*Pain Medicine*, 21(5), 2020, 918–921
doi: 10.1093/pm/pnz354
Advance Access Publication Date: 23 January 2020
**Original Research Article**





# Update of a Study of Not Ceasing Anticoagulants for Patients Undergoing Injection Procedures for Spinal Pain

**Stephen Endres, MD,* Karlee Hefti, CMA,* Erika Schlimgen, BS,* and Nikolai Bogduk, MD, PhD, DSc†**

*Pain Clinic of Northwestern Wisconsin, Eau Claire, Wisconsin, USA; †Faculty of Medicine and Health Sciences, The University of Newcastle, New South Wales, Australia

*Correspondence to:* Nikolai Bogduk, Faculty of Medicine and Health Sciences, The University of Newcastle, PO Box 431, East Maitland 2323, New South Wales, Australia. E-mail: nbogduk@bigpond.net.au.

Conflicts of interest: The authors have no conflicts of interest pertaining to any subject matter in this study.

Disclosures: The authors have no financial or other interests related to this study.

## Abstract

**Objectives.** To determine prevalence rates of hemorrhagic complications in patients who either ceased or continued anticoagulants during interventional pain procedures. **Methods.** A total of 1,936 consecutive patients were prospectively monitored during a total of 12,723 injection procedures. The prevalence of hemorrhagic complications was tallied for a variety of procedures performed on patients who ceased or continued various anticoagulants. **Results.** No hemorrhagic complications occurred in any patient who continued anticoagulants. Sufficiently large sample sizes were obtained to conclude that, in patients who continued warfarin or clopidrogel during lumbar transforaminal injections and for lumbar facet procedures, the zero prevalence of complications had 95% confidence intervals of 0% to 0.3%. This prevalence was significantly lower than the risk of medical complications in patients who ceased warfarin. **Conclusions.** Lumbar transforaminal injections and lumbar facet injections have a very low rate of hemorrhagic complications when patients continue to take anticoagulants.

**Key Words:** Spine; Pain; Injection; Anticoagulant

## Introduction

With respect to the logistics required, some questions in pain medicine can be relatively easy to answer. For example, to prove that a treatment is more effective than sham treatment, a study may require sample sizes of only 20 patients, if the treatment has a high success rate. Other questions require larger studies.

An example pertinent to the practice of interventional pain medicine is the alleged risk of hemorrhagic complications in patients who undergo invasive spine procedures while taking anticoagulant medications. Because of the perceived risk of such complications, eminent bodies have published guidelines for the cessation of anticoagulants for patients scheduled for spine procedures [1–5]. The implied conjecture of these guidelines is that complications will be encountered if anticoagulants are not discontinued. However, such complications could be rare.

In order to prove that some event is rare, large studies are required. Not only must the observed prevalence be rare, but the 95% confidence intervals of that prevalence must also be rare.

A previous study investigated the prevalence of hemorrhagic complications in patients who continued to take anticoagulants while undergoing spinal injection procedures [6]. The data collected showed that no complications occurred in patients who continued to take anticoagulants, but, tragically, medical complications occurred in a small number of patients who ceased anticoagulants, as recommended by the guidelines.

In that study, the sample sizes were substantial but not large. This limited the statistical confidence with which it could be concluded that spine procedures were safe to conduct in patients who continued anticoagulants and safer than ceasing anticoagulants. Therefore, the chief investigator continued to collect data. The present report

**Table 1.** The various indications for taking anticoagulants in patients who were scheduled to undergo one or more interventional pain medicine procedures

| Cardiac | | Cerebrovascular | |
|---|---|---|---|
| Atrial fibrillation | 599 | Stroke | 82 |
| Coronary artery disease | 379 | Transient ischemic attacks | 24 |
| Stent placement | 253 | Venous | |
| Valve replacement | 51 | | |
| Myocardial infarction | 40 | Deep vein thrombosis | 146 |
| Coronary artery bypass | 49 | Pulmonary embolism | 134 |
| Pacemaker | 5 | Blood clots | 47 |
| Septal defect | 2 | Miscellaneous | |
| Cardiomegaly | 1 | | |
| Vascular | | Factor V | 29 |
| | | Pulmonary disease | 20 |
| Hypertension | 84 | Other conditions | 18 |
| Peripheral vascular disease | 29 | | |

constitutes an update of that previous study [6], but it also constitutes the final report of data.

## Methods

The methods of the study have been reported in detail previously [6]. In essence, the chief investigator elected not to cease anticoagulants when intuitively he felt that it was safe to do so for certain spine procedures. Meanwhile, his partners in the same practice abided by the guidelines and ceased anticoagulants for similar procedures. Data were collected on the occurrence of any hemorrhagic complications attributable to the procedure performed and any other complications in patients continuing or ceasing anticoagulants.

For the previously published study [6], data were collected from January 1, 2005, to December 31, 2015. Additional data were collected from January 1, 2015, to December 31, 2018. The present study collates both sets of data.

## Results

The previous study enrolled 1,383 patients (723 males and 660 females). During the subsequent period, 553 new patients were enrolled (331 males and 222 females, for a combined total of 1,936 patients).

Table 1 summarizes the indications for anticoagulant therapy in the combined group. The most frequent indications were cardiac, venous, peripheral vascular, and cerebrovascular disorders.

These patients each underwent one or more injection procedures, not all of which were procedures in the spine (Table 2). Many underwent trigger point injections, or peripheral procedures such as injections into joints or bursae. Some underwent cervical, thoracic, or sacroiliac procedures, but in numbers too small for meaningful statistical analysis. Nevertheless, during none of the 2,263 of these procedures did any patient who continued anticoagulant therapy suffer any hemorrhagic event.

**Table 2.** Summary data on the number and location of injection procedures performed, according to if anticoagulants were discontinued or continued

| Anticoagulant | Procedure | | | | Total |
|---|---|---|---|---|---|
| | Nonspinal | | Spinal | | |
| | Trigger Point | Joints, Bursa | Other | Lumbar | |
| Discontinued | 34 | 567 | 601 | 2,672 | 3,827 |
| Continued | 802 | 300 | 1,161 | 7,004 | 8,896 |

Larger numbers of patients underwent injections in the lumbar spine. Table 3 summarizes the procedures performed, the anticoagulants used, and if they were discontinued or continued. The largest numbers of patients used warfarin or clopidogrel. Much smaller numbers of patients used other anticoagulants.

Table 3 shows that the chief investigator was willing to continue anticoagulants for lumbar transforaminal injections and facet injections but was reluctant to do so for radiofrequency neurotomy and interlaminar injections. Nonetheless, no hemorrhagic complications were encountered for any procedure in any patient who continued anticoagulants. The chief investigator considered it safe to continue anticoagulants for lumbar transforaminal injections if a 25-gauge spinal needle was used, the number of adjustments within the intervertebral foramen was kept to a minimum, and close attention was paid to any vascular uptake during the injection of a test dose of contrast medium.

The numbers of patients who continued warfarin or clopidogrel were large enough to calculate meaningful prevalence data. Table 4 shows that the zero prevalence of complications when performing transforaminal injections or facet injections has 95% confidence intervals of 0.0% to 0.3% when warfarin is continued and 0.0% to 0.4% when clopidogrel is continued.

Among the patients who *ceased* anticoagulants, none suffered any complications from their injection, but nine suffered medical complications before their procedure. These consisted of one fatal myocardial infarction, one fatal stroke, five nonfatal strokes, one pulmonary embolism, and one nonfatal myocardial infarction. These complications occurred only in patients who ceased warfarin. The prevalence of these complications was nine in 1,886 (0.48%), with a 95% confidence interval of 0.2% to 0.9%.

With respect to the risks of continuing or ceasing Warfarin, the present data are sufficiently robust to allow a statistical comparison. Using the confidence intervals of the difference between two proportions, the risk rate of ceasing warfarin (0.2% to 0.9%) is significantly greater than the risk rate of continuing warfarin (0.0% to 0.3%) for transforaminal injections or facet injections.

## Discussion

The results of the present study demonstrate several relevant features. Some pertain to the conduct of the study.

**Table 3.** The numbers of patients taking various anticoagulants and the lumbar procedures that they underwent, according to if they continued or discontinued anticoagulants for the conduct of that procedure

| Anticoagulant | Lumbar Transforaminal Injection | Lumbar Facet Injection | Radiofrequency Neurotomy | Interlaminar Injection | Total |
|---|---|---|---|---|---|
| Warfarin | | | | | |
| Discontinued | 502 | 330 | 639 | 175 | 1,646 |
| Continued | 1,666 | 1,928 | 47 | 17 | 3,658 |
| Clopidogrel | | | | | |
| Discontinued | 206 | 152 | 423 | 42 | 823 |
| Continued | 1,168 | 1,394 | 56 | 12 | 2,630 |
| Aspirin/dipyridamole | | | | | |
| Discontinued | 25 | 0 | 6 | 4 | 35 |
| Continued | 20 | 27 | 0 | 0 | 47 |
| Rivaroxaban | | | | | |
| Discontinued | 2 | 0 | 28 | 2 | 32 |
| Continued | 114 | 86 | 6 | 0 | 206 |
| Dabigatran | | | | | |
| Discontinued | 21 | 8 | 6 | 8 | 43 |
| Continued | 25 | 16 | 0 | 0 | 41 |
| Cilostazol | | | | | |
| Discontinued | 2 | 0 | 6 | 0 | 8 |
| Continued | 23 | 10 | 0 | 1 | 34 |
| Apixaban | | | | | |
| Discontinued | 2 | 2 | 72 | 0 | 76 |
| Continued | 120 | 200 | 36 | 0 | 356 |
| Enoxaparin | | | | | |
| Discontinued | 5 | 0 | 0 | 2 | 7 |
| Continued | 4 | 0 | 0 | 0 | 4 |
| Ticagrelor | | | | | |
| Discontinued | 0 | 0 | 0 | 2 | 2 |
| Continued | 18 | 9 | 0 | 0 | 27 |
| Prasugrel | | | | | |
| Discontinued | 0 | 0 | 0 | 0 | 0 |
| Continued | 1 | 0 | 0 | 0 | 1 |
| Total | | | | | |
| Discontinued | 765 | 492 | 1,180 | 235 | 2,672 |
| Continued | 3,159 | 3,670 | 145 | 30 | 7,004 |

"Lumbar facet injections" encompasses medial branch blocks and intra-articular injections.

**Table 4.** The number of patients who continued to take anticoagulants during the procedures listed and the number of complications encountered, their prevalence, and the 95% confidence intervals of that prevalence

| Drug Discontinued | Procedure | Number | Complications | | |
|---|---|---|---|---|---|
| | | | Number | Prevalence, % | 95% CI, % |
| Warfarin | Lumbar transforaminal injections | 1,666 | 0 | 0 | 0.0–0.3 |
| | Lumbar facet blocks | 1,928 | 0 | 0 | 0.0–0.3 |
| Clopidogrel | Lumbar transforaminal injections | 1,168 | 0 | 0 | 0.0–0.4 |
| | Lumbar facet blocks | 1,394 | 0 | 0 | 0.0–0.3 |

CI = confidence interval.

Others pertain to the practice of ceasing or continuing anticoagulants.

With respect to conducting studies, the experience of the present study shows that it is difficult to recruit large numbers of patients for every procedure of interest and for every anticoagulant of interest. The present data were collected over a period of 14 years but are still insufficient to support conclusions about many procedures and many of the drugs. The reasons for this include that patients using anticoagulants are not common, and become fewer when stratified by particular anticoagulants and by particular procedures. That in turn depends on the procedures that the physician offers, the referral rate for particular procedures, and the prevalence of the conditions for which particular procedures apply.

The fact that no hemorrhagic complications were encountered in any patients who continued anticoagulants suggests that spine procedures might be safe in such

patients, but confident conclusions in this regard require large numbers of patients. To establish that a zero prevalence of complications that has confidence limits <0.1% would require a sample size in excess of 5,000.

Such samples were not, and could not be, achieved in the present study. To achieve large numbers for every procedure of interest, an externally funded, multicenter study would be required, with paid staff monitoring all eligible patients and maintaining a large database over a long time. In contrast, the present study was self-funded in a single practice. No amount of continued monitoring could generate the numbers required. For that reason, the present study was closed.

Nevertheless, the study has provided meaningful data at least for two agents and two procedures. Earlier studies that measured the risk of complications in patients undergoing epidural injections while continuing nonsteroidal anti-inflammatory drugs concluded that a risk rate of 1% was acceptable [7,8]. By way of comparison, the present study has shown that the risk of hemorrhagic complications from lumbar transforaminal injections and lumbar facet injections lies between 0.0% and 0.3%, which is three times lower than the proposed safe rate. Therefore, against this benchmark, lumbar transforaminal injections and lumbar facet injections can be considered safe when performed in patients taking anticoagulants.

In contrast, however, the present study reiterates the warning of its predecessor [6]. Ceasing warfarin carries a nonzero risk of severe medical complications. The present study is now sufficiently powered to show that, although this risk rate is small, it is significantly greater than the risk rate of continuing warfarin.

One possible consolation in this regard is that all the medical complications encountered in the present study occurred during the first 10 years. No such complications occurred during the three years of the second phase of data collection. The reasons for this were not investigated, but it could be that physicians have become more reluctant to allow their patients to cease anticoagulants simply in order to undergo an invasive procedure. Additionally, they may feel that the intended procedure poses less risk than does ceasing anticoagulants. Cardiologists and others may have become aware of the risks of interrupting warfarin for reasons other than invasive spinal procedures [9].

The most recent edition of the anticoagulation guidelines of the American Society of Regional Anesthesia and Pain Medicine, together with other societies [10], reclassified lumbar medial branch blocks and lumbar radiofrequency neurotomy as low-risk procedures. The recommendation for these procedures is that anticoagulants not be discontinued. The results of the present study vindicate this recommendation for medial branch blocks, but they also strongly invite lumbar transforaminal injections to be added to the category of low-risk procedures.

## References


1. Horlocker TT, Wedel DJ, Benzon H, et al. Regional anesthesia in the anticoagulated patient: Defining the risks (the Second ASRA Consensus Conference on Neuraxial Anesthesia and Anticoagulation). Reg Anesth Pain Med 2003;28:172–97.
2. Breivik H, Bang U, Jalonen J, Vigfusson G, Alahuhta S, Lagerkranser M. Nordic guidelines for neuraxial blocks in disturbed haemostasis from the Scandinavian Society of Anaesthesiology and Intensive Care Medicine. Acta Anaesthesiol Scand 2010;54:15–41.
3. Gogarten W, Vandermeulen E, Van Aken H, Kozek S, Llau JV, Samama CM. Regional anaesthesia and antithrombotic agents: Recommendations of the European Society of Anaesthesiology and Intensive Care Medicine. Eur J Anaesthesiol 2010;27 (12):999–1015.
4. Horlocker TT, Wedel DJ, Rowlingson JC, et al. Regional anesthesia in the patient receiving antithrombotic therapy or thrombolytic therapy. American Society of Regional Anesthesia and Pain Medicine Evidence-Based Guidelines (Third Edition). Reg Anesth Pain Med 2010;35(1):64–101.
5. Narouze S, Benzon HT, Provenzano DA, et al. Interventional spine and pain procedures in patients on antiplatelet and anticoagulant medications. Guidelines from the American Society of Regional Anesthesia and Pain Medicine, the European Society of Regional Anaesthesia and Pain Therapy, the American Academy of Pain Medicine, the International Neuromodulation Society, the North American Neuromodulation Society, and the World Institute of Pain. Reg Anesth Pain Med 2015;40:182–212.
6. Endres S, Shufelt A, Bogduk N. The risks of continuing or discontinuing anticoagulants for patients undergoing common interventional pain procedures. Pain Med 2017;18(3):403–9.
7. Horlocker TT, Wedel DJ, Schroeder DR, et al. Preoperative antiplatelet therapy does not increase the risk of spinal hematoma associated with regional anesthesia. Anesth Analg 1995;80 (2):303–9.
8. Horlocker TT, Bajwa ZH, Ashraf Z, et al. Risk assessment of hemorrhagic complications associated with nonsteroidal antiinflammatory medications in ambulatory pain clinic patients undergoing epidural steroid injection. Anesth Analg 2002;95 (6):1691–7.
9. Raunsø J, Selmer C, Olesen JB, et al. Increased short-term risk of thrombo-embolism or death after interruption of warfarin treatment in patients with atrial fibrillation. Eur Heart J 2012;33 (15):1886–92.
10. Narouze S, Benzon HT, Provenzano D, et al. Interventional spine and pain procedures in patients on antiplatelet and anticoagulant medications (second edition): Guidelines from the American Society of Regional Anesthesia and Pain Medicine, the European Society of Regional Anaesthesia and Pain Therapy, the American Academy of Pain Medicine, the International Neuromodulation Society, the North American Neuromodulation Society, and the World Institute of Pain. Reg Anesth Pain Med 2018;43:225–62.