The Safety of Anticoagulation Continuation in Electroconvulsive Therapy– A Systematic Review and Proportional Meta-Analysis

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Abstract

Background: Physiologic changes during electroconvulsive therapy (ECT) raise concern for intracranial bleeding, particularly in patients on anticoagulation. We conducted a systematic review and proportional meta-analysis on bleeding and thromboembolic outcomes in this patient population.

Methods: Ovid MEDLINE, Embase, Cochrane Library, and APA PsycInfo were searched to identify relevant studies. A proportional meta-analysis was conducted on the incidence of intracerebral hemorrhage (ICH), thromboembolic events, and bleeding.

Results: Nine studies were included: one retrospective cohort study and eight case series. 772 ECT sessions were reported. No ICH event was reported. The pooled incidence was 0.21% (95% CI 0.01-0.66), 0.83% (95% CI 0.32-1.59), and 1.44% (95% CI 0.33-3.20) for ICH, bleeding, and thromboembolic events respectively.

Conclusion: Although the evidence regarding the safety of continuing anticoagulation during ECTs is of low quality, primarily from case series, the pooled ICH incidence of less than 1% (0.21%) is a valuable reference for informed healthcare decisions.

Résumé

Contexte: Les changements physiologiques survenant au cours de l’électrochoc soulèvent des inquiétudes quant aux hémorragies intracrâniennes, en particulier chez les patients recevant une anticoagulothérapie. Nous avons réalisé une revue systématique et une méta-analyse proportionnelle sur les conséquences hémorragiques et thromboemboliques chez cette population de patients.

Méthodologie: Une recherche a été effectuée dans les bases de données Ovid MEDLINE, Embase, Cochrane Library et APA PsycInfo pour relever les études pertinentes. La méta-analyse proportionnelle a été réalisée sur la fréquence des hémorragies cérébrales, des événements thromboemboliques et des saignements.

Résultats: Neuf études ont été retenues, soit une étude de cohorte rétrospective et huit séries de cas. On rapporte 772 séances d’électrochoc. Aucune hémorragie cérébrale n’est signalée. La fréquence regroupée est...
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Introduction

Electroconvulsive therapy (ECT) is widely used for the treatment of severe depression, bipolar disorder, psychotic disorders, catatonia, and neuroleptic malignant syndrome. Research has shown that ECT is effective in achieving remission in 50% to 60% of patients with depression, as opposed to 10% to 40% remission rates with pharmacotherapy or psychotherapy. A typical ECT course consists of six to twelve treatments administered twice to thrice a week.

During ECT, a small electric current is delivered to induce generalized tonic–clonic seizure under general anesthesia following the administration of a fast-acting anesthetic agent and a muscle relaxant agent. In the clonic phase of seizure activity, there is a transient increase in blood pressure, heart rate, and doubling of cerebral blood flow due to a catecholamine surge. These physiologic changes cause concern for intracranial bleeding, particularly in patients on anticoagulation therapy. In patients with generalized tonic–clonic seizures outside of the ECT context, clinical manifestations, electroencephalographic, and neuroimaging findings of ictal and postictal states show similarities with ECT-induced seizures. Yet, only a few case reports documented seizure development before intracerebral hemorrhage (ICH). Data on blood pressure changes are scarce in this population because seizure-related movements prevent reliable blood pressure monitoring throughout the tonic–clonic phase; in one study, ictal hypertension was observed in 15 out of 57 (26.3%) seizures. Among patients undergoing ECT, the management of anticoagulation therapy has not been extensively studied, with the most relevant literature being case reports and case series. In patients requiring ECT taking vitamin K antagonists (VKA), heparin and its derivatives, or direct oral anticoagulants (DOACs), the safety of continuation of anticoagulation has not been systematically evaluated. We reviewed the available literature on the reported bleeding and thromboembolic outcomes in patients undergoing ECT based on their anticoagulation status.

Methods

This systematic review was performed by the Cochrane Handbook for Systematic Reviews of Interventions and reported following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement for interventions.

Study Eligibility

Studies were included if the following criteria were met: original article, had patients undergoing ECT with indications for therapeutic anticoagulation, reported more than one subject, and reported the number of bleeding and thromboembolic events. Studies of patients less than 18 years of age and studies where all patients had discontinued anticoagulation before ECT were excluded. There were no restrictions on language or date of publication. We included articles published as full manuscripts or conference abstracts. When the study methods were unclear, we attempted to contact the authors for clarification.

Literature Search

We worked with a librarian to develop a search strategy using comprehensive terms relevant to anticoagulation and electroconvulsive therapy, outlined in Appendix A. We searched Ovid MEDLINE (1946 to March 30, 2022), Embase (1947 to March 30, 2022), Cochrane Library, and APA PsycInfo (1806 to week four of March 2022) for relevant articles.

Study Selection

Our search output was imported to Rayyan.ai. Two independent reviewers (L.D. and D.D.) screened titles and abstracts...
in duplicate to screen for possible eligibility. The citations selected during the screening process then underwent full-text review in duplicate by the two independent reviewers to determine eligibility for our systematic review. Any disagreement during both abstract screening and full-text review was resolved by consensus.

**Data Collection and Quality Assessment**

Two independent reviewers (L.D. and D.D.) undertook data extraction and assessed the quality of the included studies; any disagreement was resolved by consensus. We recorded bleeding and thromboembolic events. Quality assessment was performed using the validated Newcastle-Ottawa Scale (NOS) for cohort studies. NOS is a nine-star scale developed to assess the quality of nonrandomized studies based on the selection of participants, comparability, and outcome ascertainment. The NOS assigns a maximum of four stars for selecting participants, two stars for comparability, and three stars for outcome ascertainment. Nine stars on the NOS would reflect the highest study quality. Case series were evaluated by the same tool, understanding that a lower score is expected because of the study design. Follow-up duration was considered adequate if the patients were followed until 48 hours after an ECT session or the end of an ECT treatment course.

**Study Outcomes**

The primary outcome was the incidence of ICH during an ECT treatment course. Secondary outcomes included any other bleeding events and thromboembolic events. Bleeding events refer to any reported symptomatic ICH confirmed on imaging and further directly or endoscopically observed bleeding, such as epistaxis and gastrointestinal bleeding. Thromboembolic events include any reported pulmonary embolism (PE), deep vein thrombosis (DVT), other venous thromboembolism (VTE), and arterial thrombosis. Efforts were made to contact the authors when study outcomes were unclear.

**Statistical Analysis**

Without randomized control trials (RCTs) investigating bleeding and thromboembolic outcomes in anticoagulated patients undergoing ECT, we conducted a proportional meta-analysis to assess the incidence of these specific outcomes. We pooled the effect sizes from all included studies to obtain a more robust estimate of the incidence of bleeding and thromboembolic events. We performed statistical analyses using MedCalc® Statistical Software version 22.009 (MedCalc Software Ltd, Ostend, Belgium; https://www.medcalc.org; 2023). We used random effects models to pool the study results for each outcome. We calculated a proportion (%) with a 95% confidence interval (CI) for the estimated value of the combined effect size. We quantified the degree of heterogeneity using the I² index. We viewed any I² ≥ 30% as representing meaningful heterogeneity.

**Results**

The literature search identified a total of 808 citations (Figure 1). After all titles and abstracts were screened, the full texts of 30 citations were further assessed to determine eligibility. Based on the eligibility criteria, nine published studies were included in our review. The characteristics of the nine included studies are described in Table 1. Manuscripts were published between 1989 and 2021, with 95 patients and 772 ECT sessions. Of the nine included studies, eight were case series, and one was a retrospective cohort study. Most were considered similar in terms of patient population. The mean age was 69.6; 64% of patients were female. The most common indications for anticoagulation were DVT and PE (n=47), followed by atrial arrhythmia (n=45). One study included eight patients in duplicate to screen for possible eligibility. The citations selected during the screening process then underwent full-text review in duplicate by the two independent reviewers to determine eligibility for our systematic review. Any disagreement during both abstract screening and full-text review was resolved by consensus.

**Characteristics of Included Studies**

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Table 1. Study Characteristics.

<table>
<thead>
<tr>
<th>Study</th>
<th>Study Design</th>
<th>Year of publication</th>
<th>Number of Patients</th>
<th>Mean age</th>
<th>Number of Female Patients</th>
<th>Choice of AC</th>
<th>Indication of AC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td></td>
<td></td>
<td>95</td>
<td>69.6</td>
<td>64 (67%)</td>
<td>Warfarin (n=66, 69%) DOAC (n=22, 23%) Heparin (n=3, 3%) ≥ 1 agent (n=2, 2%) None (n=2, 2%)</td>
<td>VTE (n=47, 49%) Afib/A flutter (n=44, 46%) Others (n=13, 14%)*</td>
</tr>
<tr>
<td>Centanni et al., 2021</td>
<td>Retrospective cohort study</td>
<td>2021</td>
<td>32</td>
<td>71.5</td>
<td>19</td>
<td>Warfarin (n=23) Rivaroxaban (n=5) Apixaban (n=4)</td>
<td>Afib (n=18, 56%) VTE (n=14, 44%)</td>
</tr>
<tr>
<td>Hirata et al., 2019</td>
<td>Case series</td>
<td>2019</td>
<td>8</td>
<td>60.9</td>
<td>6</td>
<td>Edoxaban (n= 3) Edoxaban or Heparin (n=1) Rivaroxaban (n=2) Apixaban (n=2)</td>
<td>VTE (n=8, 100%)</td>
</tr>
<tr>
<td>Hirata et al., 2020</td>
<td>Case series</td>
<td>2020</td>
<td>2</td>
<td>NR, aged 66-78</td>
<td>2</td>
<td>Edoxaban (n=2)</td>
<td>VTE (n=2, 100%)</td>
</tr>
<tr>
<td>Inagawa et al., 2018</td>
<td>Case series</td>
<td>2018</td>
<td>5</td>
<td>55.2</td>
<td>5</td>
<td>Rivaroxaban (n=2) Heparin or Warfarin (n=1)</td>
<td>VTE (n=5, 100%)</td>
</tr>
<tr>
<td>Mehta et al., 2004</td>
<td>Case series</td>
<td>2004</td>
<td>35</td>
<td>71.0</td>
<td>25</td>
<td>Warfarin</td>
<td>Afib (n=17, 49%) VTE (n=15, 43%) CHF (n=8, 23%) Mechanical valve (n=4, 11%)*</td>
</tr>
<tr>
<td>Petrides and Fink, 1996</td>
<td>Case series</td>
<td>1996</td>
<td>6</td>
<td>73.7</td>
<td>4</td>
<td>Warfarin (n=4) None (n=2)</td>
<td>Afib (n=4, 67%) A flutter (n=1, 17%) Mechanical valve (n=1, 17%)</td>
</tr>
<tr>
<td>Schmidt et al., 2014</td>
<td>Case series</td>
<td>2014</td>
<td>2</td>
<td>79.0</td>
<td>0</td>
<td>Dabigatran</td>
<td>Afib (n=2, 100%)</td>
</tr>
<tr>
<td>Suzuki et al., 2008</td>
<td>Case series</td>
<td>2008</td>
<td>2</td>
<td>63.0</td>
<td>2</td>
<td>Warfarin (n=1) Heparin (n=1)</td>
<td>VTE (n=2, 100%)</td>
</tr>
<tr>
<td>Tancer and Evans, 1989</td>
<td>Case series</td>
<td>1989</td>
<td>3</td>
<td>69.0</td>
<td>1</td>
<td>Warfarin</td>
<td>Afib (n=2, 67%) VTE (n=1, 33%)</td>
</tr>
</tbody>
</table>

AC: anticoagulation. NR: not reported. Afib: atrial fibrillation. A flutter: atrial flutter. VTE: venous thromboembolism such as DVT and PE.

*: the Mehta et al. study did not specify how many patients had overlapping indications.

in whom the indication for anticoagulation was congestive heart failure and four patients in whom the indication was mechanical heart valve. Still, it did not specify whether there were overlapping indications. Another study only included patients with known cerebral aneurysms. Six studies included patients on warfarin or heparin requiring therapeutic level monitoring. Overall, 66 patients were on warfarin, 22 on DOACs, three on heparin, one on heparin or edoxaban depending on the patient's ability to take oral medications, one on heparin and warfarin without further details on timing, and 2 were not anticoagulated in the setting of atrial fibrillation.

Quality Assessment

The one retrospective cohort study compared patients on DOACs with those on warfarin and was thus considered to lack a control group for this review. The case series also lacked control groups. The quality rating is summarized in Table 2. Seven studies were assigned five stars on the NOS scale, losing points: having a representative control group, demonstrating the absence of outcome at the start of the study, and controlling for confounding factors. Two studies were assigned four stars on the NOS scale, losing additional points on having a representative study population and follow-up adequacy.
Table 2. Study Quality Assessment using the Newcastle-Ottawa Scale (NOS).

<table>
<thead>
<tr>
<th>Study</th>
<th>Study Design</th>
<th>Selection</th>
<th>Comparability</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Cohort Represent-</td>
<td>Control Represent-</td>
<td>Exposure Ascertainment</td>
</tr>
<tr>
<td>Centanni et al., 2021</td>
<td>Retrospective cohort study</td>
<td>*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hirata et al., 2019</td>
<td>Case series</td>
<td>*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hirata et al., 2020</td>
<td>Case series</td>
<td>*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inagawa et al., 2018</td>
<td>Case series</td>
<td>*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mehta et al., 2004</td>
<td>Case series</td>
<td>*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Petrides and Fink, 1996</td>
<td>Case series</td>
<td>*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Schmidt et al., 2014</td>
<td>Case series</td>
<td>*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Suzuki et al., 2008</td>
<td>Case series</td>
<td>*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tancer and Evans, 1989</td>
<td>Case series</td>
<td>*</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

NOS is a nine-star scale developed to assess the quality of nonrandomized studies based on the selection of participants, comparability, and outcome ascertainment. A maximum of four stars are assigned for the selection of participants, two stars for comparability, and three stars for outcome ascertainment.

Primary Outcome
A total of 772 ECT treatments were reported, of which 725 (94%) were conducted while patients were on anticoagulation, and the remainder were conducted off anticoagulation. No ICH events were reported (Table 3). The pooled estimated risk of ICH in 772 ECT treatments, CI 0.01 (95% CI 0.01 to 0.66, $I^2 = 0\%$) (Figure 2).

Secondary Outcomes
There was a total of four bleeding events in patients taking anticoagulation throughout ECTs (Table 3). The pooled estimated risk of bleeding in 772 ECT treatments was 0.83% (95% CI 0.32 to 1.59, $I^2 = 0\%$) (Appendix B). Centanni et al. described a patient on rivaroxaban and venlafaxine who experienced gastrointestinal bleeding, as well as another patient on warfarin and fluoxetine developing hemoptysis secondary to epistaxis with an international normalized ratio (INR) of 1.9. Mehta et al. reported 35 patients undergoing ECT on warfarin. One patient experienced lower gastrointestinal bleeding from angiodysplasia, but after cauterization of the culprit lesion, warfarin was resumed, and ECT took place without further bleeding events. Another patient in the same study experienced self-limited subconjunctival hemorrhage. The exact INR at the bleeding time in these two patients was not reported. The overall INR in all patients ranged from 0.9 to 4.9 (mean 2.3 ± 0.7), subtherapeutic (less than 2.0 defined by the study) in 36% patients, therapeutic (2.0-3.5 defined by the study) in 61% of patients, and supratherapeutic (greater than 3.5 defined by the study) in 3% patients.
A total of seven thromboembolic events were reported. The pooled estimated risk of thromboembolic events in 772 ECT treatments was 1.44% (95% CI 0.33 to 3.20, I² = 51.52%) (Appendix C). One in a sub-therapeutically anticoagulated patient, five *de novo* thromboembolic events in patients without pre-existing indication for anticoagulation, and one in a patient whose anticoagulation therapy was held before an ECT session (Table 3). A patient on warfarin in the case series by Mehta et al. developed a popliteal artery thrombosis in the context of consistently subtherapeutic INR (less than 2.0 defined by the study).19 Hirata et al. reported in their case series three patients without prior indications for anticoagulation developing DVT and PE during the ECT course, who were subsequently started on DOACs.16 Similarly, Suzuki et al. reported a patient diagnosed with PE after the third ECT treatment necessitating anticoagulation; ECT was resumed five days after anticoagulation initiation.22 Inagawa et al. reported one patient with two thromboembolic events: the patient developed a proximal DVT after the first ECT treatment, for which she was started on intravenous heparin; the heparin was held for six hours before the second ECT.

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**Table 3. Study Outcomes.**

<table>
<thead>
<tr>
<th>Study</th>
<th>Total Number of ECT Sessions</th>
<th>Number of Sessions on AC</th>
<th>Number of Sessions off AC</th>
<th>Number of Bleeding Events</th>
<th>Type of Bleeding</th>
<th>Type of Thromboembolic Events</th>
<th>Type of Thromboembolism</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>772</td>
<td>725 (93.9%)</td>
<td>47 (6.1%)</td>
<td>4</td>
<td></td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>Centanni et al., 2021</td>
<td>247 (32.0%)</td>
<td>247 (32.0%)</td>
<td>0</td>
<td>2 (50%)</td>
<td>- GI bleed</td>
<td>- PE, DVT (n=1)</td>
<td></td>
</tr>
<tr>
<td>Hirata et al., 2019</td>
<td>92 (11.9%)</td>
<td>68 (8.8%)</td>
<td>24 (3.1%)</td>
<td>0</td>
<td>- Epistaxis</td>
<td>- DVT (n=2)</td>
<td></td>
</tr>
<tr>
<td>Hirata et al., 2020</td>
<td>14 (1.8%)</td>
<td>10 (1.3%)</td>
<td>4 (0.5%)</td>
<td>0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inagawa et al., 2018</td>
<td>14 (1.8%)</td>
<td>12 (1.6%)</td>
<td>2 (0.3%)</td>
<td>0</td>
<td></td>
<td>2 (28.6%)</td>
<td>DVT after 1st session, then PE after 2nd session</td>
</tr>
<tr>
<td>Mehta et al., 2004</td>
<td>284 (36.8%)</td>
<td>284 (36.8%)</td>
<td>0</td>
<td>2 (50%)</td>
<td>- Lower GI bleed due to angiodyplasia</td>
<td>1 (14.3%)</td>
<td>Popliteal artery thrombosis</td>
</tr>
<tr>
<td>Petrides and Fink, 1996</td>
<td>46 (6.0%)</td>
<td>32 (4.1%)</td>
<td>14 (1.8%)</td>
<td>0</td>
<td></td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Schmidt et al., 2014</td>
<td>16 (2.1%)</td>
<td>16 (2.1%)</td>
<td>0</td>
<td>0</td>
<td></td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Suzuki et al., 2008</td>
<td>32 (4.1%)</td>
<td>29 (3.8%)</td>
<td>3 (0.4%)</td>
<td>0</td>
<td></td>
<td>1 (14.3%)</td>
<td>PE (suspected)</td>
</tr>
<tr>
<td>Tancer and Evans, 1989</td>
<td>27 (3.5%)</td>
<td>27 (3.5%)</td>
<td>0</td>
<td>0</td>
<td></td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>


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**Figure 2. Proportional meta-analysis of the risk of ICH.**

No ICH was observed in any of the studies. The pooled estimate of ICH in 772 ECT treatments was 0.21%, and 95% CI with the random effects model was 0.01 to 0.66.
session to prevent brain hemorrhage, and the patient was subsequently found to have a pulmonary embolism, resulting in termination of the ECT course. Further details relevant to outcomes are reported in Appendix D.

Discussion

In this first study reviewing bleeding and thromboembolic outcomes among patients undergoing ECT with an indication for anticoagulation, it is noteworthy that most (94%) of the ECT treatments in the nine studies included were conducted while patients remained on therapeutic anticoagulation. No ICH events and very few bleeding events were reported. On the other hand, there was a more significant number of thromboembolic events, though most occurred during the ECT course in patients without prior indications for anticoagulation.

Our Study of Other Studies

The theoretical risk of ICH in patients taking anticoagulation is based on the brief increase in blood pressure due to ECT. Our results are in keeping with data presented by Mehta et al., where the authors detected no ICH in their case series of 284 ECT treatments on warfarin despite having observed a significant increase in peak systolic and diastolic blood pressures during ECT by 26 mmHg (95% CI 21.2-30.7 mmHg) and 19.4 mmHg (95% CI 6.6-32.3 mmHg) respectively. We included studies where patients were on other forms of anticoagulation, such as DOACs, and found similar results. Compared to other reviews on the same topic, we searched for relevant studies on more databases and included more studies in this review. To our knowledge, this is the first systematic review to employ a proportional meta-analysis to determine the effect size of bleeding and thromboembolic events in anticoagulated ECT patients.

Interpretation

ECTs have been described as the most efficacious treatment modality in psychiatry. ECTs are superior to pharmacotherapy for the treatment and management of major unipolar depression. Using ECTs has demonstrated its high efficacy by decreasing readmission rates, hospitalizations, length of stay, and the overall depression burden. Despite robust evidence supporting the efficacy of ECT, its uptake remains limited by safety concerns such as memory loss, ICH, and death.

In a series of 20,000 ECT treatments published in 1964, one case of ICH in a severely catatonic patient was described, making ICH an exceedingly rare complication expected to occur in 0.005% of patients. In 1991, Weisberg et al. reported a case of intraparenchymal hemorrhage following ECT that was attributable to cerebral amyloid angiopathy. In 2017, a fatal case of intraparenchymal hemorrhage with intraventricular extension following ECT was described by Carlson et al.; the patient sustained a tonic-clonic seizure for 10 minutes, and no structural vascular cause was identified on imaging. These numbers support that ECT is largely safe and that ICH is an uncommon adverse event. Physicians can take several precautions to minimize the risk of ICH unrelated to anticoagulation status in patients undergoing ECT: first, screening and management of pre-existing medical conditions that may increase intracranial pressure such as systemic hypertension; second, administering appropriate anesthetic agents and muscle relaxant agents; third, using appropriate electrode-placement and stimulus-dosing; and fourth, pre- and post-ECT monitoring of vital signs. Careful evaluation of the patient’s risk profile for thromboembolism and bleeding should guide anticoagulation management and other prophylactic measures during hospitalization and ECT course.

On the other hand, hospitalized patients undergoing ECTs are at increased risk of thromboembolic events for a variety of reasons, such as physical restraints, immobilization, and catatonia. DVT incidence can be as high as 25.3% in patients with catatonia. A recent systematic review and meta-analysis of pooled observational evidence suggested that both depression and the use of antidepressants are associated with an increased risk of VTE. Pooled analyses demonstrated that the relative risk (RR) for VTE was 1.31 (95% CI, 1.13-1.53) in patients with depression versus those without depression, and the RR for VTE comparing antidepressant use with no antidepressant use was 1.27 (95% CI, 1.06-1.51). Additionally, both first- and second-generation antipsychotic medications have been linked with an increased risk of VTE. The American Psychiatric Association (APA) recommends that hospitalized patients suffering from major depressive disorder with catatonic features should be evaluated for VTE risk and considered for prophylaxis. In the context of ECT, there have been case reports of PE development following ECT, a plausible mechanism being that the muscle contractions during a generalized seizure could dislodge a peripheral thrombus despite the use of muscle relaxant agents.

In the studies reviewed in this article, it was found that five out of the seven cases of thromboembolism during the ECT course occurred in patients who did not have a prior indication for anticoagulation.
anticoagulation management before ECT was not a factor in VTE development in those cases. However, the remaining two cases occurred in patients who had insufficient anticoagulation in the context of a persistent indication for therapeutic anticoagulation at the time of ECT: one in a patient who was sub-therapeutically anticoagulated and one in a patient whose anticoagulation therapy was held. These results highlight the importance of appropriate anticoagulation management among patients with a persistent indication for therapeutic anticoagulation during their ECT and their susceptibility to adverse outcomes. However, given the high heterogeneity observed, caution must be exercised in drawing definitive conclusions based on these findings.

Weaknesses

This study has several limitations. First, the quality of evidence is poorly measured by the NOS as eight of nine included studies were case series; the remaining one retrospective cohort study compared patients on DOACs with those on warfarin; thus, its data was treated as case series for this review. The case series design reports data from a subject group without including a control population. The absence of a control group increases the risk of selection bias and limits the generalizability of results to a larger population. Furthermore, the absence of comparative studies prevented us from definitively addressing whether there is an increased risk of ICH associated with the non-interruption of anticoagulant therapy during ECT. Similarly, for thromboembolic events, our data primarily stemmed from case series of patients not on anticoagulants who were subsequently diagnosed with thromboembolic events following ECT. Consequently, our study could not provide robust recommendations for the risk-benefit assessment of interrupting anticoagulant therapy versus non-interruption in this context.

Second, reporting bias is a significant concern in case series studies. The observed heterogeneity in reporting styles and the absence of data on certain risk factors in the studies we included may have contributed to the underreporting of ICH and thromboembolic events.

Third, the sample size of 95 patients undergoing 772 ECTs was too small to detect a significant difference in outcome measures. It’s worth noting that the annual risk of ICH in patients taking direct oral anticoagulants DOACs is approximately 0.15%, whereas for those on VKAs, it stands at about 0.45%; to effectively detect a two-fold increase in ICH risk among anticoagulated patients undergoing ECT, we would need to include a much larger participant pool, including up to 31 000 patients.

Conclusions

In conclusion, the available evidence to determine the safety of continuing anticoagulation during ECTs is of low quality and derived primarily from case series. Nevertheless, the pooled incidence of ICH was demonstrated to be low, suggesting that among patients with an indication for therapeutic anticoagulation, anticoagulants may be continued throughout the ECT treatment course. Further prospective studies are required to answer this important question more definitively.

Acknowledgment

We thank Ms. Andrea Quaiattini, librarian at McGill University, for her generous help with the literature search process.

References


Appendix

A. Search Terms
B. Proportional meta-analysis of the risk of bleeding

Four bleeding events were reported. The pooled estimated risk of bleeding in 772 ECT treatments was 0.83%, and 95% CI with the random effects model was 0.32 to 1.59.

C. Proportional meta-analysis of the risk of thromboembolic events

Seven thromboembolic events were reported. The pooled estimated risk of thromboembolic events in 772 ECT treatments was 1.44%, 95% CI with the random effects model was 0.33 to 3.20.
<table>
<thead>
<tr>
<th>Study</th>
<th>Total ECT Sessions</th>
<th>Number of ECT Sessions</th>
<th>On AC</th>
<th>Off AC</th>
<th>Follow-up Period (hrs)</th>
<th>Antiplatelet Agents</th>
<th>Concurrent Antidepressant or Antipsychotic Use</th>
<th>Use of Physical Restraint</th>
<th>Type of Thromboembolic Events</th>
<th>Bleeding Events on AC</th>
<th>Bleeding Events off AC</th>
<th>Type of Bleeding</th>
<th>Blood Pressure升降</th>
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<td>Centanni et al., 2021</td>
<td>247</td>
<td>68</td>
<td>24</td>
<td>NR</td>
<td>48-120</td>
<td>ASA (n=5)</td>
<td>Low-dose ASA, NSAIDs within two days of ECT in 19247 sessions</td>
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<td>Pre-ECT: 1/2</td>
<td>1/1</td>
<td>1/1</td>
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<td>4</td>
<td>NR</td>
<td>5</td>
<td>NSAIDs (n=2)</td>
<td>NR</td>
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<td>0/0</td>
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ECT: Electroconvulsive therapy; AC: anticoagulation; NR: not reported; ASA: aspirin; NSAIDs: non-steroidal anti-inflammatory drugs; SBP: Systolic blood pressure.