetic nerve block                 |                                                                                          |
| Epidural corticosteroid injections      |                                                                                          |
| Sympathetic nerve block                 |                                                                                          |
| Intrathecal injection                   |                                                                                          |
| Spinal cord stimulation                 |                                                                                          |
| Painful diabetic polyneuropathy         | Spinal cord stimulation                                                                   |
| Carpal tunnel syndrome                  | Local injections with corticosteroids                                                     |
| Meralgia paraesthetica                  | Lateral femoral cutaneous nerve (LFCN) infiltration with local anesthetic ± corticosteroid |
| Phantom pain                            | Pulsed RF treatment of the stump neuroma Pulsed RF treatment adjacent to the spinal ganglion (DRG) |
| Traumatic plexus lesion                 | Spinal cord stimulation                                                                   |
| Pain in patients with cancer            | Intrathecal medication delivery                                                           |
| Pain in chronic pancreatitis            | Epidural medication delivery                                                              |
| Chronic refractory angina pectoris      | Cervical cordotomy                                                                        |
| Ischemic pain of the extremities and Raynaud's phenomenon | Neurolytic plexus coeliacus block                                                       |
| Pain in chronic pancreatitis            | Neurolytic nervus splanchnicus block                                                     |
|                                         | Neurolytic plexus hypogastricus block                                                     |
|                                         | Intrathecal phenolization of lower sacral roots of cauda equine                           |
|                                         | Vertebroplasty                                                                            |
|                                         | Kyphoplasty                                                                              |
|                                         | Spinal cord stimulation                                                                   |
|                                         | Spinal cord stimulation                                                                   |
|                                         | Spinal cord stimulation                                                                   |

DRG, dorsal root ganglion; FBSS, failed back surgery syndrome; RF, radiofrequency.