PAIN MEDICINE CASE REPORTS

ISSN 2768-5152

Volume 9, Number 2, pp. 147-150

Bridging Antiplatelet Therapy With Cangrelor in Spinal Cord Stimulator Trial and Implant for Patient With Refractory Angina: A Case Report

Marshall Yuan, PharmD[1], Angie Kuang, BS[2], and David Hao, MD[3]

Background: Antiplatelet medications increase the risk of neuraxial bleeding during spinal cord stimulator (SCS) trials and implants, necessitating adequate discontinuation. However, interrupting antiplatelet therapy is undesirable in patients at high risk for thromboembolism. Cangrelor, a novel nonthienopyridine adenosine triphosphate analog, has a rapid onset and offset that can be used to bridge antiplatelet therapy prior to procedures involving neuraxial access, minimizing the risk of subtherapeutic anticoagulation.

Case Report: We present the case of a 44-year-old man with an extensive cardiac history who underwent neuromodulation for refractory angina. The patient was transitioned from prasugrel to cangrelor, with cangrelor being discontinued 3 hours prior to the tunneled SCS trial and subsequent implant. He showed no signs of any complications, including neurological issues, related to bleeding.

Conclusions: This case illustrates the successful use of cangrelor as an antiplatelet bridge prior to a neuraxial procedure.

Key words: Cangrelor, spinal cord stimulator, spinal hematoma, antiplatelet bridge, neuraxial access

BACKGROUND

Anticoagulant and antiplatelet therapy in patients undergoing neuraxial procedures is a concern due to the potentially increased risk of hemorrhagic complications. Spinal cord stimulation (SCS) is indicated for patients with chronic pain that is refractory to other treatment options and involves implant of electrodes into the epidural space (1). Potential-associated risks include electrode migration, infection, spinal cord injury, and hemorrhage (2). A systematic review from 2011 (3) reported a 0.19% incidence rate of epidural hematoma associated with paddle leads, resulting in major neurological deficits, limited neurological deficits, and no neurological deficits at 63%, 19%, and 18%, respectively. A 2023 meta-analysis (4) of 40 studies reported an incidence of 0.81% for any hematoma following SCS, with a 0.32% occurrence of neuraxial bleeding.

Studies (5) have shown that patients receiving unfractionated heparin < 1 hour after a lumbar puncture had higher incidences of spinal hematomas. Multiple case reports (6) have also reported the occurrence of spontaneous spinal epidural hematomas in patients on anticoagulants and antiplatelets. Due to the risk of neuraxial bleeding, the American Society of Regional Anesthesia and Pain Medicine (ASRA) has developed guidelines recommending medication-hold intervals tailored to specific drugs, with extended intervals recommended for high-risk procedures like SCS. Retrospective studies (7) have demonstrated that patients managed with an appropriate "anticoagulant hold" do not exhibit an

From: [1]Robert Wood Johnson Medical School, Piscataway, NJ; [2]Drexel University College of Medicine, Philadelphia, PA; [3]Department of Anesthesia, Critical Care and Pain Medicine, Massachusetts General Hospital, Harvard Medical School, Boston, MA

Corresponding Author: Marshall Yuan, PharmD, E-mail: marsyuan55@yahoo.com
Disclaimer: There was no external funding in the preparation of this manuscript.
Conflict of interest: Each author certifies that he or she, or a member of his or her immediate family, has no commercial association (i.e., consultancies, stock ownership, equity interest, patent/licensing arrangements, etc.) that might pose a conflict of interest in connection with the submitted manuscript.
Patient consent for publication: Consent obtained directly from patient(s).
This case report adheres to CARE Guidelines and the CARE Checklist has been provided to the journal editor.
Accepted: 2025-02-06, Published: 2025-04-30

increased risk of hemorrhagic complications compared to those who are not anticoagulated.

Thienopyridines, including clopidogrel, prasugrel, and ticlopidine, are adenosine diphosphate receptor antagonists that inhibit platelet aggregation and are used to prevent cerebrovascular thromboembolic events. ASRA guidelines recommend that thienopyridines be stopped 7 to 10 days prior to spine and pain procedures (8). European Society of Anesthesiology and Intensive Care guidelines recommend holding clopidogrel for 5 to 7 days and prasugrel for 7 days before neuraxial procedures (9). These recommendations align with the guidelines of the Society of Interventional Radiology, which recommend holding clopidogrel for at least 5 days and prasugrel for 7 days for those at high risk of bleeding (10). American Society of Interventional Pain Physicians guidelines recommend preoperatively holding clopidogrel for 5 days and prasugrel for 7 days prior to high-risk spinal pain interventions, such as SCS (11).

Cangrelor is a novel nonthienopyridine adenosine triphosphate analog that reversibly and rapidly antagonizes the P2Y12 receptor to prevent platelet activation and aggregation. It is currently US Food and Drug Administration-indicated to prevent periprocedural myocardial infarction (MI), coronary revascularization, and stent thrombosis in percutaneous coronary intervention (PCI) (12). Studies comparing cangrelor against other similar antiplatelet agents have shown greater or comparable efficacy and safety (12,13). Subanalysis of the original CHAMPION PHOENIX study demonstrated that, in high-risk patients with prior MI, cangrelor resulted in a decrease in the primary endpoint of death, MI, ischemia-driven revascularization, and stent thrombosis at 48 hours following PCI compared to clopidogrel, without increased bleeding (13). A meta-analysis (14) of the clinical efficacy of cangrelor and other P2Y12 inhibitors demonstrated no differences in cardiovascular death, MI, major adverse cardiac events, stent thrombosis, and bleeding while on cangrelor therapy. Antiplatelet effects of cangrelor are observed within 2 minutes, achieving 90% to 95% platelet inhibition. With a half-life of 2.9 to 5.5 minutes, cangrelor is rapidly metabolized, with 80% of platelet activity recovered in 60 minutes and 90% of platelet activity recovered in 90 minutes (8). It currently costs $749.00 per 50 mg vial (15).

Cangrelor's pharmacokinetic profile makes it an ideal option for bridging antiplatelet therapy in surgical patients at high risk of thromboembolic complications. Current ASRA guidelines recommend holding clopidogrel for 5 to 7 days and prasugrel for 7 to 10 days prior to neuraxial procedures. In contrast, cangrelor offers a practical alternative for bridging therapy, as it can be discontinued just 3 hours before neuraxial access. For high-risk interventions, such as SCS placement, an interval > 3 hours is preferred for cangrelor. Cangrelor may be restarted 24 hours after conclusion of the neuraxial block or procedure (8). The American Heart Association expert opinion on switching P2Y12 inhibitors recommends a dosing of 0.75-μg·kg-1·min-1 infusion without a bolus, derived from study that established this dose yielded a similar degree of platelet inhibition to clopidogrel (16). The current ASRA recommendations for cangrelor holds prior to neuraxial intervention are classified as grade 2C and are based on pharmacokinetic elimination data. To our knowledge, no prior case reports have assessed the efficacy of cangrelor in facilitating neuraxial access for SCS procedures. This case demonstrates the safe and effective use of cangrelor as bridging antiplatelet therapy in a patient undergoing a tunneled SCS trial and implant, in alignment with guideline recommendations.

CASE

We present the case of a 44-year-old man with early-onset multivessel coronary artery disease (CAD) status post multiple coronary interventions, and chronic neuropathic pain following laminectomy in 2003. Over the past 2 years, he has undergone 10 cardiac catheterizations, including 5 interventions and the placement of 9 stents. Despite maximal antianginal therapy, his anginal pain remained refractory to medical management. The patient presented to the emergency department with severe chest pain nonresponsive to sublingual nitroglycerin. He underwent repeat coronary angiography, which demonstrated patent stents and no intervenable coronary lesions, with stable coronary anatomy. He received maximal medical therapy with intravenous nitroglycerin and heparin, but his chest pain remained severe and unrelieved. Coronary angiography with intravascular ultrasound demonstrated underexpanded stents in the left anterior descending artery, for which percutaneous transluminal angioplasty was performed. His anginal pain temporarily improved postprocedure. However, he experienced recurrent angina approximately one week later and presented again with worsening chest pain, diaphoresis, and dyspnea. Repeat coronary angiography revealed underexpansion of the diagonal branch stent, which was addressed with balloon angioplasty.

During this procedure, the patient was started on daily prasugrel.

Given his persistent refractory angina, the pain management team was reconsulted to explore neuromodulation, and an inpatient tunneled trial was arranged. To facilitate neuraxial access, prasugrel was transitioned to cangrelor, allowing for a 7-day discontinuation of prasugrel. At the end of this hold, cangrelor was paused for the recommended 3-hour period, and the patient was taken to the operating room (OR) for a tunneled trial of SCS. A midline incision was made and dissection to the posterior thoracolumbar fascia was performed. Both electrodes were introduced via Tuohy needles placed at the T12/L1 level. The first electrode was advanced to the middle of the T3 vertebral body, while the second electrode was advanced to the top of the T2 vertebral level. Paresthesia mapping confirmed that the stimulation effectively overlapped the painful region, providing adequate pain coverage. A flank pocket was created, and the electrodes were tunneled from the back to the pocket site. They were connected to extensions, which were coiled and secured within the pocket. The extension electrodes were tunneled across the back and exited through a stab incision. Cangrelor was restarted 24 hours after the procedure.

The patient reported a 75% improvement over the following week and described successfully aborting severe episodes by adjusting the stimulator during attacks. He then returned to the OR for permanent implantation of the SCS generator. Postoperatively, he was transitioned to clopidogrel with a loading dose. Postprocedural monitoring was completed with daily neuro checks and was unremarkable for signs indicative of neuraxial hematoma. His Canadian Cardiovascular Society classification for angina improved from Class IV to Class I. His angina class remained between Classes I and II on 6-month follow-up. The patient described in this study provided informed consent to be included in this case report.

CONCLUSIONS

The use of cangrelor as bridge therapy has been documented in patients undergoing various procedural interventions, first established in a study investigating cangrelor as a bridge for thienopyridine-treated patients prior to a coronary artery bypass graft (CABG) (17). A prospective study (18) of 24 high-risk thrombotic patients evaluated cangrelor bridging after dual antiplatelet therapy discontinuation for intermediate- and high-risk surgeries, including pulmonary lobectomy, prostatectomy, nephrectomy, hip replacement, and nonemergent CABG or mitral valve repair. One cardiac death occurred from ST-segment elevation myocardial infarction and 9 patients required blood transfusion, but no fatal or life-threatening bleeds occurred (18). Another prospective study (19) demonstrated the feasibility of cangrelor as a bridging therapy for CAD patients undergoing cardiac and noncardiac surgeries. Among 27 patients (24 cardiac and 3 noncardiac), the median cangrelor hold time was 6.75 hours (range: 4 to 10.75 hours). Bleeding events occurred in 2 cardiac surgery patients, while no bleeding complications were reported in noncardiac patients (19). This case report is, to our knowledge, the first to evaluate the safety and efficacy of cangrelor as bridge therapy in a patient undergoing neuraxial access for SCS.

The patient's history of early-onset CAD, 10 cardiac catheterizations, and 9 stents underscores a high risk for coronary stent thrombosis. Beyond antiplatelet therapy, he had no significant bleeding risk factors. Patients with high thrombotic risk are ideal candidates for cangrelor in this context. Bleeding during neuraxial procedures is most often associated with coagulation disorders or anticoagulant use. Other factors, such as advanced age, male gender, spinal anatomical abnormalities, and the Charlson Comorbidity Index, have also been linked to an increased risk of spinal hematoma, though these associations are less well established (20). The patient was closely monitored in the postoperative period for any signs or symptoms of neuraxial bleeding. Early identification of potential indicators of spinal hematoma is crucial to ensure prompt intervention and reduce the risk of adverse outcomes. A review of case reports on spinal hematoma following neuraxial anesthesia found that nearly 50% of initial symptoms appeared within 24 hours, and approximately 70% within 72 hours (21).

In patients requiring neuraxial access with significant ischemic risk factors, the primary advantage of cangrelor over other antiplatelets, such as clopidogrel, lies in its regimen flexibility due to its rapid pharmacokinetic profile, while maintaining comparable clinical efficacy. Additionally, several studies (21) have reported spontaneous spinal hematomas associated with clopidogrel, potentially encouraging the consideration of alternative options like cangrelor. However, this difference may reflect the widespread use of clopidogrel compared to the limited adoption of cangrelor, warranting ongoing surveillance as more

data on cangrelor becomes available. The primary risk of cangrelor remains bleeding. A pooled analysis of 3 trials involving percutaneous coronary interventions found that while cangrelor was not significantly associated with Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Arteries (GUSTO) moderate or severe bleeding events, it did increase rates of less severe bleeding, such as GUSTO mild bleeding and Acute Catheterization and Urgent Intervention Triage Strategy major bleeding (22). These mixed findings underscore the need for further research and careful evaluation to identify the patient populations that would derive the greatest benefit from cangrelor therapy, considering the potential for increased bleeding risk.

Current guidelines are primarily based on expert opinion. Future research should prioritize generating primary data on the use of cangrelor as a bridging antiplatelet therapy in patients undergoing neuraxial procedures. Patients at high thrombotic risk who require neuraxial access may benefit from cangrelor's favorable pharmacokinetic profile, but further research is essential to clarify its safety and efficacy in this context. As pain medicine evolves and novel invasive modalities are introduced, optimizing the management of medically complex patients becomes increasingly critical, particularly when the risk-benefit balance remains uncertain. This case highlights the potential of cangrelor as a bridging antiplatelet therapy for patients undergoing neuraxial access for SCS.

REFERENCES

1. Dydyk AM, Tadi P. Spinal cord stimulator implant. In: *StatPearls [Internet].* StatPearls Publishing, Treasure Island, FL 2024.
2. Garg I, Wang D. Complications of spinal cord stimulator trials and implants: A review. *Curr Pain Headache Rep* 2023; 27:837-842.
3. Levy R, Henderson J, Slavin K, et al. Incidence and avoidance of neurologic complications with paddle type spinal cord stimulation leads. *Neuromodulation* 2011; 14:412-422; discussion 422.
4. West T, Driver CN, D'Souza RS. Incidence of neuraxial and non-neuraxial hematoma complications from spinal cord stimulator surgery: Systematic review and proportional meta-analysis. *Neuromodulation* 2023; 26:1328-1338.
5. Ruff RL, Dougherty JH Jr. Complications of lumbar puncture followed by anticoagulation. *Stroke* 1981; 12:879-881.
6. Horlocker TT, Vandermeuelen E, Kopp SL, Gogarten W, Leffert LR, Benzon HT. Regional anesthesia in the patient receiving antithrombotic or thrombolytic therapy: American Society of Regional Anesthesia and Pain Medicine Evidence-Based Guidelines (Fourth Edition). *Reg Anesth Pain Med* 2018; 43:263-309.
7. Khan H, Kumar V, Ghulam-Jelani Z, et al. Safety of spinal cord stimulation in patients who routinely use anticoagulants. *Pain Med* 2018; 19:1807-1812.
8. 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; 43:225-262.
9. Kietaibl S, Ferrandis R, Godier A, et al. Regional anaesthesia in patients on antithrombotic drugs: Joint ESAIC/ESRA guidelines. *Eur J Anaesthesiol* 2022; 39:100-132.
10. Patel IJ, Rahim S, Davidson JC, et al. Society of Interventional Radiology consensus guidelines for the periprocedural management of thrombotic and bleeding risk in patients undergoing percutaneous image-guided interventions-part II: Recommendations: Endorsed by the Canadian Association for Interventional Radiology and the Cardiovascular and Interventional Radiological Society of Europe. *J Vasc Interv Radiol* 2019; 30:1168-1184 e1.
11. Kaye AD, Manchikanti L, Novitch MB, et al. Responsible, safe, and effective use of antithrombotics and anticoagulants in patients undergoing interventional techniques: American Society of Interventional Pain Physicians (ASIPP) guidelines. *Pain Physician* 2019; 22:S75-S128.
12. Feng KY, Mahaffey KW. Cangrelor in clinical use. *Future Cardiol* 2020; 16:89-102.
13. Eisen A, Harrington RA, Stone GW, et al. Cangrelor compared with clopidogrel in patients with prior myocardial infarction - insights from the CHAMPION trials. *Int J Cardiol* 2018; 250:49-55.
14. Westman PC, Lipinski MJ, Torguson R, Waksman R. A comparison of cangrelor, prasugrel, ticagrelor, and clopidogrel in patients undergoing percutaneous coronary intervention: A network meta-analysis. *Cardiovasc Revasc Med* 2017; 18:79-85.
15. Jensen IS, Wu E, Cyr PL, et al. Cost-Consequence analysis of using cangrelor in high angiographic risk percutaneous coronary intervention patients: A US hospital perspective. *Am J Cardiovasc Drugs* 2022; 22:93-104.
16. Angiolillo DJ, Rollini F, Storey RF, et al. International expert consensus on switching platelet P2Y(12) receptor-inhibiting therapies. *Circulation* 2017; 136:1955-1975.
17. Angiolillo DJ, Firstenberg MS, Price MJ, et al. Bridging antiplatelet therapy with cangrelor in patients undergoing cardiac surgery: A randomized controlled trial. *JAMA* 2012; 307:265-274.
18. Rossini R, Masiero G, Fruttero C, et al. Antiplatelet therapy with cangrelor in patients undergoing surgery after coronary stent implantation: A real-world bridging protocol experience. *TH Open* 2020; 4:e437-e445.
19. Kairouz V, Patel P, Franchi F, et al. Cangrelor as an antiplatelet bridging strategy in patients with coronary artery disease undergoing cardiac and non-cardiac surgery. *J Am Coll Cardiol* 2018; 71:A75.
20. Vandermeulen EP, Van Aken H, Vermylen J. Anticoagulants and spinal-epidural anesthesia. *Anesth Analg* 1994; 79:1165-1177.
21. Lagerkranser M, Lindquist C. Neuraxial blocks and spinal haematoma: Review of 166 cases published 1994 - 2015. Part 2: Diagnosis, treatment, and outcome. *Scand J Pain* 2017; 15:130-136.
22. Steg PG, Bhatt DL, Hamm CW, et al. Effect of cangrelor on periprocedural outcomes in percutaneous coronary interventions: A pooled analysis of patient level data. *Lancet* 2013; 382:1981-1992.