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Epidural hematoma risks associated with ceasing vs maintaining anticoagulant and/or antiplatelet medications for cervical and thoracic interlaminar epidural steroid injections

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ABSTRACT

Background: There is a lack of substantiated evidence to support or refute the risks of ceasing vs maintaining anticoagulant and/or antiplatelet medications (ACAP) prior to cervical and thoracic interlaminar epidural steroid injections. The ACAP medication is frequently stopped pre-procedure due to concerns for potential bleeding complications, particularly epidural hematomas (EH). This article provides evidence regarding EH incidence in this population.

Methods: Data for this study was collected retrospectively on all patients from September 19, 2009–Jun 16, 2017 who were scheduled for an Interlaminar Cervical and/or Thoracic Epidural Steroid Injections (IL-CTESI) and were on an ACAP medication at the time a procedure was scheduled. All possible adverse outcomes were then retrospectively analyzed via extensive data mining of the electronic medical record system with special emphasis on EHs.

Results: 591 IL-CTESI were performed on patients taking ACAP medications. In total, 351 patients ceased their ACAP medication prior to the procedure and 240 maintained ACAP medication. Our findings demonstrate that there were no clinically relevant incidents of EHs in either cohort.

Conclusions: This data gives critical insight into the post-procedural EH risk for patients who had continued or stopped taking their ACAP medications prior to their IL-CTESI. The results from this study suggest re-evaluating the potential post-procedural EH risks associated with continuing vs ceasing these medications.

1. Introduction

Interlaminar Cervical and Thoracic Epidural Steroid Injections (IL-CTESIs) are minimally invasive elective procedures that have been shown to reduce cervico-thoraic and upper limb radicular pain and symptoms in appropriately selected patients with functionally disabling pain despite conservative care. About 200,000 IL-CESIs are performed per year in the US Medicare populations [1]. IL-CTESIs have been proven to reduce 50% of the Visual Numeric Scale (VNS) and Oswestry Disability Index (ODI) scores by greater than or equal to 50% for up to 3 months with limited quality extending beyond this time frame of analysis [2–4]. However, it is important to note that IL-CESIs have associated risks [9]. Similarly, interlaminar thoracic epidural steroid injections (IL-TESI) are postulated to have similar indications, though these are less frequent clinically and there is a paucity of outcomes and risk literature as a result of this.

IL-CTESI risks include puncturing the dura, spinal cord and/or epidural veins. The epidural veins are more densely packed laterally and form an arcuate pattern. Although there is no direct risk from injecting into the epidural veins, damage to these blood vessels during IL-CTESI

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have been reported to cause epidural hematomas (EHs) [5,6].

The true incidence of clinically relevant EH related to IL-CTESI is unknown. However, early anesthesia-based literature reported that the incidence of epidural hematoma after accessing the lumbar epidural space via an interlaminar approach for epidural blocks was 1 in 150,000 [9,10]. Although the clinical EH incidence is quite low, interventional physicians tend to err on the side of caution since the potential consequences of clinically relevant EH causing spinal cord injury and associated neurologic compromise can be devastating.

Clinically relevant EH signs and symptoms immediately post IL-CTESI procedure include pain, weakness, numbness, difficulty walking, loss of bowel and/or bladder control and paralysis. If immediately identified, clinically relevant EH can be treated by emergent surgical evacuation. Potential long term consequences of clinically relevant EHs include irreversible neurological deficits. EHs can lead to paraplegia and even potential death if not emergently decompressed [7–29]. To reduce EH risk, pain management providers have recommended cessation of anticoagulants and/or antiplatelet (ACAP) medication prior to IL-CTESI [30,31].

The conventional wisdom is that the risks associated with ACAP medication cessation to prevent potential EHs outweighs the risk of stopping the ACAP medications despite the medical indications. Hence guidelines historically have often recommended ACAP medication cessation prior to IL-CTESI [30,31]. However, the basis of these recommendations is limited by a paucity of literature on the true incidence of clinically relevant EH following IL-CTESI. Even more, the risk of clinically relevant EH in patients on ACAP has not been quantified.

The purpose of this present study is to investigate the clinically relevant EH rate in patients taking ACAP medications who maintain or stop their ACAP medications prior to their IL-CTESI.

2. Methods

The present study was conducted at OSS Health, a private multi-specialty practice in York, Pennsylvania serving a population of about 500,000 people. Data for this study was collected retrospectively on all patients from September 19, 2009–June 16, 2017 who were scheduled for an IL-CTESI and were on an ACAP medication. These patients were identified by a search of our Medent Electronic Medical Record (EMR) (Auburn, NY) for generated ACAP forms. These ACAP forms at OSS Health are generated every time a patient is on an ACAP medication and is scheduled for an interventional procedure at our pain center.

Institutional Review Board (IRB) approval was obtained prior to data collection via the OSS Health IRB committee. All spinal procedures were performed in accordance with the Practice Guidelines of the ASRA and Spine Intervention Society using fluoroscopic guidance and performed at the OSS Health pain center [30,31].

This data captures the ACAP medication management of six different pain management physicians for IL-CESI and IL-TESI. Two physicians were board certified in Anesthesiology and four physicians were board certified in Physical Medicine and Rehabilitation (PM&R). All six physicians had individualized management protocols of ACAP medication management. These protocols were based on either ASRA or SIS guidelines but with deviations due to individual patient comorbidities, anatomy, age and type of procedure being performed [30,31].

Whether the ACAP medication were ceased or maintained was determined based on the clinical judgment of the interventional physician weighing relevant guidelines and a shared decision process with the patients. The most recent available literature during the study duration suggested that the potential thromboembolic risk of holding ACAP medications was potentially greater than the EH risk associated with continuing the ACAP medication. This led to many cases in which ACAP medications were continued in an effort to optimize patient safety. When ACAP medication was held, the cessation timeline was in accordance with ASRA guidelines at that time [30].

After the decision to cease or maintain medication was made, it was documented and included in the generated ACAP form, and categorized accordingly. Patients on Coumadin had their INR checked within at least 72hrs of the procedure regardless of whether the medication was ceased or maintained. Medication level assays, PT, aPTT, platelet function, or bleeding times were not recorded.

Every medication or combination was independently recorded as part of the chart review. For data analysis, a patient's medications were then grossly classified as being on antiplatelet medication, anticoagulant medication, or both antiplatelet and anticoagulant medication.

For this study, patients who had ACAP forms and an IL-CTESI were analyzed and documented. Patient charts were retrospectively reviewed as to whether ACAP medications were ceased or maintained for the IL-CTESI. For patients on warfarin therapy, INR was reviewed from the charts retrospectively. An INR on the day of the procedure or the day prior to the procedure was considered in our analysis.

Major adverse outcomes including but not limited to new neurologic deficits, clinically detected hematomas, hospitalization, death, or any other patient concerns were recorded and analyzed.

All patients who underwent a procedure were routinely followed immediately post procedure for new signs or symptoms and by telephone within 72 h of the procedure. Patients were also instructed to call for issues such as increased pain, new onset neurologic dysfunction, bleeding or signs of infection. Patients were then routinely scheduled for a two week follow up encounter post procedure.

This data was gathered by reviewing post-procedure phone calls, post procedure follow ups, urgent care follow ups, patient portal messages and local hospital visits. If the above protocol did not result in post-procedural information in the OSS Health EMR, any potential encounter information was then searched (with permission) at our two local major medical institutions. To further minimize patients lost to follow-up (LTFU), we also searched for patients on local obituary lists and even called patients or their families by phone.

Patient outcomes were tracked up to 90 days post procedure. The 90-day mark was chosen as a reference point based on previous ACAP data that shows that 99.99% of complications following the cessation of medication happens within a 90-day window [31–35]. For purposes of this study, 90-day follow up is also appropriate in capturing any EH related to the procedure.

Every procedure was counted as a unique encounter. For patients that received multiple procedures over the time period, each procedure was counted as a unique count.

3. Statistical methods

Basic patient demographics including age and gender were recorded.

The overall incidence of EH was calculated as a simple proportion. A binomial exact calculation was performed to report a 95% confidence interval for incidence as an estimate of the proportion with a dichotomous result in this single sample. In cases wherein the numerator is 0, a one-sided 97.5% confidence interval was calculated to determine the upper bound of the 95% confidence interval, whereas the lower bound of the confidence interval remained 0.

4. Results

We performed 592 IL-CESI and IL-TESI between September 19, 2009 and Jun 16, 2017 on patients identified as having pre-procedure ACAP medications. There was only one patient lost to follow-up, who underwent a C7-T1 interlaminar ESI whilst continuing their Apixaban. Because they were lost to follow-up they were not included in the analysis, resulting in 591 included in our data. 49.9% of patients were male, with an average age of 68.2 years old. 561 procedures were performed at C7-T1, 4 were performed at C6-7, and 26 were performed in the thoracic spine. In total, 351 patients ceased their ACAP medication prior to the procedure and 240 maintained ACAP medication. Of those that ceased ACAP medications, 195 were on Antiplatelet (AP)

medications, 103 were on Anticoagulant (AC) medications, and 53 were on both AP and AC medications. 190 patients maintained AP medication, 36 maintained AC medications, and 14 maintained AC and AP medications. This is further stratified in Table 1.

The most common ACAP medication or medication combinations encountered were aspirin (159 total, 110 maintained), clopidogrel and aspirin combination therapy (143 total, 43 maintained), warfarin (142 total, 21 maintained), clopidogrel (90 total, 28 maintained), and warfarin and aspirin combination therapy (54 total, 12 maintained) (Table 2).

35 patients were instructed to maintain warfarin (or warfarin plus antiplatelet therapy), with available INR data on 22 of the those patients. 13 were missing INR data. Of the 22, the mean INR was 1.87.11 maintained an INR between 2 and 3, 6 had an INR between 1.4 and <2, and 5 had an INR of less than 1.4. Of note, INR data was also available on 2 additional patients that was drawn between 48 and 72 h prior to the procedure, whose values were 3.7 and 3.4.

124 patients were instructed to cease warfarin therapy. 45 patients are missing INR data. Of the 79 patients with available INR data, the mean INR was 1.28.7 patients had an INR between 2 and 3, 11 patients had an INR between 1.4 and <2, and the remaining 61 had an INR of 1.3 or less.

No clinically relevant EHs were noted in the patient cohort (0/591, 0%, 95% CI 0.0–0.62%) (Table 3). In patients who maintained AC or AP medication overall, the rate of clinically relevant EH was 0/240 (0%, 95% CI 0–1.5%). In patients who maintained AP medication, AC medication, or AC and AP combination therapy, the rate of clinically relevant EH was 0/190 (0%, 95% CI 0–1.9%), 0/36 (0%, 95% CI 0–9.7%) and 0/14 (0%, 95% CI 0–23.1%) respectively.

5. Discussion

Here we present the largest cohort published to date showing the risk of clinically relevant EH in patients taking ACAP medications prior to undergoing IL-CESI or IL-TESI stratified by whether the medication was ceased or maintained. We acknowledge the risk of EH is serious given the catastrophic nature of such a complication. Accordingly, guidelines have focused on medication management strategies to mitigate the risk of EH. Notably, in this cohort, we estimate the overall risk of EH to be 0% (95% CI 0.0–0.62%), with patients who maintain ACAP or medications for IL-CESI or IL-TESI to be 0% (95% CI 0–1.5%) [37].

We are only presenting data for post-procedural *clinically relevant* EHs. We painstakingly reviewed post-procedural patient data for any neurologic symptoms, or other clinical information suggesting a change from baseline. Asymptomatic EHs, information that would *not* generally be clinically relevant, was not captured in this study.

York, PA is geographically well situated for this type of study. Our two local institutions are UPMC Memorial Hospital and Wellspan York Hospital which serve a population of about 500,000. The next closest hospitals are 45 min away so it is a relatively closed system. Hence most patient data was available for review and for this study out of 591 patients, only one patient was lost to follow up.

This data should not be construed to say the risk of EH following ILESI is 0%, as numerous publications have demonstrated that this complication does occur [7–29]. However, when considering the relative risks of ceasing or maintaining ACAP medications, the current literature is insufficient to accurately quantify these risks. The relatively large 'n' and subsequent 95% confidence intervals in this study does provide data that can guide that discussion. In theory, if the upper limit of the risk of developing a hematoma after ILESI while maintaining ACAP medications is less than the lower limit of the risk of a thrombotic complication occurring should ACAP medications be ceased prior to the procedure this would call into question guidelines that are currently aimed primarily at preventing EH.

ACAP cessation has its associated risks as well. ACAP medications are typically prescribed to reduce thrombotic/ischemic events such as Myocardial infarction (MI), Deep Vein Thrombosis (DVT), Pulmonary Embolism (PE), Cerebrovascular Events (CVA), and even death associated with these events [32]. Anticoagulants derive their effect by acting at various sites of the coagulation cascade. Antiplatelet medication works by blocking platelet aggregation. Stopping both AC and AP medications will increase the frequency of these ischemic/thrombotic events and can even result in a hypercoagulable state [32–37]. Such complications can be equally if not more catastrophic than a EH. Moreso, an EH is treatable if diagnosed within a timely manner, wherein complications such as MI, PE, and CVA have a much shorter window duration of therapeutic opportunity.

Regarding the patients on warfarin therapy (or warfarin plus antiplatelet therapy), it was clear that not all patients had an INR that was in the therapeutic range (for those instructed to maintain), or below the therapeutic range (for those instructed to cease). While it does reflect clinical practice, patients may not be in the therapeutic range for various reasons: They do not always follow physician instructions in addition to the notorious challenges with dosing warfarin in a way that results in a stable INR. This does limit some generalizability of the warfarin data in this study. In the truest sense, in terms of intent to treat, this does reflect what may be expected when patients are instructed to cease or maintain warfarin therapy. From an accuracy perspective, however, this higher than expected INR in the cease cohort theoretically could result in overestimating the hematoma risk and underestimating thromboembolic risk complications. Likewise, the lower INR in the maintain cohort

Table 1
Patients who ceased vs maintained AC or AP medication.

	Ceased	Maintained
AP	195	190
AC	103	36
Combo	53	14

Table 2
Ceased vs Maintained AC or AP medication by spinal segment.

Cervical (all C7-T1 except 4C6-7)			Thoracic		
	Ceased	Maintained		Ceased	Maintained
AP	187	178	AP	8	12
AC	101	34	AC	2	2
Combo	52	13	Combo	1	1

Table 3
Medications ceased or maintained.

Medications	Ceased	Maintained
Aggrenox	1	0
Apixaban	3	2
Apixaban and ASA	4	0
ASA 81	23	70
ASA 81+	26	40
Clopidogrel	62	28
Clopidogrel and Apixaban	1	0
Clopidogrel and ASA	80	43
Dapigatran	4	5
Dapigatran and ASA	1	0
Enoxaparin	2	1
Heparin and ASA	1	0
Pentosan	1	3
Prasugrel	0	1
Prasugrel and ASA	3	4
Rivaroxaban	12	4
Rivaroxabran and ASA	3	0
Ticagrelor and ASA	0	3
Ticlopidine	0	1
Warfarin	81	21
Warfarin and ASA	42	12
Warfarin and Clopidogrel	1	2

could underestimate the hematoma risk and overestimate the thromboembolic risk complications. In terms of the safety of maintaining warfarin therapy for CTILESI, our data set only includes 18 patients that underwent the procedure whilst having an INR in the range of 2–3. This data should not be construed to convey safety of CTILESI whilst a patient is maintained on active warfarin therapy as a total n of 18 is grossly insufficient to make safety claims regarding this practice.

This data is still limited and in and of itself cannot be used to draw certain conclusions. Another limitation of this study is its retrospective design. Some potential for recall bias exists in cases where patients or family members were contacted. Ideally, the concomitant use of reviewing medical records and the presumed fidelity of such records limit some of this bias. Much of the data collection was done so prospectively, such as the post-procedure follow up call. Even with rigorous data collection, there was some missing data as well such as the 1 patient lost to follow up and some of the missing INR data. This study would have added more strength if all data was collected prospectively. Additionally the overall 'n' of patients maintaining AC or AC/AP combination therapy for a IL-CESI or IL-ESI is low and as such the upper limit of the incidence of EH in this study is still 9.7% and 23.2% respectively. As such, this study in and of itself in no way confers safety to performing ILESI whilst patients are therapeutically anticoagulated. Moreover, this study also does not evaluate the incidence of thrombotic complications in this patient cohort, so the relative risk of ceasing versus maintaining medications cannot be ascertained by this study. Alas, given the overall low incidence of clinically relevant EH a much larger study of patients ceasing or maintaining medications which evaluates both the incidence of EH and thrombotic complications is needed, which these authors are in the process of completing. In the interim, however, being able to quantify the risk of EH following IL-CESI or IL-TESI in patients on ACAP medications can be used to guide further research and incorporated into current interpretation of the literature to add clarity to a topic that has life and death consequences and yet has sparse data.

6. Conclusion

This data gives critical insight into the clinically relevant EH risk for patients continuing or stopping their ACAP medications after receiving an IL-CTESI. The results from this study suggest re-evaluating the potential EH risks associated with continuing vs ceasing these medications. Although further research is needed in order to change guidelines, every patient has their own unique set of risk factors and this data gives evidence to support a more individualized approach to patient care in the context of IL-CTESI. Further investigation comparing the ischemic events associated with ACAP medication cessation also needs to be performed.

Declaration of competing interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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