

Acupuncture Safety in Patients Receiving Anticoagulants: A Systematic Review

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Perm J 2015 Winter;19(1):November 3, 2014

<http://dx.doi.org/10.7812/TPP/14-057>

Abstract

Introduction: Theoretically, acupuncture in anticoagulated patients could increase bleeding risk. However, precise estimates of bleeding complication rates from acupuncture in anticoagulated patients have not been systematically examined.

Objective: To critically evaluate evidence for safety of acupuncture in anticoagulated patients.

Methods: We searched PubMed, EMBASE the Physiotherapy Evidence Database, and Google Scholar.

Results: Of 39 potentially relevant citations, 11 met inclusion criteria: 2 randomized trials, 4 case series, and 5 case reports. Seven provided reporting quality sufficient to assess acupuncture safety in 384 anticoagulated patients (3974 treatments). Minor-moderate bleeding related to acupuncture in an anticoagulated patient occurred in one case: a large hip hematoma, managed with vitamin K reversal and warfarin discontinuation following re-evaluation of its medical justification. Blood-spot bleeding, typical for any needling/injection and controlled with pressure/cotton, occurred in 51 (14.6%) of 350 treatments among a case series of 229 patients. Bleeding deemed unrelated to acupuncture during anticoagulation, and more likely resulting from inappropriately deep needling damaging tissue or to complex anticoagulation regimens, occurred in 5 patients. No bleeding was reported in 2 studies (74 anticoagulated patients): 1 case report and 1 randomized trial prospectively monitoring acupuncture-associated bleeding as an explicit end point. Altogether, 1 moderate bleeding event occurred in 3974 treatments (0.003%).

Conclusion: Acupuncture appears to be safe in anticoagulated patients, assuming appropriate needling location and depth. The observed 0.003% complication rate is lower than the previously reported 12.3% following hip/knee replacement in a randomized trial of 27,360 anticoagulated patients, and 6% following acupuncture in a prospective study of 229,230 all-type patients. Prospective trials would help confirm our findings.

Introduction

Acupuncture is a healing method intended to regulate physiologic and neurologic functioning, with the earliest archeologic evidence for acupuncture tools dating to Neolithic times, and the earliest textual evidence of acupuncture written in the Shang Dynasty (1766 BC to c1046 BC).¹ Acupuncture needle stimulation achieves its therapeutic benefits through up-regulation of processes in the cortical network and down-regulation in the limbic-paralimbic neocortical

network. Its effect on pain is a combination of simultaneous changes in sensory, cognitive, and affective pathways.²

Acupuncture is efficacious in patients with conditions for whom anticoagulant medications are often prescribed: those with cancer,³⁻⁶ atrial fibrillation,⁷⁻⁹ acute ischemic stroke,¹⁰ postischemic stroke,¹¹ postoperative pain,¹² renal disease,¹³ and critically ill intensive care patients¹⁴ or those receiving mechanical ventilation.¹⁵ Acupuncture needles used in practice range from 0.12 mm (Japanese gauge 00)

to 0.35 mm (Chinese gauge 28); however, in our data searches we identified no reports examining any effect of needle gauge on acupuncture treatment safety.

Anticoagulants are widely used in the hospital and community care settings to prevent coagulopathies and embolic phenomena, with demonstrated safety. Meta-analysis of randomized trials comparing anticoagulant prophylaxis with no treatment in 19,958 hospitalized (not perioperative) patients showed a nonsignificant increase in major bleeding.¹⁶ Older but commonly used anticoagulants include clopidogrel for recent stroke or cardiac stents; warfarin for prevention of thromboembolism in patients with atrial fibrillation¹⁷ or with history of deep-vein thrombosis or pulmonary embolism¹⁸; and low-molecular-weight heparin, unfractionated heparin, or vitamin K antagonists for prevention of thromboembolism in long-term inpatients¹⁹ and those with cirrhosis²⁰ or cancer.^{21,22} Newer drugs include the Factor X inhibitors (fondaparinux, rivaroxaban, and apixaban) for atrial fibrillation and prevention of surgery-associated coagulopathy^{23,24} and direct thrombin inhibitors (hirudin and its derivatives, argatroban, elagatran, abigatran) for atrial fibrillation and venous thromboembolism.²⁵

To place our review in a broader context of patients receiving low-molecular weight heparin or vitamin K antagonists, the safety of surgical procedures far more invasive than acupuncture has been closely examined. A Cochrane meta-analysis of 27,360 anticoagulated patients found 123 bleeding events per 1000 patients (12.3%) occurring in the

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4 to 6 weeks following total hip or knee replacement.²⁶

The risk of procedure-related bleeding in anticoagulated patients receiving acupuncture may be lower, but the question has not yet been definitively investigated. We therefore conducted this meta-analysis to review all identifiable peer-reviewed medical publications and critically examine the safety of acupuncture in patients receiving anticoagulant therapy.

Materials and Methods

We searched PubMed, EMBASE, the Physiotherapy Evidence Database, and Google Scholar to identify potentially relevant citations. Search terms for our PubMed and EMBASE searches are listed in the Sidebars: PubMed Search Terms and EMBASE Search Terms.

We searched other databases with comparable terms. Two reviewers screened all citations and conferred with a third when disagreements arose in deciding on inclusion or exclusion of citations. Exclusion criteria were as follows: no discussion of both anticoagulants AND acupuncture, no quantifiable data, anticoagulant use not confirmed, and adverse events not reported.

We ordered 39 articles that were potentially relevant and, upon review of the full-text copies and exclusions (Figure 1), identified 11 that met inclusion criteria: reporting on the combination of acupuncture and 1 or more anticoagulants. After data extraction, we conferred to assess these 11 articles and, combining clinical judgment with literature assessment criteria, graded them by quality of reporting and apparent likelihood of a causal relationship between anticoagulant exposure and acupuncture-associated bleeding. To facilitate clear risk stratification, these articles were grouped into likelihood of certainty that the outcome (bleeding event) was attributable to the co-exposure (acupuncture, in patients receiving anticoagulants). We assessed that likelihood of certainty on the basis of the elapsed time between anticoagulant dosing and acupuncture as well as on the quality and thoroughness of documentation of each therapy in the published manuscripts. Data from the

full-text articles were then extracted into table format (Table 1).²⁷⁻³⁸

Results

Systematic Search

Our systematic search yielded 11 relevant citations (Figure 1): 2 randomized trials,^{29,33} 3 retrospective case series,^{28,34,36} 5 case reports,^{27,31,32,37,38} and 1 practice description.³⁵ Because we did not find multiple studies with control patients or before-after comparisons, quantitative meta-analysis was not performed, and we report the results as a systematic review (Table 1).

Articles with Quality of Reporting Allowing Assessment of Safety of Acupuncture in Anticoagulated Patients

We sought clear documentation of time between anticoagulation and acupuncture therapy as well as an adequate description of adverse events observed. We found seven publications with quality

PubMed Search Terms

("anticoagulant"[MeSH Terms] OR "anticoagulant"[All Fields] OR "anticoagulants"[MeSH Terms] OR "anticoagulants"[All Fields] OR "anticoagulants"[Pharmacological Action]) OR ("warfarin"[MeSH Terms] OR "warfarin"[All Fields]) OR ("heparin"[MeSH Terms] OR "heparin"[All Fields]) OR ("clopidogrel"[Supplementary Concept] OR "clopidogrel"[All Fields]) OR ("enoxaparin"[MeSH Terms] OR "enoxaparin"[All Fields]) OR ("aspirin, dipyridamole drug combination"[Supplementary Concept] OR "aspirin, dipyridamole drug combination"[All Fields] OR "aggrenox"[All Fields]) AND ("acupuncture"[MeSH Terms] OR "acupuncture"[All Fields] OR "acupuncture therapy"[MeSH Terms] OR "acupuncture therapy"[All Fields]) OR "acupuncture therapy"[All Fields])

EMBASE Search Terms

([anticoagulant OR anticoagulants OR warfarin OR coumadin OR heparin OR clopidogrel OR enoxaparin OR aggrenox] AND acupuncture)

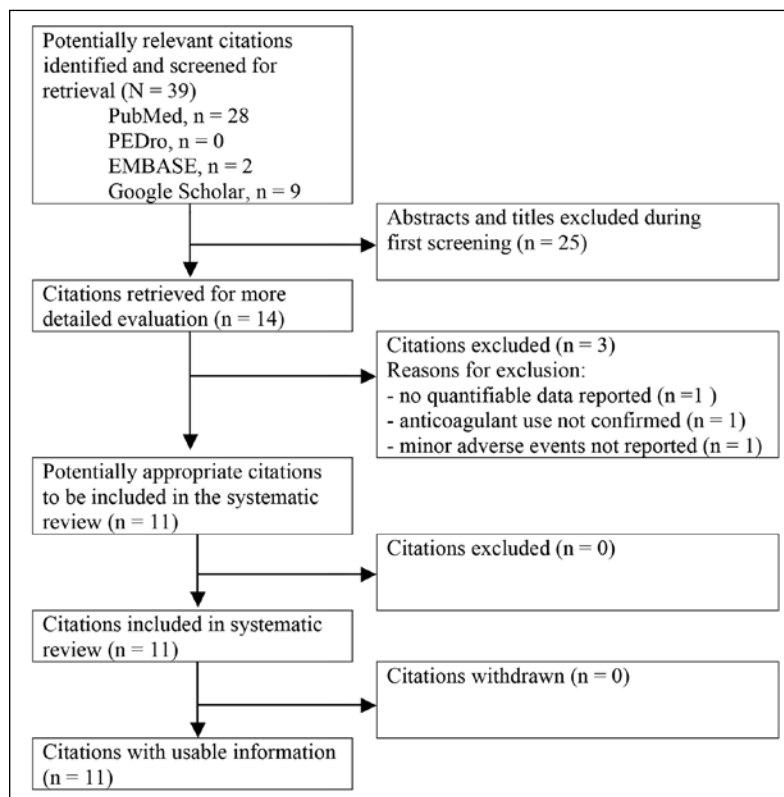


Figure 1. QUOROM Statement flow diagram. Safety of acupuncture in patients receiving anticoagulants: a systematic review.

PEDro = Physiotherapy Evidence Database.

Table 1. Published data on acupuncture complications in patients receiving anticoagulant medication therapy

Author, year	Sample size	Study type	Patients	Anticoagulants specified	Acupuncture method	Complication	Complication management	Time between anticoagulant and acupuncture	Notes
Quality of reporting sufficient to allow assessment of acupuncture safety in anticoagulated patients									
Minor-moderate bleeding related to acupuncture in an anticoagulated patient									
Kenz, ²⁷ 2012	N = 1	Case report	82-year-old woman	Warfarin	Not specified	Hematoma, right buttock/upper thigh	Warfarin stopped, oral vitamin K given	Concurrent	Attribution of bleeding to acupuncture is reasonable
Minor blood-spot bleeding typical for any needling procedure and not normally considered a problem in medical practice									
Miller, ²⁸ 2012	N = 229 (350 tx)	Retrospective case series	106 men 123 women age 29-95 years	Warfarin	Not specified	Drop of blood after needle withdrawal in 14.6% (n = 51)	Pressure with cotton-tipped swab (for n = 50); not specified for the remaining patient	Concurrent	Cases directly observed. No difference in bleeding between high INR vs low (14.3% vs 14.6%)
Bleeding unlikely related to acupuncture and more likely the result of multi-agent fibrinolytics									
Li, ²⁹ 2003	N = 80	RCT	Age 42-74 years, gender unspecified	Dextran/aspirin in all, randomized to: scalp acupuncture urokinase saline placebo	Scalp, and GB20	Intracranial hemorrhage: 1 case in dextran/aspirin + scalp acupuncture group, 2 cases in dextran/aspirin + urokinase group, and 1 case in dextran/aspirin + saline placebo	Not specified	Concurrent	Reported 3% complication rate is less than the rate reported by AHA/ASA as typical in acute ischemic stroke patients receiving multi-agent fibrinolytics without acupuncture ³⁰
Bleeding caused by inappropriately deep needling, certain to have occurred even in patients not receiving anticoagulants									
Nishimura, ³¹ 2008	N = 1	Case report	81-year-old woman	Limaprost alfadex	Not specified	Bleeding from rupture of extensor tendons by acupuncture needle	Decompression surgery	Concurrent	Likely due to inappropriately deep needling regardless of anticoagulant therapy
Lee, ³² 2005	N = 1	Case report	75-year-old woman	Warfarin and aspirin	Not specified	Cecal intradural hematoma	Right hemicolectomy	Concurrent	Very likely the result of inappropriately deep needling
No bleeding observed									
Xu, ³³ 2005	N = 70	RCT	Age 39-78 years (mean 61.4 years)	LMW heparin, urokinase	CV17, P6, Sp6, P4	No serious AEs, however minor AEs not reported	Not specified	Concurrent	Minor adverse events not reported
Sciammarella ³⁴ 2002	N = 4 (51 tx)	Case series	4 women age 56-84 years	Warfarin	Not specified	Bruise size typical for acupuncture, 1 person	Not specified	Concurrent	No patients had posttreatment external bleeding
Quality of reporting insufficient to allow assessment of acupuncture safety in anticoagulated patients or to draw conclusions									
Lu, ³⁵ 2008	N = "over 6000"	Practice description	Not specified	Not specified	Not specified	"... does not increase the chance of bleeding ..."	Not specified	Not specified	No quantifiable data reported
Rapson, ³⁶ 2003	N = "several hundred"	Retrospective case series	Not specified	Warfarin and heparin	Not specified	No bleeding in any patient	Not needed	Concurrent	Author treated all cases
Smith, ³⁷ 1986	N = 1	Case report	68-year-old man	Warfarin	Not specified	Anterolateral intracompartmental hemorrhage	Decompression fasciotomy	Not specified	Inappropriately deep needling. Time between acupuncture and anticoagulant unspecified.
Han, ³⁸ 2010	N = 1	Case report	60-year-old woman	Warfarin	Not specified	Intramuscular hematoma in left calf	Mannitol	Not specified	Deep needling. Time from anticoagulant to acupuncture not clear

Abbreviations: AEs = adverse events; AHA/ASA = American Heart Association/American Stroke Association; INR = international normalized ratio; LMW = low-molecular-weight; RCT = randomized controlled trial; tx = treatments.

of reporting sufficient to assess whether the safety of acupuncture was influenced by concurrent anticoagulant therapy (Table 1).^{27-29,31-34}

Minor bleeding typical to that seen in both acupuncture and medication injection (a drop of blood managed simply with pressure and cotton-tipped swab) was observed in 51 (14.6%) of 350 treatments among a case series of 229 patients.²⁸ The bleeding was not clinically significant and stopped with pressure as would typically be applied after an injection of medication. Moderate bleeding in one deep needling event was likely exacerbated by the presence of warfarin anticoagulation, which was managed by oral vitamin K to reverse anticoagulation.²⁷

Significant bleeding (most likely related to aggressive anticoagulation and not to acupuncture) was reported in a randomized trial comparing two different acupuncture methods in the treatment of 80 patients with acute ischemic cerebral infarction up to 6 hours after attack, in which intracranial hemorrhage was a reported outcome. Patients were randomized to three groups: A) dextran/aspirin + scalp acupuncture, B) dextran/aspirin + urokinase, and C) dextran/aspirin + saline placebo. The authors reported 4 cases of intracranial hemorrhage: 1 case in the dextran/aspirin + scalp acupuncture group, 2 cases in the dextran/aspirin + urokinase group, and 1 case in the dextran/aspirin + saline placebo group.^{29,30}

Significant bleeding apparently caused by inappropriately deep needling (likely to have happened even if the patient had not been anticoagulated) was observed in 2 case reports: acute carpal tunnel syndrome including bleeding from rupture of several extensor tendons of the hand the day after acupuncture in an 81-year-old woman receiving (unspecified) anticoagulant therapy, managed surgically³¹; and multiple small hematomas on the inner membrane of the appendix in a 75-year-old woman following acupuncture with long needles placed at a depth that repeatedly pierced the intestine wall.³²

The remaining 2 high-quality reports documented no acupuncture-induced bleeding. In a trial of 70 patients random-

ized to either aspirin/low-molecular-weight heparin anticoagulation, or anticoagulation combined with acupuncture, there were no serious adverse events reported, although the article did not include reporting of minor adverse events.³³ In a retrospective chart review of the outcomes of 4 women who presented to a solo-practice physician's office to receive acupuncture for pain relief, all 4 patients were receiving warfarin for underlying conditions. Cumulatively, the 4 women received 51 acupuncture treatments without electrical stimulation at local and distal acupuncture points. After treatment, none of the patients demonstrated any bleeding or bleeding-related problems, either as observed by the physician-acupuncturist or through self-report, except for an occasional asymptomatic bruised area at an acupuncture site on the upper back on one patient.³⁴

Articles with Quality of Reporting Insufficient to Assess Safety of Acupuncture in Anticoagulated Patients or to Draw Conclusions

In a practice review conducted at the Dana Farber Cancer Institute (Boston, MA), the authors reported that in their experience in treatment of more than 6000 oncology patients, acupuncture did not increase the chance of bleeding (rates not specified) in oncology patients receiving anticoagulants.³⁵ In a retrospective case series of several hundred patients by a physician acupuncturist at a Toronto spinal cord injury rehabilitation hospital, the author reported her personal experience during an 11-year period, observing not a single incident of bleeding from acupuncture in anticoagulated patients; however, this was a letter to the journal editor and may have been written more from memory than formal retrospective case record review.³⁶ In addition, 2 case reports noted hematoma³⁸ and compartmental hemorrhage³⁷ caused by giving warfarin to acupuncture patients, but the time between acupuncture and anticoagulation was not specified. Because of the poor quality of reporting in these 4 articles, we were unable to draw conclusions and withdrew them from the review set.

Discussion

We determined that 7 of the 11 articles identified in our systematic search provided reporting of sufficient quality to critically assess our research question: does acupuncture in anticoagulated patients present a higher-than-expected risk of bleeding? Of the anticoagulated patients treated with acupuncture discussed in the 7 articles, there were 58 bleeding events documented in 3974 treatments among 384 acupuncture patients, a bleeding complication rate of 1.4%. This compares very favorably with the 12.3% bleeding complication rate in patients anticoagulated with low-molecular-weight heparin or vitamin K antagonists who receive total hip or knee replacement. Remarkably, the 1.4% acupuncture bleeding complication rate is lower than the 6% rate documented in a large prospective observational study of 229,230 patients, a diverse group without restrictive exclusion criteria.³⁹

The majority of acupuncture bleeding events found in our study were either an asymptomatic bruise³⁴ or a minor drop of blood typical of any needling procedure and managed with pressure and cotton.²⁸ However, the bleeding was not clinically significant and stopped with pressure. By our assessment, the only serious bleeding events were the result of either inappropriately deep needling (for two patients)^{31,32} or mixtures of anticoagulation regimens.²⁹ In the randomized trial by Li et al.,²⁹ each group observed intracranial hemorrhage: dextran/aspirin + scalp acupuncture (one case), dextran/aspirin + urokinase (two cases), and dextran/aspirin + saline placebo (one case). These observations do not support assigning causation of hemorrhage to the combination of acupuncture and anticoagulants but rather suggest anticoagulant combinations were a larger problem.

The remaining 2 high-quality reports documented no acupuncture-induced bleeding. In a trial of 70 patients randomized either to aspirin/low-molecular-weight heparin anticoagulation alone or to anticoagulation combined with acupuncture, the authors reported that there were no serious adverse events (however, they did not include data on minor adverse events).³³ The second was

a retrospective chart review of the outcomes of 4 women given acupuncture for pain relief (totaling 51 acupuncture treatments), with only an occasional asymptomatic bruised area at an acupuncture site on the upper back on 1 patient.^{34,36}

For the 4 remaining cases that we identified, the relationship between the bleeding event and the combination of acupuncture and anticoagulants was indeterminable. Two case reports documented calf compartment syndrome following acupuncture, but we determined causation was not assessable because the duration between acupuncture and anticoagulation was not specified.^{37,38} Unfortunately the final publication, a 6000-patient retrospective practice review, which could have been well positioned to comprehensively address the question of the safety of acupuncture in patients receiving anticoagulants, was lacking in reporting depth and assessment of causation was not possible.³⁵

Conclusion

Given that 56 of 384 patients (3974 treatments; 1.4%) experienced minor bleeding and only 1 patient (0.02%) experienced serious bleeding likely related to the combination of anticoagulant therapy and acupuncture, the evidence identified and assessed in our systematic review suggests acupuncture has a high degree of safety in patients receiving anticoagulant therapy. The fact that the only significant bleeding occurred in patients whose acupuncturist caused tendon and organ damage underscores the importance of respecting appropriate needling location and depth. A prospective randomized trial similar to the one randomized trial³³ we identified but that monitored for both minor and major bleeding events following acupuncture in anticoagulated patients, would help to confirm the findings of our systematic review.

Our systematic review noted a large difference between our observed complication rate and that of Witt et al.³⁹ To further clarify the differences between that article and our own favorable safety observations within our own institution, we plan on following up this review with retrospective and then prospective

analyses of original patient data on the safety of acupuncture in anticoagulated patients. ♦

Disclosure Statement

The author(s) have no conflicts of interest to disclose.

Acknowledgment

Mary Corrado, ELS, provided editorial assistance.

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