



## Review Article

# Hand and wrist surgery without suspending warfarin or oral antiplatelet – systematic review<sup>☆</sup>



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## ABSTRACT

To assess, through a systematic literature review, whether or not it is necessary to suspend antithrombotic medications (warfarin, aspirin, and clopidogrel) to perform elective wrist and hand surgeries. The search for articles was performed using a combination of keywords in the databases available, without scientific design constraints, being selected series with five or more surgeries; the selected articles were analyzed regarding serious (need for surgical treatment) and mild complications (without surgery). Seven articles were retrieved and analyzed; 410 wrist and hand surgeries were performed in patients on warfarin or aspirin and clopidogrel, with three serious complications (0.7%) and 38 mild (9.2%); 2023 surgeries were performed in patients without use of antithrombotics, with zero serious and 18 (0.8%) minor complications. Patients using warfarin or oral antiplatelet (aspirin, clopidogrel, and aspirin associated with clopidogrel) need not suspend the medication to undergo wrist and hand surgery.

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## Cirurgia da mão e do punho sem suspender varfarina ou antiplaquetários orais – Revisão sistemática

## RESUMO

Avaliar, por meio de revisão sistemática da literatura, se há ou não necessidade de suspender medicamentos antitrombóticos (varfarina, AAS e clopidogrel) para a realização de procedimentos eletivos de cirurgia do punho e da mão. A busca de artigos foi feita por meio da combinação de palavras-chave nas bases de dados disponíveis, sem restrições de desenho científico, sendo selecionadas séries com cinco ou mais cirurgias; os artigos selecionados foram analisados em relação às complicações graves (necessidade de tratamento cirúrgico)

## Palavras-chave:

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e leves (sem necessidade de tratamento cirúrgico). Sete artigos foram encontrados e analisados; 410 cirurgias do punho e da mão foram feitas em pacientes em uso de varfarina ou AAS e clopidogrel e observou três complicações graves (0,7%) e 38 leves (9,2%); 2.023 cirurgias foram feitas em pacientes sem uso dos antitrombóticos, apresentaram zero complicações graves e 18 leves (0,8%). Pacientes em uso de varfarina ou antiplaquetários orais (AAS, clopidogrel e AAS associado a clopidogrel) não necessitam suspender a medicação para ser submetidos a cirurgias do punho e da mão.

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## Introduction

The indication of continuous use of oral antithrombotic drugs for the treatment or prevention of cardiovascular and cerebrovascular diseases has increased in recent decades.<sup>1,2</sup> Antithrombotic drugs are distributed in two groups: anticoagulants, warfarin being the most used, and antiplatelets, with acetylsalicylic acid (ASA) and clopidogrel alone or in combination, commonly used in the prevention of thrombotic diseases. The adjustment of warfarin dosage to keep the patient in an anticoagulated state, prevent thrombotic diseases, and avoid causing serious bleeding is a complex treatment that requires control through regular International Normalized Ratio (INR) testing; warfarin suspension and reintroduction are even more difficult, and may lead to the development of new thrombotic events or hyperanticoagulation with bleeding risk. Suspension and reintroduction of oral antiplatelet agents (ASA and clopidogrel) also present a high risk of thrombotic diseases, as well as of thrombosis or bleeding.<sup>3-6</sup>

Patients taking antithrombotic medications that require surgery put physicians in a dilemma: stopping antithrombotic medication to avoid excessive bleeding, but increasing the risk of thromboembolic disease, or maintaining the antithrombotic medication to prevent thromboembolism, but increasing the risk of bleeding. Clinical experiences and meta-analysis studies indicate two groups of situations: surgeries and invasive procedures with a low risk of bleeding (*e.g.*, endoscopy, cataract surgery, arthrocentesis, and dermatological surgeries) do not require discontinuation of antithrombotic therapy, and surgeries with increased risk of bleeding require the suspension of oral antithrombotic medication and, depending on the risk of thrombosis, a transition period with heparin.<sup>4,7,8</sup> The present study aimed to assess whether it is necessary to suspend antithrombotic drugs (warfarin, aspirin, and clopidogrel) for elective surgical procedures of the wrist and hand, through a systematic review.

## Material and methods

The search strategy for the databases used the terms hand surgery and anticoagulant or anticoagulants or indirect thrombin inhibitors or platelet aggregation inhibitors or blood platelet antiaggregants or platelet antiaggregants or blood platelet aggregation inhibitors or platelet inhibitors or antiplatelet agents or antiplatelet drugs or platelet antagonists

or blood platelet antagonists or warfarin or clopidogrel or ticlopidine or aspirin or acetylsalicylic acid. The strategy was adapted to search in MEDLINE (PubMed), Embase, Scopus, LILACS, SciELO, and Cochrane Library (Reviews and Trials) databases.

There was no period limitation for the study; the searches were carried out until December 2015.

Articles that directly addressed the study topic, *i.e.*, wrist and hand surgery and the use or suspension of anticoagulants or antiplatelet agents, were selected through the analysis of their titles and, when necessary, abstracts retrieved through the search strategies in databases.

There were no restrictions regarding study design. However, only articles with sample size (patients or surgeries) equal to or greater than five patients operated on using warfarin or antiplatelet drugs (ASA and clopidogrel) were selected.

The bibliographic references of the selected articles were analyzed in search of other studies that may not have been previously retrieved.

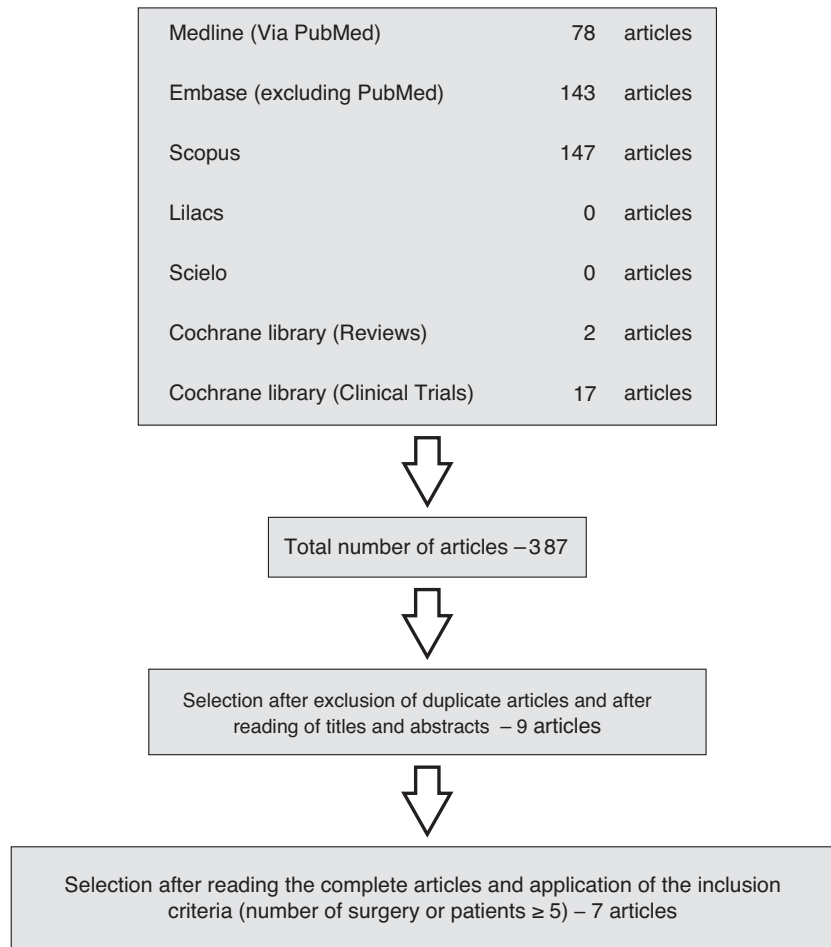
The articles were analyzed and the following characteristics were recorded: sample size (number of surgeries or patients); type of surgery; use of tourniquet; type of antithrombotic medication (warfarin, antiplatelet associated with warfarin, ASA, clopidogrel, or ASA associated with clopidogrel); and number and severity of complications.

The complications assessed were those directly related to the effects of warfarin and antiplatelet agents (clopidogrel and ASA) on blood coagulation during surgery and up to two weeks postoperatively: excessive bleeding and bruising. Complications that were treated only with conservative methods were considered as mild; those that required reoperation were considered as severe.

## Results

A total of 387 articles were selected. After analyzing the titles and abstracts and excluding duplicate studies, nine articles were selected. After reading their full texts, two were excluded, as the sample size was less than five surgeries or patients. The analysis of the references of the nine articles did not retrieve any new papers. The final number of articles included for analysis was seven (Fig. 1).

The study by Smith and Hooper<sup>9</sup> was classified as a retrospective cohort. All surgeries were performed with the use of a tourniquet. The sample (surgeries) included: 1370 surgeries without antithrombotic medication (843 for carpal



**Fig. 1 – Studies retrieved on hand and wrist surgery in patients using antithrombotic drugs (warfarin, aspirin, and clopidogrel).**

tunnel syndrome [CTS] and 527 for Dupuytren contracture); 22 in use of warfarin in patients with INR  $< 3$  (nine for CTS and 13 for Dupuytren contracture); and one in use of clopidogrel (Dupuytren contracture). The patient in use of clopidogrel who underwent surgery for Dupuytren contracture presented excessive bleeding treated conservatively, thus characterized as a mild complication. All other patients operated on (1370 without antithrombotic medication and 22 with warfarin) did not present excessive bleeding or bruising complications.

Wallace et al.<sup>10</sup> conducted a non-controlled clinical retrospective series. All surgeries were performed with the use of a tourniquet. The sample (surgeries) included: 55 patients in use of warfarin (INR between 1.3 and 2.9; 17 for CTS, 12 for Dupuytren contracture, five for trigger finger, and 21 other surgeries). Two patients (one operated for CTS and one who underwent a trapeziectomy) developed hematoma, which was conservatively treated, thus indicating a mild complication.

Jivan et al.<sup>11</sup> conducted a retrospective case-control study. The patients were operated with the use of a tourniquet. All patients underwent surgery for CTS, 48 without the use of antithrombotic medication and 48 using ASA. No bleeding or bruising complications were observed in both groups.

Edmunds and Avakian<sup>12</sup> conducted a non-controlled, prospective clinical series. The patients were operated with

the use of a tourniquet. The sample (surgeries) consisted of 57 patients using warfarin (INR between 1.4 and 3.2), 40 using clopidogrel, and 24 using clopidogrel and ASA. The surgeries performed were: 59 for CTS, 12 for Dupuytren contracture, five for trigger finger, and 45 other surgeries. Six patients (five using clopidogrel and one using clopidogrel and ASA) presented excessive bleeding conservatively treated, thus characterizing a mild complication; one patient on clopidogrel with a diagnosis of Vaughan-Jackson syndrome, who underwent resection of the distal ulna, tenosynovectomy, and tendon transfer, presented a hematoma that required surgical treatment, thus characterizing a severe complication.

Boogaarts et al.<sup>13</sup> conducted a retrospective cohort study. Patients were operated on without tourniquet, with local anesthesia using epinephrine. All patients underwent surgery for CTS; 423 did not use antithrombotic medication, 25 had their antiplatelet medication suspended, and six were operated on while using antiplatelet medication; of the 31 patients on antiplatelet medication (25 suspended and six non-suspended), 30 were on ASA and one was using clopidogrel. Therefore, only six patients using ASA or clopidogrel were operated. No bleeding or bruising complications were observed in any operated patients.

Bogunovic et al.<sup>5</sup> conducted a prospective cohort study. The patients were operated with the use of a tourniquet. The sample (surgeries) included 107 patients who did not use antithrombotic medication (39 for CTS, 23 for trigger finger, and 45 for other surgeries) and 107 operated on while using antiplatelet medication (48 for CTS, 21 for trigger finger and 38 for other surgeries). Among the patients using antiplatelet agents, 76 used ASA, five used clopidogrel, and 11 used clopidogrel and ASA. No serious complications were observed in patients who did not use antiplatelet medication. One of the patients using antiplatelet medication presented severe bleeding requiring reoperation (the patient had rheumatoid arthritis and was using a high dose of ASA, and underwent arthrodesis of the wrist and tenosynovectomy). The rates of conservatively treated bruising (which did not require surgery and were characterized as mild complications) were 14% for patients who did not use medication and 17% in those who used antiplatelet agents; this difference was not statistically significant. No infection or dehiscence of surgical wound was observed in the group of patients using antiplatelet agents. The ecchymosis size, digital sensitivity, and Quick-Dash presented statistically similar results in operated patients using antiplatelet agents vs. those who were not.

Bogunovic et al.<sup>6</sup> conducted another prospective cohort study on this issue, this time addressing warfarin. The sample included 50 surgeries in patients using warfarin alone (32) or associated with ASA (18; 27 for CTS, two for trigger finger, five for mass or synovial cysts resection, four for tendon surgeries, and 12 for bone surgeries) and 50 surgeries in patients who did not use antithrombotic medication (21 for CTS, eight for trigger finger, three tendon surgeries, three for de Quervain tenosynovitis, one wrist arthroscopy, three soft tissue surgeries, and 11 bone surgeries). The mean INR in patients using warfarin was 2.3. All surgeries were made with the use of a tourniquet and local anesthetic was injected without epinephrine at the surgical site. No serious complications were observed in patients who did not use antithrombotic medication. In patients using warfarin, one serious complication requiring a new surgical intervention was observed (patient submitted to carpectomy of the first row who developed hematoma and compression of the median nerve four days after surgery). Regarding mild complications that did not require hospitalization or reoperation, patients using warfarin had a higher incidence of bruising only at two weeks postoperatively, which paired with the group that did not use antithrombotic medication at four weeks. There were no relevant clinical differences between the groups regarding pain, edema, and upper limb dysfunction.

Tables 1 and 2 present summaries of the results from the seven articles included.

The indication for the use of warfarin and antiplatelet agents in the seven studies analyzed were atrial fibrillation, cardiomyopathy, mitral valve prosthesis, coarctation of the aorta, venous thromboembolism, valvular prosthesis, atrioventricular communication, primary prevention of coronary disease, secondary prevention of coronary disease, combined secondary prevention of coronary and cerebrovascular diseases, pulmonary thrombosis, deep venous thrombosis, thrombotic disorders, cardiovascular disease, peripheral vascular disease, and neurovascular disease.

## Discussion

The analysis of the results of the seven selected studies addressed hand and wrist surgeries in patients using warfarin or oral antiplatelet agents (ASA and clopidogrel) indicates that the frequency of severe complications, defined as bleeding or bruising requiring surgical treatment, was extremely low – three in 410 (0.7%). The three serious complications occurred in patients undergoing complex surgical wrist procedures (wrist arthrodesis associated with tenosynovectomy; resection of the distal ulna associated with tenosynovectomy and tendon transfer; and first-row carpectomy); one patient used high-dose ASA, one used clopidogrel, and one used warfarin.<sup>5,6,12</sup> Bogunovic et al.<sup>5</sup> emphasize the similarity of the situation of patients using antiplatelet agents, in which serious complications were observed in those with rheumatoid arthritis undergoing bone procedures. In the 184 surgeries performed on patients using warfarin, one serious complication was observed.<sup>6</sup>

Mild complications, defined as bleeding or bruising that did not require surgical treatment, occurred in 35 out of 410 surgeries (8.5%). The prospective studies by Bogunovic et al.<sup>5,6</sup> including a control group (patients who did not use antiplatelet agents or warfarin) presented the largest amount of mild complications, but the authors adopted a broad definition of the term hematoma (“any bulging with palpable fluid collection, regardless of size”) Edmunds and Avakian<sup>12</sup> reported six minor complications in patients using clopidogrel and ASA, subjectively defined as “excessive intraoperative bleeding.” Stone et al.<sup>14</sup> analyzed the results of over 10,000 patients undergoing major arterial surgery in use of clopidogrel alone or in combination with ASA, and did not find evidence of excessive intraoperative bleeding.

The four studies reporting surgery in patients using warfarin<sup>6,9,10,12</sup> adopted INR equal to or less than three as a parameter to perform the surgery without suspending anticoagulant; apparently, the selection of the INR value was determined subjectively. The four studies showed an INR variation from 1.3 to 3.2. Wallace et al.<sup>10</sup> reported two mild complications, and the INR ranged from 1.3 to 2.9. The study by Bogunovi et al.<sup>6</sup> presented a case with serious complication in which the INR was 2.1 preoperatively and 5.4 on the fourth day after the operation, when the complication was detected. Although the INR parameter of less than or equal to 3 or 3.5 is subjective, the observed results suggest that this limit is safe.

The seven studies analyzed had low levels of evidence, as only three were prospective studies presenting better detailing and care in design and execution; these studies reported more cases of mild and severe complications, probably due to the fact that the definitions of the complications were more precise.<sup>5,6,12</sup>

The risks of thrombotic diseases with the suspension of warfarin or antiplatelet agents depend on multiple factors, starting immediately after the suspension, and can last for months. Drug reintroduction is difficult and undergoes risks. Bell et al.,<sup>15</sup> in a study conducted in Canada on the use of medications after surgery, concluded that patients with long-term use of warfarin have the potential risk of unintentional discontinuation of medications after elective surgery. Therefore,

**Table 1 – Characteristics and summary of results of the seven articles.**

Authors	Type of study	Tourniquet use	AT	Number of surgeries		Mild complications		Severe complications		Total complications
				With AT	Without AT	With AT	Without AT	With AT	Without AT	
Smit and Hooper <sup>9</sup> (2004)	Cohort study (retrospective)	Yes	Warfarin (INR $\leq$ 3) and clopidogrel	23 (22 with warfarin and 1 with clopidogrel)	1.370	1 (Bleeding/clopidogrel)	Zero	Zero	Zero	1 (4.3%) (With AT)
Wallace et al. <sup>10</sup> (2004)	Non-controlled clinical series (retrospective)	Yes	Warfarin (INR 1.3–2.9)	55	Does not refer	2 (hematoma)	Does not refer	Zero	Zero	2 (3.6%) (With AT)
Jivan et al. <sup>11</sup> (2008)	Case-control studies (retrospective)	Yes	ASA	48	48	Zero	Zero	Zero	Zero	Zero (with and without AT)
Edmunds and Avakian <sup>12</sup> (2010)	Non-controlled clinical series (prospective)	Yes	Warfarin (INR 1.4–3.2) clopidogrel and ASA + clopidogrel	121 (57 warfarin, 40 with clopidogrel, and 24 with clopidogrel + ASA)	Does not refer	6 (bleeding; 5 clopidogrel and 1 with ASA + clopidogrel)	Does not refer	1 (hematoma/clopidogrel)	Zero	7 (5.8%) (With AT)
Boogaarts et al. <sup>13</sup> (2010)	Cohort study (retrospective)	No (local anesthesia with epinephrine)	ASA	6	448	Zero	Zero	Zero	Zero	Zero (with and without AT)
Bogunovic et al. <sup>5</sup> (2013)	Cohort study (prospective)	Yes	clopidogrel, ASA, and ASA + clopidogrel	107	107	15 (hematoma)	13 (hematoma)	1 (bleeding/high dose of ASA)	Zero	16 (15%) with AT 13 (12.1%) without AT
Bogunovic et al. <sup>6</sup> (2015)	Cohort study (prospective)	Yes	Warfarin (mean INR 2.3); 18 warfarin + ASA	50 (32 warfarin and 18 with warfarin + ASA)	50	14 (hematoma)	5 (hematoma)	1 (hematoma + median nerve compression)	Zero	15 (30%) with AT 5 (10%) without AT
Total				410	2023	38 (9.2%)	18 (0.8%)	3 (0.7%)	Zero	41 (10%) with AT 18 (0.8%) without AT

AT, antithrombotic.

**Table 2 – Summary and aggregation of the results of the seven articles.**

Surgeries using warfarin, warfarin + ASA, or antiplatelet agents (AAS; clopidogrel; AAS + clopidogrel): 410 Mild complications: 38 (9.2%) Severe complications: three (0.7%)
Surgeries using warfarin: 184 Mild complications: 16 (8.6%) Severe complications: one (0.5%)
Surgeries using antiplatelet agents (AAS; clopidogrel; AAS + clopidogrel): 226 Mild complications: 22 (9.7%) Severe complications: two (0.9%)
Surgeries without the use of antithrombotics (warfarin, warfarin + ASA, ASA, clopidogrel, ASA + clopidogrel): 2023 Mild complications: 18 (0.8%) Severe complications: zero

physicians should be extremely cautious before suspending the use of these medications.<sup>2-4,7</sup>

The ideal study, which was not retrieved in the literature, would prospectively compare the results of patients using antithrombotic drugs with those of patients who had the use of these drugs suspended.

The limitations of the present study, due in part to the methodological restrictions of the articles selected, hinder more emphatic conclusions regarding the need to suspend antithrombotic drugs for wrist and hand surgeries. However, the studies analyzed suggest that wrist and hand surgeries with low risk of bleeding, involving soft parts, finger joints, and tubular bones, can be performed without suspending warfarin or antiplatelet agents (ASA and clopidogrel). Furthermore, the studies suggest the following practices in the surgical management of patients taking antithrombotic drugs: in order not to discontinue warfarin, patients should have INR less than or equal to three on the eve of surgery, and patients on antiplatelet agents (ASA and clopidogrel) may present greater intraoperative bleeding and require greater hemostasis care.

More randomized and controlled studies, especially with groups with and without antithrombotic suspension, are necessary to elucidate this theme. Moreover, the introduction of antithrombotic treatment with anticoagulant and antiplatelet association, as well as the advent of new anticoagulants, also requires new studies on wrist and hand surgery without the suspension of these drugs.<sup>16,17</sup>

### Final considerations

Patients taking warfarin or oral antiplatelet agents (ASA, clopidogrel, and ASA associated with clopidogrel) do not need to discontinue the medication to undergo hand and wrist surgeries.

### Conflicts of interest

The authors declare no conflicts of interest.

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