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Risk of complications due to antithrombotic agents in cutaneous surgery: a systematic review and meta-analysis

Fabian David Scherer, Corinna Dressler, Gabriela Avila Valles, Alexander Nast

Division of Evidence-Based Medicine, Department of Dermatology, Venereology and Allergology, Charité – Universitätsmedizin Berlin, Corporate member of Freie Universität Berlin, Humboldt-Universität zu Berlin, and Berlin Institute of Health, Berlin, Germany

Summary

Background and objectives: We aimed to determine the risk of complications during cutaneous surgery for the perioperative discontinuation in comparison to the continuation of antithrombotic agents and the bridging of vitamin K antagonists with heparin in comparison to their continuation.

Methods: We conducted a systematic review, searching three databases for eligible studies. Methods followed the Cochrane Handbook. We used RoB 2 and ROBINS-I to assess risk of bias. The quality of evidence was judged (GRADE). Fixed-effect meta-analyses were performed.

Results: Two randomized-controlled trials and 19 prospective cohort studies were included. It is uncertain whether, compared to its discontinuation, continuing acetylsalicylic acid (risk difference (RD) 0.004, 95 % confidence interval (CI) –0.003 to 0.019) perioperatively increases the risk of significant postoperative bleedings (SPB). Compared to its discontinuation, continuing phenprocoumon perioperatively may increase the risk of SPB (RD 0.02, 95 % CI 0.00 to 0.05). Bridging phenprocoumon with heparin perioperatively may increase the risk of SPB when compared to its continuation (RD 0.07, 95 % CI 0.01 to 0.22). No evidence was found regarding bleeding risks for direct oral anticoagulants.

Conclusions: No clear indications of major risks of bleedings when continuing antithrombotic agents during minor skin surgeries were identified. However, the quality of evidence was very low.

Introduction

There has been a steady rise in the number of patients requiring therapy with anticoagulants or antiplatelet agents for various acute and chronic conditions. Perioperative management of these drugs continues to be a challenge in patients undergoing dermatologic surgery [1, 2]. Between 2013 and 2018 prescriptions of oral anticoagulants increased by 56 % in Germany [3]. However, this increase was not uniformly present in all classes of anticoagulants. Since 2013 prescriptions of phenprocoumon, a vitamin K antagonist, have been steadily declining – from 77 % to 32 % of all prescribed anticoagulants in 2018. In contrast, the use of factor Xa (rivaroxaban, apixaban, edoxaban) and thrombin (dabigatran) inhibitors, classified as direct oral anticoagulants (DOACs), almost quintupled [3]. Today, DOACs are the most frequently prescribed form of oral anticoagulation [3].

Furthermore, an ever longer life-expectancy is also forecasted to lead to substantial increases in incidence rates for both melanoma and nonmelanoma skin cancer in European countries over the coming decades [4]. Hence, the number of skin surgeries is expected to rise.

A survey from 2017 among hospital-based and office-based dermatologists in Germany found that there was significant heterogeneity with respect to the perioperative management of antithrombotic agents [5]. For example, for large excisions 63.9 % of hospital-based dermatologists continued phenprocoumon treatment, whereas 27.9 % bridged

it perioperatively with heparin and 6.6 % discontinued the anticoagulant around the time of the surgery. 57.8 % of office-based dermatologists continued acetylsalicylic acid (ASA) when performing large excisions, 26.5 % discontinued the antiplatelet therapy for such procedures and 12.2 % referred such patients to a colleague.

The aim of this systematic review was to evaluate whether (Question 1) the perioperative discontinuation in comparison to the continued use of antithrombotic agents and (Question 2) the bridging of vitamin K antagonists with heparin in comparison to their continued use during cutaneous surgery changes the risk of complications. We updated an existing systematic review [6] to inform the update of the German evidence-based (S3) guideline for the management of antithrombotic agents in cutaneous surgery [2].

Methods

The systematic review and meta-analyses were conducted in line with the Cochrane Handbook 6.0 [7]; for details, see Online Supplementary File 1. A protocol was registered (PROSPERO database ID: CRD42020167337) [8]. We reported in line with the PRISMA statements [9, 10], the Cochrane style manual [11, 12] and the advice of the Cochrane Consumer and Communication Group [13].

MEDLINE (Ovid), Embase (Ovid) and the Cochrane Library were systematically searched for potentially eligible studies (see protocol for search strategies). Two reviewers independently screened the identified records. The PICO/eligibility criteria for studies are shown in Table 1. We only included studies written in English, French, German, or Spanish. Data extraction was done independently by two reviewers. Table 2 shows the outcome definitions of perioperative bleeding complications. Study risk of bias assessments were performed (RoB 2 [14] and ROBINS-I [15] tool).

Meta-analysis was performed when two or more studies were available and I^2 was lower than 60 % [16]. I^2 is a measure of heterogeneity of the included studies [16]. Study results were pooled using a fixed-effect analysis model with the Mantel-Haenszel method using ReviewManager 5.4 [17]. The risk differences (RD) and risk ratios (RR) with corresponding 95 % confidence intervals (CI) were calculated.

The quality of evidence for each outcome was evaluated using the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) approach [18] utilizing GRADEpro GDT [19]. The quality can be downgraded 1 or 2 levels due to "risk of bias, imprecision, inconsistency, indirectness, [or] publication bias" (p. 405) [20]. The final quality of evidence can be very low, low, moderate or high (e.g. very low means that "[t]he true effect is likely to be substantially different from the estimate of effect" (p. 404) [20]).

Results

Our searches identified 1,514 records for question 1 (Q 1) and 57 records for question 2 (Q 2). Twenty studies were included for Q 1 (1 randomized controlled trial [RCT], 19 prospective cohort studies) and 2 for Q 2 (1 RCT, 1 prospective cohort study; see Figure 1). See Online Supplementary File 2 for lists of included and excluded records with reasons for exclusion.

For Q 1 no studies were identified which compared the thrombin inhibitor dabigatran or the factor Xa inhibitors rivaroxaban, apixaban, or edoxaban against a control group not taking any antithrombotics perioperatively.

The included studies used different descriptions to report the bleeding complications. In order to group bleeding events for the meta-analyses, an attempt to match the different terms to the outcome definitions (Table 2) was made. The results of the outcome matching can be found in the Online Supplementary File 2. Table 3 shows an overview of all included studies.

Tables and figures displaying further study information, outcome data, the respective risk of bias assessments as well as GRADE evidence profiles and forest plots for all 16 comparisons can be found in the Online Supplementary File 2.

The following five comparisons were judged to have the highest clinical relevance. All studies included in the following comparisons are prospective cohort studies with the exception of Engheta et al. [21]. This study is an RCT assessing thromboembolic events comparing ASA versus no ASA.

Comparison: ASA versus no ASA

- Excessive intraoperative bleeding (Figure 2a): Two studies [22, 23] including 354 participants reported on this outcome. Continuing ASA perioperatively may increase the risk of excessive intraoperative bleedings (RD 0.07, 95 % CI 0.01 to 0.13; quality of evidence: very low).
- Uncontrollable intraoperative bleeding: No events occurred in either the ASA group (n = 40) or in the comparator group (n = 20) in the one study [23] reporting on this outcome. Due to imprecision, it is uncertain whether the perioperatively continued use of ASA increases the risk of uncontrollable intraoperative bleedings (RD 0.00, 95 % CI –0.07 to 0.07; quality of evidence: very low).
- Minor postoperative bleeding (Figure 2b): A meta-analysis of four studies [22–25] with 606 participants was conducted. Due to imprecision, it is uncertain whether the perioperative continuation of ASA increases the risk of minor postoperative bleedings (RD 0.003, 95 % CI –0.05 to 0.04; quality of evidence: very low).
- Significant postoperative bleeding (Figure 2c): Seven studies reported on this outcome. Two studies [26, 27], which did not report an event in either study arm, were not included in the meta-analysis (n = 280). Data collected

Table 1 Eligibility criteria for studies. The criteria were obtained from the German guideline for the management of antithrombotic agents in cutaneous surgery [36]. *Abbr.:* RCTs, randomized controlled trials.

Patients	Inclusion: Any patients undergoing cutaneous surgery were considered.	
Intervention	Inclusion: Question 1: Monotherapy or combination therapy with any of the following medications: – Platelet aggregation inhibitors: acetylsalicylic acid, clopidogrel, ticlopidine, ticagrelor, prasugrel, cilostazol, dipyridamole – Vitamin K antagonists: phenprocoumon, warfarin, acenocoumarol – Thrombin inhibitors: dabigatran, argatroban, desirudin, bivalirudin – Low molecular weight heparins: enoxaparin sodium, dalteparin sodium, nadroparin calcium, reviparin sodium, tinzaparin sodium, certoparin sodium – Unfractionated heparins: heparin sodium, heparin calcium – Heparinoids: danaparoid sodium – Factor Xa inhibitors: rivaroxaban, apixaban, edoxaban, fondaparinux At least one of the listed medications had to be taken by the participants prior to the operation without the perioperative thromboembolic prophylaxis having been the indication for said drugs.	Question 2: Perioperative discontinuation of a vitamin K antagonist (phenprocoumon, acenocoumarol, warfarin) and bridging with unfractionated heparin (heparin sodium, heparin calcium) or with low molecular weight heparin (enoxaparin sodium, dalteparin sodium, nadroparin calcium, reviparin sodium, tinzaparin sodium, certoparin sodium)
Comparator	Inclusion: Question 1: – Placebo – No treatment – Perioperative discontinuation of one or more of the medications listed above – Comparison of any of the above mentioned interventions	Question 2: Perioperative continuation of a vitamin K antagonist (phenprocoumon, acenocoumarol, warfarin)
Outcomes	Inclusion: Primary outcome measures – Proportion of patients with perioperative bleeding – Proportion of patients with a perioperative thromboembolic event Secondary outcome measures – Perioperative mortality – Proportion of patients with wound dehiscence, wound infection, skin graft or flap failure, and erythema – Cosmetic outcome as reported – Quality of life (Skindex, Dermatology Life Quality Index) and quality adjusted life years as reported At least one of the listed outcomes had to be reported.	
Study design	Inclusion: RCTs; controlled clinical trials; prospective cohort studies with a comparison group; prospective interventional studies with a retrospectively matched control group Exclusion: Retrospective studies; case studies; case series; studies with less than 10 patients per study arm	

Table 2 Outcome definitions of perioperative bleeding complications.

Outcome term	Outcome definition
Excessive intraoperative bleeding	"[S]ignificant [intraoperative] bleeding that was difficult to control" (p. 757) [21]
Uncontrollable intraoperative bleeding	"Severe [intraoperative] bleeding necessitating termination of procedure" (p. 523) [22]
Minor postoperative bleeding	Postoperative bleeding that was managed by patients themselves [23]
Significant postoperative bleeding	Postoperative bleeding that "requir[ed] some form of professional medical help [...] or compromis[ed] the surgical outcome" (p. 215) [23]
Any postoperative bleeding	Any kind of postoperative bleeding

by Eichhorn et al. [28] could not be pooled because they reported bleedings per procedure (n = 176). Four studies [22, 24, 29, 30] with 4037 participants were pooled for meta-analysis. Due to imprecision, it is uncertain whether the perioperative continuation of ASA increases the risk of significant postoperative bleedings (RD 0.004, 95 % CI –0.003 to 0.019; quality of evidence: very low).

– Thromboembolic events: One study including 73 participants reported zero thromboembolic events [21]. Details on how these were monitored were not provided. Due to imprecision, it is uncertain whether continuing ASA perioperatively increases the risk of thromboembolic events (RD 0.00, 95 % CI –0.05 to 0.05; quality of evidence: very low).

Comparison: Clopidogrel versus no clopidogrel

– Significant postoperative bleeding (Figure 2d): Three studies [27, 29, 30] including a total of 1,593 participants were pooled. Due to imprecision, it is uncertain whether continuing clopidogrel perioperatively increases

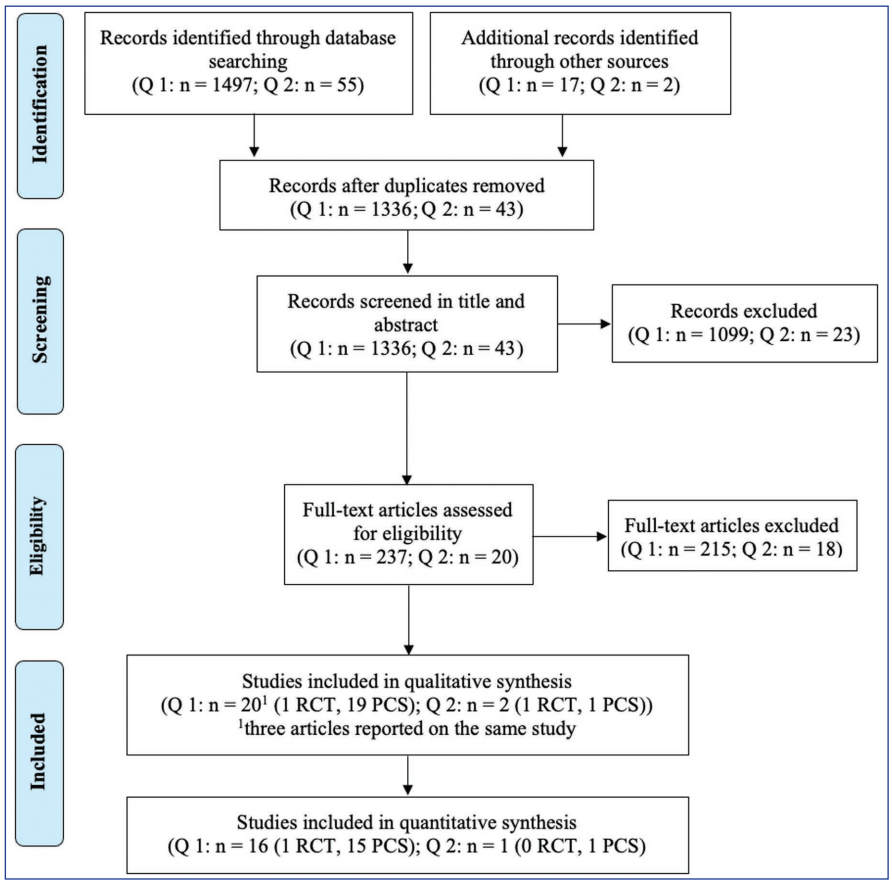

Figure 1 Study selection process for Q 1 and Q 2 depicted in a PRISMA flow diagram [9].
Abbr.: Q 1, question 1; Q 2, question 2; RCT, randomized controlled trial; PCS, prospective cohort study.

Table 3 Overview of included studies (ASA, acetylsalicylic acid).

Author (Year)	Study arms	Number of participants	Outcomes as matched to our categories (see Table 2)
Alcalay (2001)	Warfarin Control	16 77	– Excessive intraoperative bleeding – Any postoperative bleeding
Bartlett (1999)	ASA Control	52 119	– Minor postoperative bleeding – Significant postoperative bleeding – Any postoperative bleeding
Billingsley (1997)	ASA Warfarin Control	81 12 213	– Excessive intraoperative bleeding – Minor postoperative bleeding – Significant postoperative bleeding
Blasdale (2007)	Warfarin Control	65 92	– Excessive intraoperative bleeding – Uncontrollable intraoperative bleeding – Minor postoperative bleeding – Significant postoperative bleeding – Any postoperative bleeding
Bordeaux (2011)	ASA and clopidogrel ASA and warfarin Control	50 37 1027	– Any postoperative bleeding
Dixon (2007)	ASA ASA and warfarin Warfarin Control	334 11 67 1982	– Any postoperative bleeding
Eichhorn (2014)	ASA Control	91 85	– Significant postoperative bleeding
Engheta (2016)	ASA Placebo	38 38	– Any postoperative bleeding – Thromboembolic events
Gowrishankar (2017)	Rivaroxaban Warfarin	15 44	– Minor postoperative bleeding – Significant postoperative bleeding – Any postoperative bleeding
Harbottle (2014)	Warfarin Control	86 87	– Minor postoperative bleeding – Significant postoperative bleeding – Any postoperative bleeding
Kargi (2002)	ASA Warfarin Control	37 21 44	– Minor postoperative bleeding
Koenen (2017)	ASA ASA and clopidogrel ASA and phenprocoumon Clopidogrel Discontinued ASA Discontinued clopidogrel Discontinued phenpro-coumon Phenprocoumon Phenprocoumon bridged with heparin Control	1267 28* 47* 105 240 12 71 657 54* 4769	– Significant postoperative bleeding

Continued

Table 3 Continued.

Author (Year)	Study arms	Number of participants	Outcomes as matched to our categories (see Table 2)
Kramer (2010)	ASA Clopidogrel Warfarin Control	228 32 28 2073	– Any postoperative bleeding
Lam (2001)	Warfarin Warfarin bridged with heparin	26**	– Excessive intraoperative bleeding – Any postoperative bleeding – Thromboembolic events
Lawrence (1994)	ASA Control	40 20	– Excessive intraoperative bleeding – Uncontrollable intraoperative bleeding – Minor postoperative bleeding – Any postoperative bleeding
O'Neill (2014)	ASA ASA and clopidogrel Clopidogrel Warfarin Warfarin and 1 – 2 antiplatelets Control	881 67 56 161 58 1184	– Significant postoperative bleeding
Shalom (2003)	ASA Control	41 212	– None of the primary outcomes of this systematic review were assessed
Shalom (2008)	ASA Warfarin Control	228 28 2073	– Any postoperative bleeding
Shipkov (2017)	ASA Clopidogrel Control	14 12 224	– Significant postoperative bleeding
Sun (2017)	ASA Discontinued ASA Control	26 16 55	– Significant postoperative bleeding – Any postoperative bleeding
Syed (2004)	Warfarin Control	55 55	– Minor postoperative bleeding – Significant postoperative bleeding – Any postoperative bleeding

*For this study arm only the percentage of patients experiencing postoperative bleeding was reported. Conservative estimates of the number of events and the group size were calculated by finding the lowest possible values for both denominator (events) and counter (size) which deliver a percentage equal to the one reported when rounded.
**Study arm sizes were not reported.

the risk of significant postoperative bleedings (RD 0.02, 95 % CI –0.02 to 0.05; quality of evidence: very low).

Comparison: ASA & clopidogrel versus neither ASA nor clopidogrel

– Significant postoperative bleeding (Figure 3a): Pooled analysis of the two studies [29, 30] reporting on this outcome included 6,048 participants. Due to imprecision, it is uncertain whether continuing this dual antiplatelet therapy perioperatively increases the risk of significant postoperative bleedings (RD 0.01, 95 % CI –0.02 to 0.03; quality of evidence: very low).

Comparison: Phenprocoumon versus no phenprocoumon

– Significant postoperative bleeding (Figure 3b): One study [30] with 728 participants reported on this outcome. Continuing phenprocoumon perioperatively may increase the risk of significant postoperative bleedings (RD 0.02, 95 % CI 0.00 to 0.05; quality of evidence: very low).

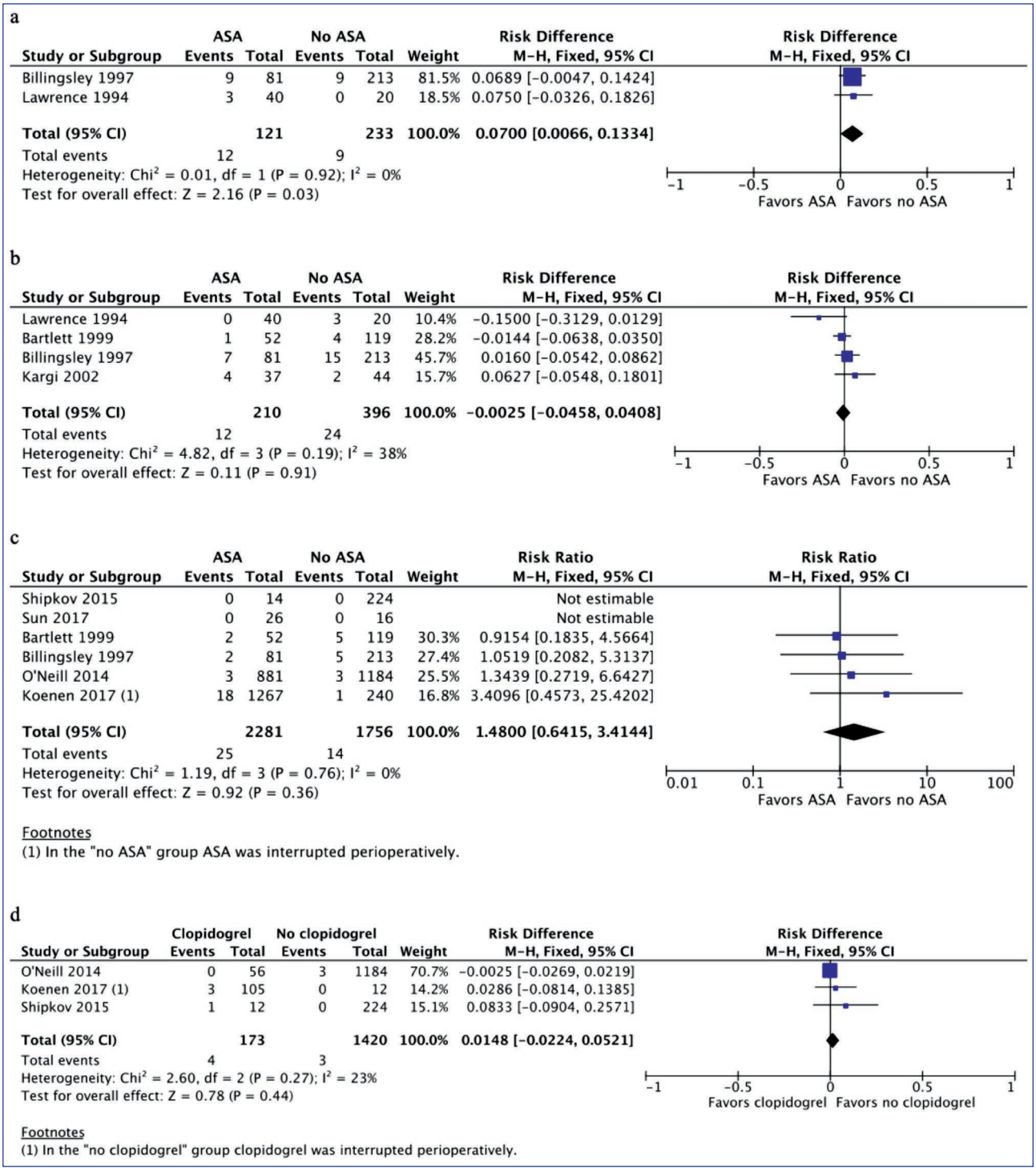

Figure 2 Forest plots. ASA versus no ASA – Excessive intraoperative bleeding (a); ASA versus no ASA – Minor postoperative bleeding (b); ASA versus no ASA – Significant postoperative bleeding (c); Clopidogrel versus no clopidogrel – Significant postoperative bleeding (d).

Abbr.: ASA, acetylsalicylic acid; M-H, Mantel-Haenszel; 95% CI, 95% confidence interval.

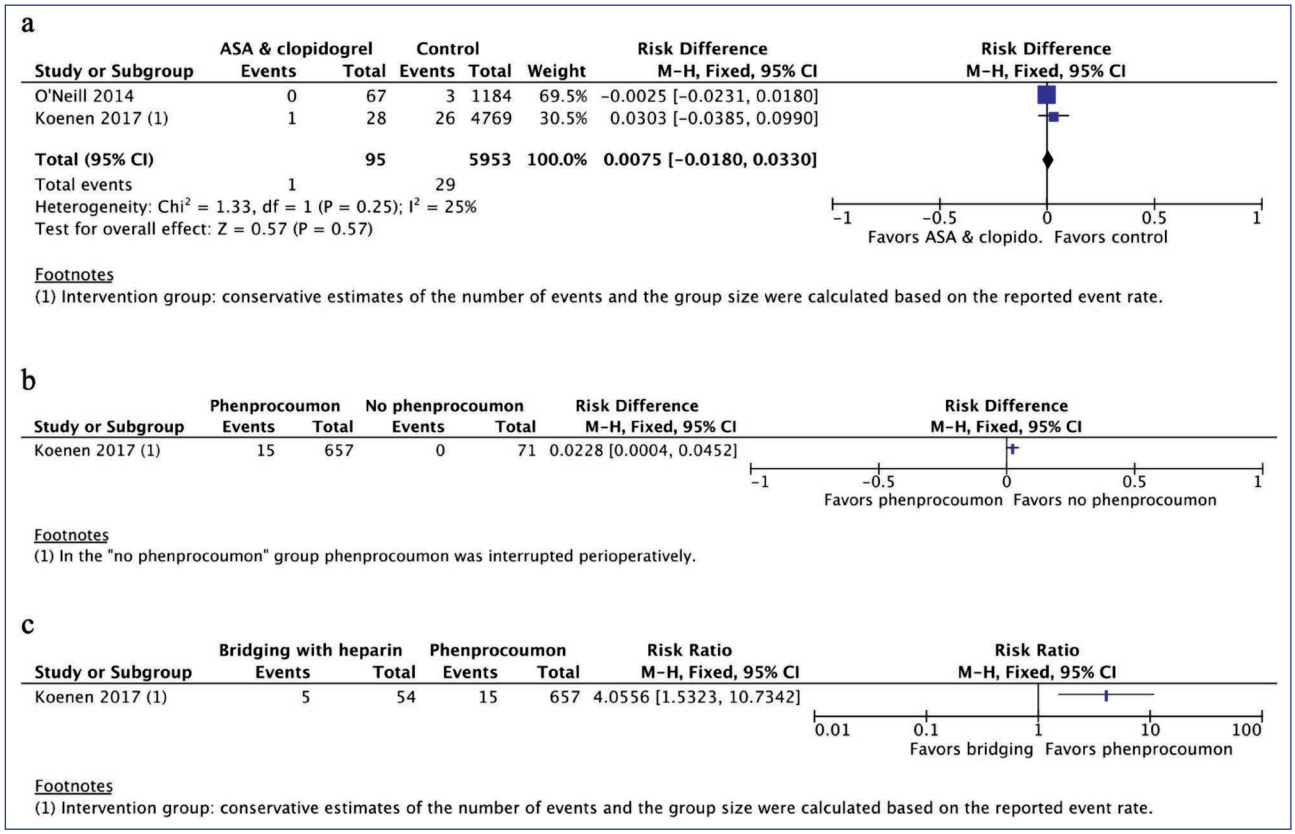

Figure 3 Forest plots. ASA & clopidogrel versus neither ASA nor clopidogrel – Significant postoperative bleeding (a); Phenprocoumon versus no phenprocoumon – Significant postoperative bleeding (b); Bridging phenprocoumon with heparin versus phenprocoumon - Significant postoperative bleeding (c).
Abbr.: ASA, acetylsalicylic acid; M-H, Mantel-Haenszel; 95% CI, 95% confidence interval.

Comparison: Bridging phenprocoumon with heparin versus phenprocoumon

– Significant postoperative bleeding (Figure 3c): One study [30] with 711 participants reported on this outcome. Bridging phenprocoumon with heparin perioperatively may increase the risk of significant postoperative bleedings when compared to its continuation (RD 0.07, 95 % CI 0.01 to 0.22; quality of evidence: very low).

No studies were identified that compared the perioperative continuation with the discontinuation of direct oral anticoagulants in patients undergoing cutaneous surgery.

All outcomes reported in the 19 cohort studies were judged as having a serious risk of bias. Similarly, all outcomes in the included RCTs were considered as having a high risk of bias. In six studies outcome data for at least one of the outcomes as defined in Table 2 was missing [21, 22, 30–33]. In three of these studies, it was not clear to which study arm the participants with missing outcome data belonged [21, 32, 33].

Four studies reported the occurrence of bleeding complications per procedure [28, 31, 34, 35]. Therefore, they could not be pooled with studies reporting event rates per patient. One exception was the data for uncontrollable intraoperative bleeding for the comparison warfarin versus no warfarin because no events occurred in either study arm [34]. Another exception was Dixon et al. [31] because outcome data was also reported as number of bleeds on first procedures and was therefore treated as "per patient" data.

Discussion

We conducted a systematic review of the literature regarding the perioperative risk of complications due to antithrombotic agents in cutaneous surgery. We included two RCTs and 19 prospective cohort studies. Despite the fact that the correct perioperative management of antithrombotic agents is a frequent clinical decision in cutaneous surgeries, the evidence available to guide these decisions is still surprisingly sparse.

In an exercise to rank the importance of the different outcomes in the course of the development of the German guideline for the management of anticoagulants and antiplatelet agents in cutaneous surgery, the outcomes "excessive intraoperative bleeding", "uncontrollable intraoperative bleeding", "significant postoperative bleeding", and "thromboembolic events" were determined to be of critical importance [36]. "Minor postoperative bleeding" was deemed as important.

For ASA, the included studies suggest an increased rate of excessive intraoperative bleedings.

It is uncertain whether, compared to its discontinuation, continuing ASA perioperatively increases the risk of either uncontrollable intraoperative bleeding, minor postoperative bleeding, significant postoperative bleeding, or thromboembolic events as no differences were found. Limited evidence and imprecision hamper any strong conclusions.

For clopidogrel with or without ASA versus no use/interrupted use, no difference was found regarding the rates of significant postoperative bleedings, again based on very low quality evidence.

Continuing phenprocoumon perioperatively versus no use/interrupted use, may lead to an increase in the risk of significant postoperative bleedings (quality of evidence: very low). The observed increase in the risk justifies particular attention in these patients and further studies are needed. In particular, as Koenen et al. point out, a higher INR (International Normalized Ratio) might lead to more bleeding complications [30]. They note that an INR > 1.3 was found to significantly increase the rate of bleeding complications when compared to an INR ≤ 1.3.

When compared to the continued use of phenprocoumon the formerly common procedure of bridging phenprocoumon with heparin was found to increase the rate of significant postoperative bleedings (quality of evidence: very low).

Our findings with regard to bridging of vitamin K antagonists with heparin are in line with findings in previous reviews [37, 38]. The complete lack of evidence with regard to DOACs hints at a relevant research gap, especially when taking into account the strong increase in the number of patients taking these medications [3].

Comparison of our findings with existing systematic reviews is limited by relevant differences in the methods. Most published systematic reviews summarize the results narratively and do not attempt to perform meta-analysis. Our findings are corroborated by previous systematic reviews looking into the same subject. Differences are due to different methodological approaches. A systematic review by Isted et al. found no difference in bleeding risk when continuing ASA perioperatively [39]. We have found a potential increase of excessive intraoperative bleedings in our meta-analysis. Our other findings (no increased risk with ASA) are in line with Isted et al. [39]. They reported "conflicting" (p. 464) evidence regarding warfarin and clopidogrel ("are both likely associated with a small increase in rate of bleeding complications" (pp. 465–466)) [39]. Our study confirms the very low quality of the available evidence. On the contrary, our study results highlight that it is uncertain whether continuing clopidogrel perioperatively increases the risk of bleeding complications. Direct comparison of the results for vitamin K antagonists are not possible as our review focused on phenprocoumon (as it is the medication used in the German healthcare setting) whereas Isted et al. [39] only included studies with warfarin cohorts.

In Germany, recommendations for the management of antithrombotic agents in cutaneous surgery have first been published in 2015 [2]. The expert group recommended the perioperative continuation of phenprocoumon in low-risk operations or in patients without a positive bleeding history. It is recommended to preoperatively measure the INR in patients undergoing skin surgeries with an increased bleeding risk. If the INR is above the therapeutic range, they recommend to not proceed with the operation. In addition, they advised against the perioperative discontinuation of ASA and clopidogrel. Similarly, the American College of Chest Physicians suggests that vitamin K antagonists and ASA should be continued perioperatively in patients undergoing minor dermatologic procedures [40]. Furthermore, the European Heart Rhythm Association recommends that non-vitamin K antagonist oral anticoagulants should not be interrupted for small dermatologic excisions or when hemorrhages are readily manageable [41].

With the notable exception of the German evidence-based (S3) guideline [2] and its update [36], there are no guidelines available focusing on the management of antithrombotic agents during cutaneous surgery that we are aware of.

Limitations

The quality of evidence for all outcomes across all comparisons was judged to be very low. No study sufficiently controlled for potential confounders (e.g. comorbidities, age, or sex) and only one cohort study [25] reported blinding of outcome assessors. Missing outcome data in six studies [21, 22, 30–33] led to a higher risk of bias rating.

Different follow-up times for postoperative bleeding complications introduced methodological heterogeneity (range: from 24 hours [21, 22] up to 30 days [27]), but clinically the majority of bleeding complications occur during the first 24 hours postoperatively. Therefore, the quality of evidence was not downgraded due to inconsistency.

Imprecision was judged to be serious to very serious across all analyzed outcomes. The confidence intervals were generally very wide and often included both no difference between treatment groups as well as large absolute risk

increases. The "optimal information size (OIS)" (p. 582) for a meta-analysis describes the number of participants required to find a clinically relevant risk difference with sufficient power and sensitivity [42]. When the events of interest are rare, the OIS needs to be larger than when the analyzed events are more common. Bleeding complications in cutaneous surgery are relatively rare events. Therefore, no meta-analysis reached the OIS if calculated with the clinical decision thresholds used for the GRADE assessment.

Reporting on perioperative thromboembolic events was limited to the two included RCTs [21, 43], while none of the included cohort studies reported such outcomes. It might have been advantageous to define different patient population for bleeding versus thromboembolic complications [44]. On the one hand, the risk of bleeding complications is influenced by the invasiveness of the surgery. For bleeding outcomes, it is therefore reasonable to only look at patients undergoing cutaneous surgery. On the other hand, the risk of thromboembolic complications due to the interruption of any antithrombotic medication is less dependent on the kind of surgery undertaken.

Only Engheta et al. [21], Koenen et al. [30], Lam et al. [43], and Sun et al. [26] included comparison groups in which participants under regular antithrombotic therapy discontinued their medications perioperatively. All other studies included in this review had comparison groups which did not regularly take any antithrombotic drugs. Studies using the former kind of group address the clinical questions of this review more appropriately. Furthermore, comparison groups, who had not been under regular antithrombotic therapy preoperatively, tended to have lower levels of comorbidity (e.g. hypertension) [32, 45], included a higher proportion of women [27, 28, 32, 34, 45, 46], and often significantly younger participants [27, 32, 34, 45, 46] relative to other study arms in their respective trials in which drug therapy was continued perioperatively.

The findings of this systematic review are only generalizable to patients undergoing Mohs micrographic or excisional skin cancer surgery in the head and neck region because participants of included studies mainly underwent these kinds of surgeries. Hence, further large trials focusing on the perioperative management of antithrombotic medication in different types of surgeries with a high risk of bleeding complications should be conducted. Additionally, further prospective studies with a focus on the now commonly used factor Xa and thrombin inhibitors are needed.

Conclusions

The perioperative discontinuation of any antithrombotic agent can cause potentially life-threatening thromboembolic complications. Additionally, no clear indications of major or life-threatening risks for bleedings when continuing antithrombotic agents perioperatively in minor cutaneous surgeries were identified in this review. Therefore, the possible harm of such adverse effects generally outweighs the risk of manageable intra- and postoperative bleeding complications in minor skin surgeries.

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Correspondence to

Fabian Scherer
Department of Dermatology, Venereology and Allergology
Division of Evidence-Based Medicine (dEBM)
Charité – Universitätsmedizin Berlin

Charitéplatz 1
10117 Berlin, Germany

E-mail: fabian-david.scherer@charite.de

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