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Dextran-40 Reduces Partial Flap Failure: A Systematic Review and Meta-analysis for Antithrombotics after Free Flaps

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Background: Antithrombotic agents are used after free-flap surgery to prevent thrombus formation and improve flap outcomes. However, the reports vary. Therefore, this meta-analysis aimed to elucidate the need for antithrombotic agents in this context.

Methods: We searched for studies that compared the outcomes of patients undergoing free-flap surgery with or without postoperative antithrombotic agents in the PubMed, Cochrane, and ClinicalTrials.gov databases. The primary outcome was total flap failure, with secondary outcomes including partial flap failure, pedicle thrombosis, and bleeding/hematoma. The relative risks (RRs) of outcomes with or without antithrombotic use were evaluated.

Results: Fifteen studies (n = 6755 cases) were included. Antithrombotic agents did not reduce flap failure or pedicle thrombosis risks but increased bleeding and hematoma risks (RR, 1.535). Subgroup analyses by antiplatelet and anticoagulant use demonstrated results similar to those of antithrombotic use. The RR of bleeding/hematoma was 1.761 and 2.740 in the antiplatelet and anticoagulant groups, respectively. Postoperative dextran-40 administration reduced the risk of partial flap failure, with an RR of 0.535.

Conclusions: Postoperative antithrombotic, antiplatelet, or anticoagulant use did not change the risk of total/partial flap failure or pedicle thrombosis but increased the risk of hematoma/bleeding. Postoperative use of dextran-40 reduced the risk of partial flap failure. Increased intraflap blood flow may decrease the risk of partial flap failure. However, dextran-40 may cause severe pulmonary distress. Further prospective studies are required to evaluate the effects of these agents on thrombus formation, intraflap blood flow, and partial flap failure risk. *(Plast Reconstr Surg Glob Open 2024; 12:e5812; doi: 10.1097/GOX.0000000000005812; Published online 15 May 2024.)*

INTRODUCTION

Free flap surgery is effective for reconstructing extensive soft tissue and/or bone defects caused by oncological surgery, infection, or trauma. Vascular occlusion is the leading cause of flap loss, with venous thrombosis being more common than arterial occlusion.[1] Endothelial injury, hypercoagulability, and blood flow stasis may result in platelet aggregation and coagulation cascade activation, leading to thrombus enlargement and blood flow blockage (Fig. 1).[2] Accordingly, antithrombotic medications are classified based on their antithrombotic effects: antiplatelet, anticoagulant, and thrombolytic agents, respectively. After free flap surgery, aspirin, heparin, prostaglandin E1 (PGE1), and dextran-40 are commonly used antithrombotic agents to prevent vascular thrombosis.[3,4]

The total flap failure rate in the antithrombotic group is reportedly 1%–3% below that in the control

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groups.[5–8] However, antithrombotics' impact on flap success rates remain controversial owing to inconsistent findings.[4,6,9–11] Antithrombotic-related bleeding/hematoma may compress the pedicle, leading to flap ischemia or failure.[10,12–15] Higher rates of bleeding/hematoma and total flap failure in patients with post-free-flap antithrombotic therapy were observed.[9,10,15] In addition, increased rates of cardiopulmonary complications and pneumonia have been linked to long-term dextran-40 use.[16] Consequently, the risk–benefit calculus of antithrombotics remains unclear.[3,4]

Partial flap failure, with a reported incidence rate of 5%–10%, is another severe complication.[5,7–10,15,17] Contour deformity, re-exposure of vital tissues, and partial flap failure may lead to secondary reconstruction or prolonged wound care. A standard treatment to prevent partial flap necrosis is currently lacking, and few studies have examined the effects of antithrombotic use on the incidence of partial flap failure.

Takeaways

Question: Does the use of antithrombotic agents after free flap surgery reduce the risk of poor outcomes?

Findings: Postoperative antithrombotic, antiplatelet, or anticoagulant use did not change the risk of total/partial flap failure or pedicle thrombosis but increased the risk of hematoma/bleeding. Postoperative use of dextran-40 reduced the risk of partial flap failure.

Meaning: Increased intraflap blood flow may decrease the risk of partial flap failure.

Previous studies comparing the effects of antithrombotics on the risk of free-flap complications were limited by small sample sizes and low complication rates.[8,9,11,13,14] Consequently, we aimed to conduct a systematic review and meta-analysis of studies on the impact of antithrombotics

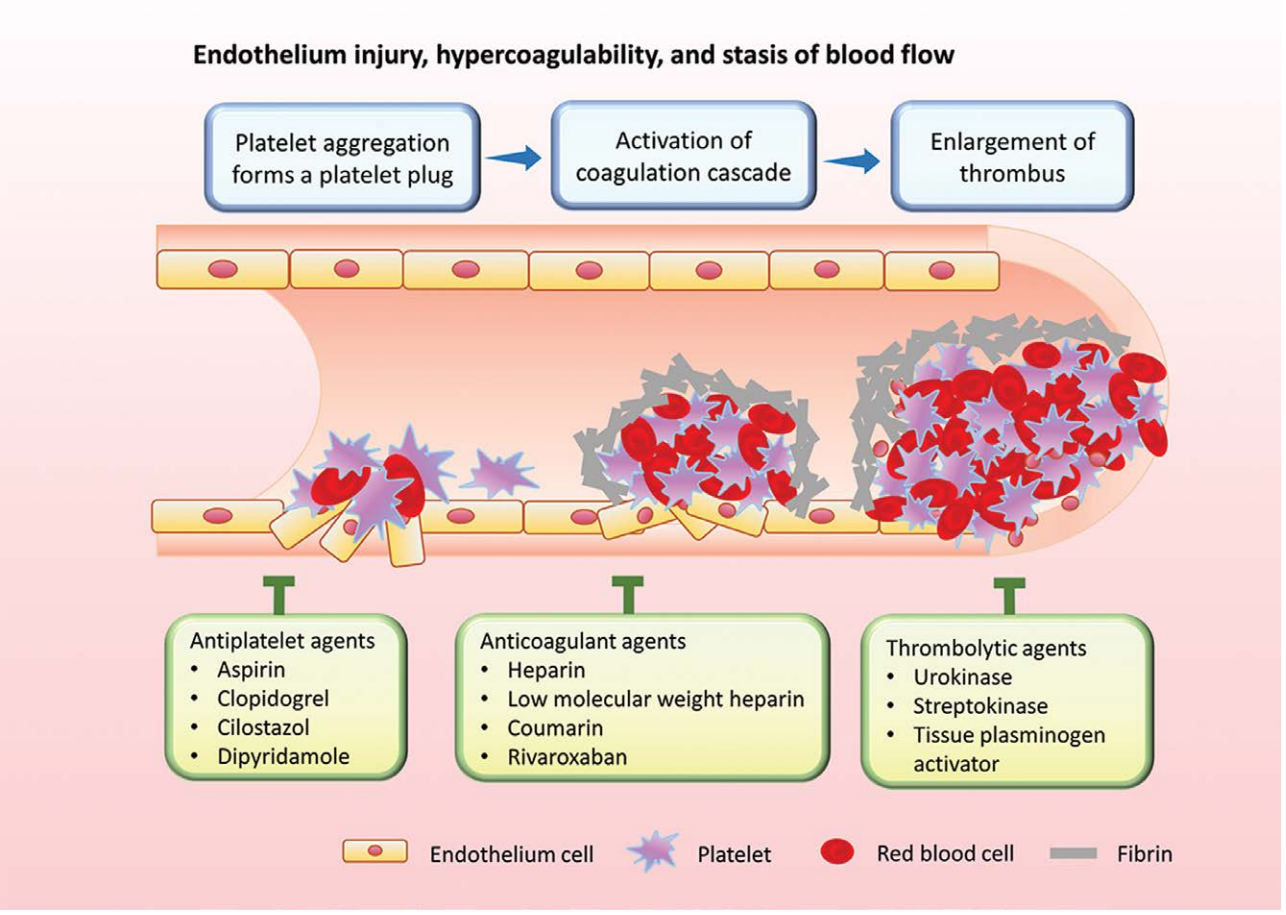

Fig. 1. Schematic of thrombus formation and antithrombotic agent mechanism of action. Endothelial injury, hypercoagulability, and blood flow stasis may lead to platelet adhesion, activation, and aggregation, ultimately forming a platelet plug. The activation of the coagulation cascade promotes fibrin formation and stabilizes the thrombus. The continued progression of these processes results in the enlargement of thrombus, blocking blood flow. Thus, antithrombotic medications can be classified into antiplatelet, anticoagulant, and thrombolytic agents based on the mechanism of action: platelet aggregation inhibition, coagulation cascade block, and thrombose dissolution promotion.

on the risk of total flap failure, partial flap failure, pedicle thrombosis, and bleeding/hematoma in patients undergoing free-flap surgery.

METHODS

This systematic review and meta-analysis were conducted in accordance with the *Cochrane Handbook for Systematic Reviews of Interventions*, version 5.1.0.[18] and followed the Preferred Reporting Items for Systematic Review and Meta-Analysis guidelines.[19] The protocol was registered in INPLASY (registration no.: INPLASY2023120013).

Electronic searches were conducted using the PubMed and Cochrane databases, and ClinicalTrials.gov for articles published before July 7, 2023. Each database was searched using the following key terms: ("free flap" OR "free tissue transfer") AND (anticoagulants OR aspirin OR heparin OR antiplatelet OR antithrombotic OR dextran OR fibrinolytic OR prostaglandin OR urokinase).

The study selection details are presented in Figure 2. After removing duplicates, 356 articles were potentially eligible for this meta-analysis. We included studies comparing the outcomes of free-flap surgery with or without postoperative antithrombotic therapy; both randomized and nonrandomized studies were eligible. The primary outcome was the total flap failure rate, and secondary outcomes were the rates of partial flap failure, pedicle thrombosis, and bleeding/hematoma. Among the shortlisted studies, only Nelson et al defined partial failure as flap loss or atrophy up to 50%, not requiring immediate re-operation.[20] Bleeding/hematoma was defined as blood loss events requiring a surgical intervention, drainage, and/or blood transfusion.[7,8,14,17,20,21] Systematic reviews; case reports; case series; letters to the editor; animal studies; and studies with fewer than 10 participants, published in languages other than English, lacking raw data for primary or secondary outcomes, or that relied on questionnaire data were excluded. After screening titles and abstracts, two authors independently reviewed the full text of 245 articles using these criteria. Disagreements on study eligibility were resolved through consensus discussions. Finally, 15 articles were included in the meta-analysis.[7–15,17,20–24]

Data Extraction

Two authors independently extracted the following variables: first author name, publication year, study type, patients' clinical and demographic characteristics (patient count, age, sex, and underlying disease), reconstruction area, antithrombotic agent used, antithrombotic therapy protocol used, and primary and secondary outcome events.

Study quality was assessed independently by two authors using the Newcastle-Ottawa scale.[25] Studies scoring more than six points, indicating high quality, were included. Any discrepancies in the assigned scores were resolved through consensus discussion. Funnel plots and Egger test were used to assess the risk of publication bias, revealing no significant publication bias regarding the risk of complications.

Statistical Analysis

Statistical analysis was conducted using the Comprehensive Meta-Analysis software, version 3.3.070 (Biostat Inc, Atlanta, Ga.). Relative risk (RR) and confidence intervals were estimated to assess the strength of the association between antithrombotic agent use and complication rates. Forest plots were used to illustrate the

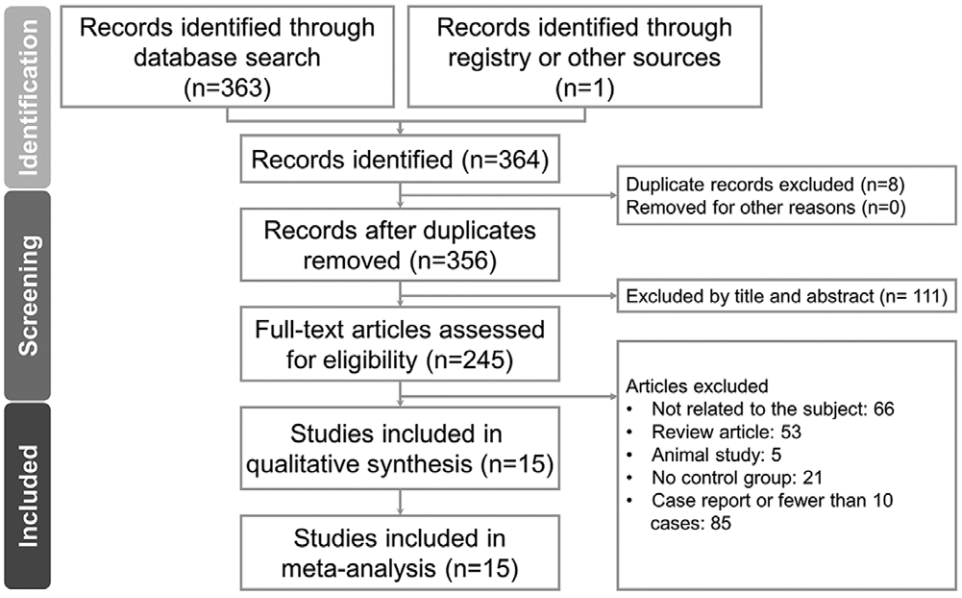

Fig. 2. Preferred reporting items for systemic reviews and meta-analysis flow diagram for the search and identification of included studies.

magnitudes of the observed effects. Outcomes were considered significant at a *P* value less than 0.05. Individual studies were weighted under the random effects statistical model to include the variation between and within the studies. We performed subgroup analyses for patients treated with antiplatelets, anticoagulants, and dextran-40, given their different mechanisms.

RESULTS

We included 15 studies comparing the effects of postoperative antithrombotic therapy in 6755 free-flap cases, including 4052 patients treated with antithrombotics.[7–15,17,20–24] Most free-flap procedures were performed for postoncological treatment reconstruction. Most reconstruction areas were the head and neck (80%), followed by the breast, lower extremities, and upper extremities (Table 1).

The rates of total flap failure, partial flap failure, pedicle thrombosis, bleeding/hematoma, and the antithrombotic regimens/protocols used are presented in Supplemental Digital Content 1.[7–15,17,20–24] (**See table, Supplemental Digital Content 1,** which shows the types and protocols of antithrombotic agents used and patient outcomes. **http://links.lww.com/PRSGO/D205**.) The types of antithrombotics used included aspirin, heparin, low-molecular-weight heparin (LMWH), unfractionated heparin (UFH), dextran-40, PGE1, ketorolac, and combinations thereof.

Antithrombotic Agents

Nine studies compared the outcomes with and without post-free-flap antithrombotic use.[7,10–12,14,15,17,21,22] The control groups in these studies did not receive antithrombotics, even for deep vein thrombosis prevention. The average total flap failure rate was 2.97% (n = 1464, range: 0.00%–5.43%) in the nonantithrombotic group and 7.78% (n = 1508, range: 0.00%–31.25%) in the antithrombotic group.[7,10,11,15,17,21,22] Antithrombotic agent use did not affect the risk of total flap failure ($P = 0.417$; Fig. 3A).[7,10,11,15,17,22]

The average rates of partial flap failure and pedicle thrombosis in the nonantithrombotic group were 11.12% (n = 902, range: 0.00%–25.00%) and 3.21% (n = 1310, range: 0.00%–8.85%), whereas those in the antithrombotic group were 4.64% (n = 709, range: 1.65%–8.19%) and 7.85% (n = 1327, range: 1.33%–31.82%), respectively.[7,10,11,17,21,22] Postoperative antithrombotics neither increased nor decreased the risk of partial flap failure ($P = 0.356$) and pedicle thrombosis ($P = 0.922$; Fig. 3B, C).[7,10,11,17,21,22]

The average bleeding/hematoma rates were 5.53% (n = 2169, range: 0.00%–25.00%) in the nonantithrombotic group and 9.22% (n = 3140, range: 0.00%–31.25%) in the antithrombotic group. Post-free-flap antithrombotics significantly increased the risk of bleeding/hematoma (RR = 1.535, 95% CI: 1.067–2.207, $P = 0.021$), relative to that in the nonantithrombotic groups (Fig. 3D).[7,10–12,14,15,17,22]

To assess whether specific types of antithrombotics reduced the risk of complications, we conducted subgroup analyses based on antiplatelets, anticoagulants, and dextran-40 use, given their different mechanisms (inhibition of platelet aggregation, inhibition of coagulation cascades, and increased blood flow with suspected fibrinolytic effect).

Antiplatelets

This antiplatelet subgroup included patients treated with aspirin, ketorolac, and PGE1, which were used in three, one, and one studies, respectively.[8,10,15,23,24] Aspirin

Table 1. Study and Patient Characteristics

				Reconstruction Area (No. Flaps)				Medical History (No. Patients)						
Author, Year	Design	Age (y)	Male/ Female	Head and Neck	Breast	Lower Limbs	Upper Limbs	Diabetes	HTN	PAOD	Trauma	Tumor	Smoker	Alcohol
Ekin et al[22]	Retrospective	49.3	40/37	—	—	—	—	5	9	—	—	68	28	4
Enajat et al[23]	Retrospective	48	0/430	0	430	0	0	—	—	—	—	—	26	—
Filipan et al[13]	Retrospective	59.9	118/58	176	0	0	0	—	—	—	—	142	—	—
Jayaprasad et al[9]	Retrospective	55.6	119/49	172	0	0	0	—	21	—	—	172	29	—
Karamanos et al[24]	Retrospective	31	125/58	0	0	144	39	50	—	21	—	—	79	—
Keith et al[14]	Retrospective	—	0/146	0	146	0	0	—	—	—	—	146	—	—
Kroll et al[7]	Retrospective	—	—/—	338	179	0	0	—	—	—	—	—	—	—
Lee et al[8]	Retrospective	43.5	79/49	0	0	128	0	15	24	—	17	41	20	—
Lighthall et al[15]	Retrospective	64.3	193/197	390	0	0	0	—	—	—	—	—	—	—
Nelson et al[20]	Retrospective	56	—/—	1	18	—	—	—	—	—	—	19	9	—
Numajiri et al[17]	Retrospective	61	149/34	183	0	0	0	—	—	—	—	183	—	—
Riva et al[10]	Retrospective	51.9	1179/54	1351	0	0	0	189	193	—	—	1351	889	—
Sun et al[21]	Retrospective	53.9	42/13	55	0	0	0	—	—	—	—	55	—	—
Wu et al[12]	Retrospective	50.5	2234/226	2460	0	0	0	171	346	—	—	—	2038	1869
Zhou et al[11]	Prospective	49.1	287/167	454	0	0	0	—	—	—	—	—	—	—

Dashes (—) indicate "not mentioned in the study."
HTN, hypertension; PAOD, peripheral arterial occlusion disease.

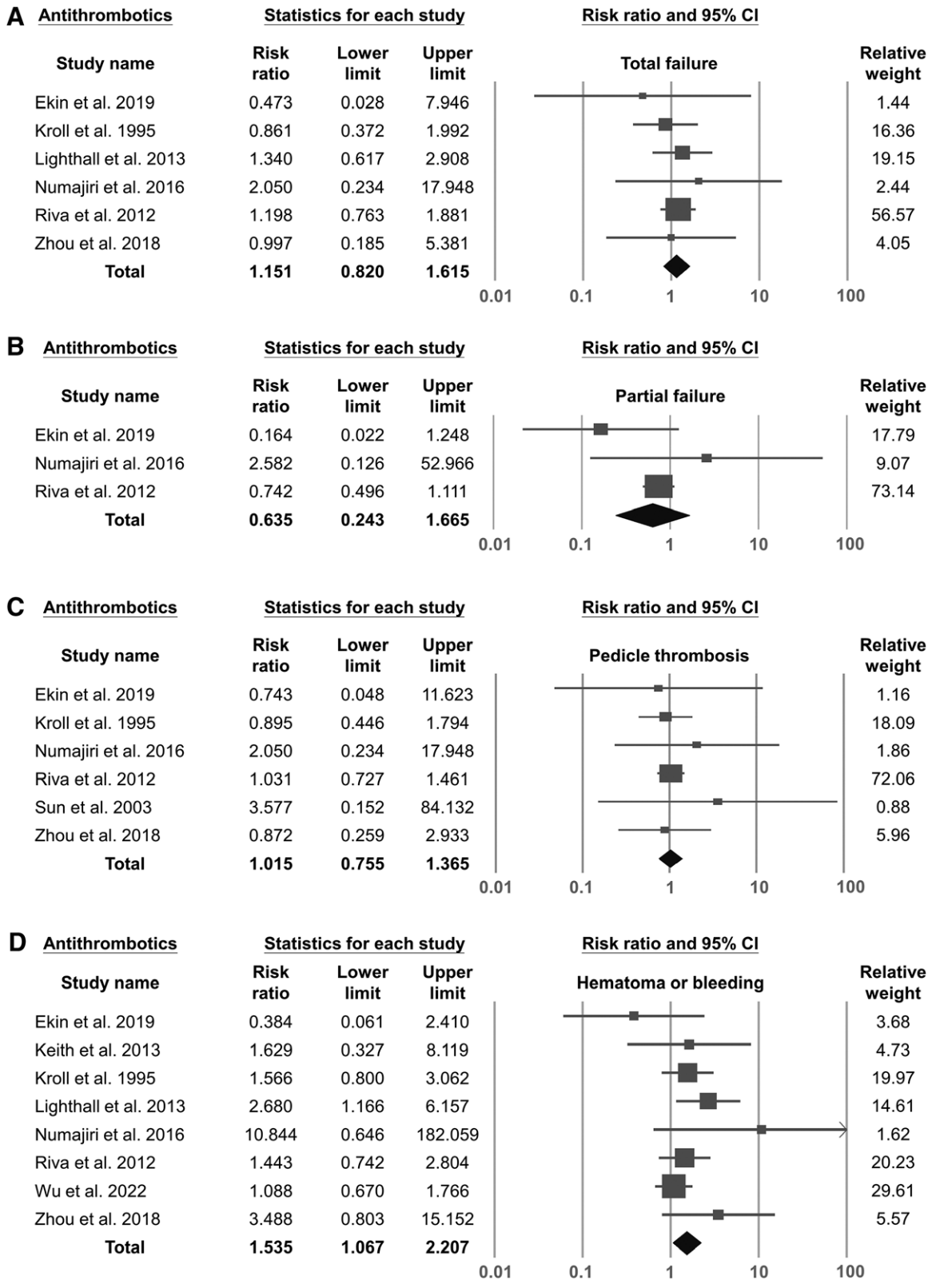

Fig. 3. Forest plot depicting patient outcomes after free flap surgery with or without postoperative antithrombotic therapy: total flap failure (A), partial flap failure (B), pedicle thrombosis (C), and hematoma or bleeding (D).

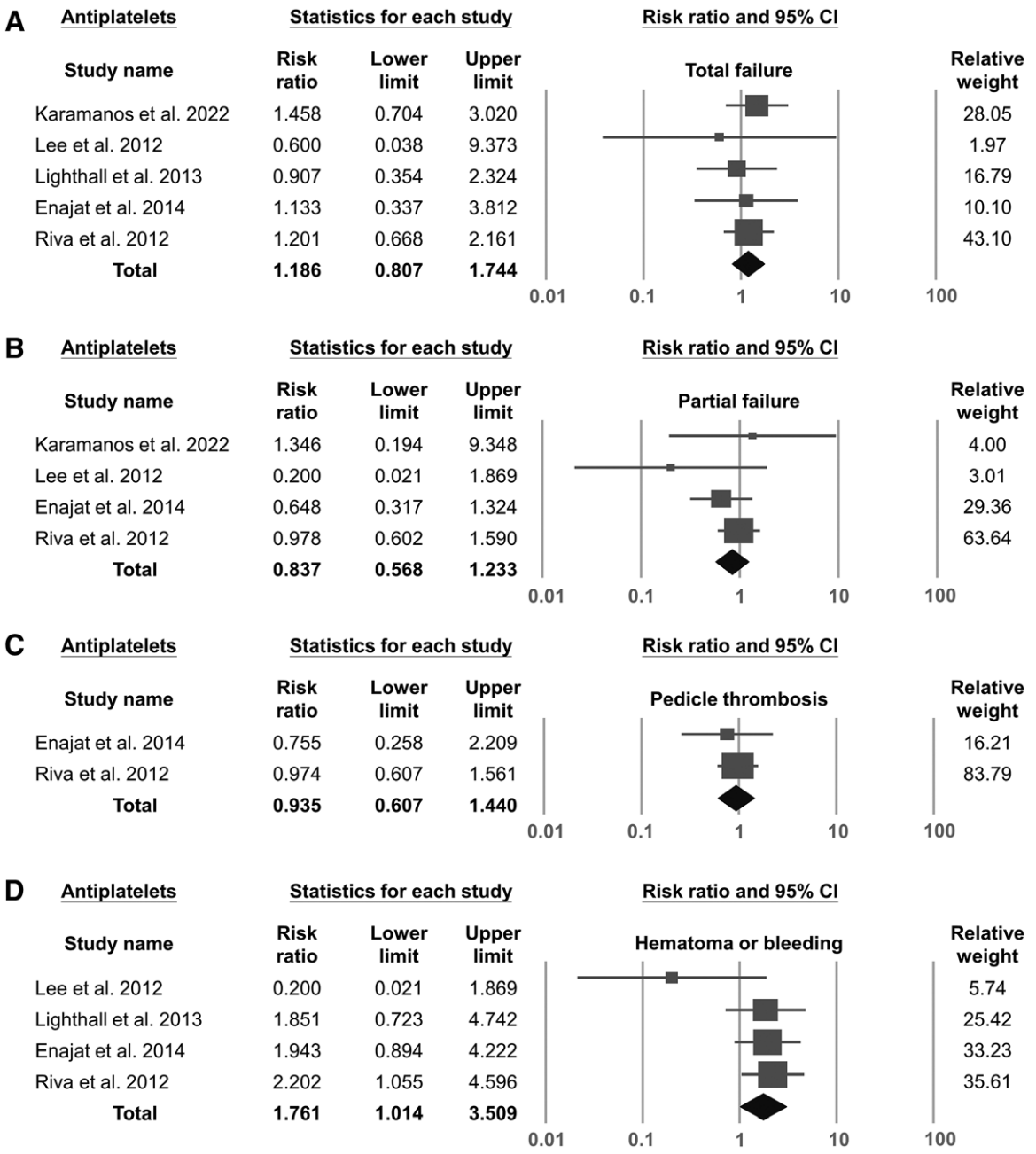

Fig. 4. Forest plot depicting patient outcomes after free flap surgery with or without postoperative antiplatelet use: total flap failure (A), partial flap failure (B), pedicle thrombosis (C), and hematoma or bleeding (D).

and ketorolac are nonsteroid antiinflammatory drugs that block the activity of cyclooxygenase-1 and thus irreversibly inhibit platelet aggregation.[26,27] PGE1 exhibits a broad range of pharmacological effects, including antithrombotic mechanisms, vasodilation, and inhibition of platelet aggregation.[28,29]

Total flap failure rates were in the range of 2.08%–11.43% in the control groups and 1.25%–16.67% in the antiplatelet groups.[8,10,15,23,24] The rates of partial flap failure and pedicle thrombosis were in the range of 1.90%–8.37% and 3.55%–8.85% in the control groups and 1.25%–8.19% and 2.68%–8.62% in the antiplatelet groups, respectively.[8,10,23,24] Antiplatelets did not affect total flap failure ($P = 0.385$), partial flap failure ($P = 0.367$), or pedicle thrombosis ($P = 0.759$) rates (Fig. 4A–C).[8,10,15,23,24]

The rates of bleeding/hematoma ranged from 2.15% to 6.25% in the control group and 1.25% to 9.20% in the antiplatelet groups.[8,10,15,23] The risk of bleeding/hematoma significantly increased (Fig. 4D) in the antiplatelet group (RR=1.761, 95% CI: 1.014–3.059, $P = 0.045$).[8,10,15,23]

A subgroup analysis based on aspirin use included three studies with a total of 481 and 458 cases treated with and without aspirin, respectively.[15,23,24] Aspirin did not affect the risk for total ($P = 0.397$) or partial ($P = 0.311$)

flap failure but significantly increased the risk of bleeding/hematoma (RR = 1.905, 95% CI: 1.047–3.467, P = 0.035).[15,23,24] (**See figure, Supplemental Digital Content 2**, which shows forest plot depicting patient outcomes after free flap surgery with or without postoperative aspirin use. **http://links.lww.com/PRSGO/D206**.)

Anticoagulants

Heparin, LMWH, and UFH were classified as anticoagulants according to their function of binding to and activating antithrombin-III, inhibiting the function of thrombin and coagulation factors.[30] Heparin, LMWH, and UFH were used in four, four, and one study, respectively, with 2497 and 1346 patients receiving and not receiving anticoagulants, respectively.[7,11,12,14,15,17,20] Partial flap failure was reported in only one study, where heparin use did not affect outcomes, and was not accounted for in a subgroup analysis.[17] Subgroup analysis for anticoagulants was separated into the use of anticoagulants, prophylactic treatments (heparin dose <400 U per hour, LMWH 4100 U per day, enoxaparin <60 mg per day, or any intervention reported for DVT prevention), and therapeutic treatments (heparin dose >500 U per hour or maintaining activated partial thromboplastin time of 55–80 s).[7,11,12,14,15,17,20]

The total flap failure and pedicle thrombosis rates ranged from 1.32% to 17.65% and 1.6% to 17.65% in the control group and 0.00% to 31.25% and 0.00% to 3.36% in the anticoagulants groups, respectively.[7,11,15,17,20] Lighthall et al observed an increased total failure rate with anticoagulant use, whereas the other four studies reported no significant difference. Overall, anticoagulants did not significantly affect total flap failure (P = 0.878) and pedicle thrombosis (P = 0.106; Figs. 5A, B).[7,11,15,17,20]

The bleeding/hematoma rate ranged from 0.00% to 5.29% and 3.53% to 31.25% in the control and anticoagulant groups, respectively.[7,11,12,14,15,17,20] Lighthall et al and Zhou et al examined 844 patients with head and neck reconstructions, reporting the highest RR of bleeding/hematoma at 7.052 and 5.033, respectively, in the anticoagulant groups, contributing to approximately 32% of the total relative weight.[11,15] Subgroup analysis revealed that the RR of bleeding/hematoma was 2.740-times higher in the anticoagulant group than in the control group (P = 0.008; Fig. 5C).[7,11,12,14,15,17,20]

Furthermore, the risk of total flap failure was unaffected in the prophylactic group (P = 0.56) but increased in the therapeutic group (RR = 3.945, 95% CI: 1.613–9.649, P = 0.003). (**See figure, Supplemental Digital Content 3**, which shows a forest plot depicting total flap failure after free flap surgery with or without prophylactic or therapeutic dose of anticoagulants. **http://links.lww.com/PRSGO/D207**.) Both groups showed increased risk of bleeding/hematoma, and the risk in the therapeutic group (RR = 5.354, 95% CI: 2.515–11.398, P = 0.024) was higher than that in the prophylactic group (RR = 2.314, 95% CI: 1.116–4.797, P = 0.000). (**See figure, Supplemental Digital Content 4,** which shows a forest plot depicting hematoma or bleeding after free flap surgery with or without prophylactic or therapeutic dose of anticoagulants. **http://links.lww.com/PRSGO/D208**.)

Dextran-40

Dextran-40 is used in post-free-flap care as a volume expander to increase blood flow at a dose of approximately 20–25 mL per hour for 3–5 days.[7,10,13] It also has antithrombotic properties by enhancing fibrinolysis.[31] Overall, five studies compared outcomes with regard to dextran-40 use, with 513 and 1258 cases treated with and without dextran-40, respectively.[7,9,10,13,21]

The total flap failure rates ranged from 2.33% to 7.59% in the control group and 3.49% to 27.27% in the dextran-40 group.[7,9,10,13,21] Kroll et al reported that dextran-40 significantly increased the risk of total flap failure and pedicle thrombosis, whereas the other studies revealed no such effects.[7,9,10,13,21] No studies revealed any association between dextran-40 and bleeding/hematoma. In subgroup meta-analysis, dextran-40 neither increased nor decreased the risk of total flap failure (P = 0.111), pedicle thrombosis (P = 0.563), and bleeding/hematoma (P = 0.170) (Fig. 6A–C).[7,9,10,13,21]

Partial flap failure in the dextran-40 group was reported in four studies, mostly in patients undergoing head and neck reconstruction.[9,10,13,21] One study was excluded from the analysis owing to the absence of partial flap failure cases.[21] The partial flap failure rate ranged from 0.00% to 8.37% in the control groups and 0.00% to 4.59% in the dextran-40 group. Riva et al reported that dextran-40 lowered the risk of partial flap failure in 283 patients after head and neck reconstruction, with the highest relative weight (90.4%) in the dextran-40 subgroup. In subgroup meta-analysis, postflap dextran-40 significantly lowered the risk of partial flap failure (RR = 0.536, 95% CI: 0.310–0.928, P = 0.026, I^2 = 0.000%; Fig. 6D).[9,10,13]

DISCUSSION

In this meta-analysis, antithrombotic agents did not reduce the risk of flap failure and pedicle thrombosis but increased the risk of hematoma and bleeding. In subgroup analysis, antiplatelets and anticoagulants were associated with RR values of 1.761, and 2.740, respectively, relative to those associated with the control groups. Notably, postoperative dextran-40 administration reduced the risk of partial flap failure.

Total flap failure is a severe complication of free-flap reconstruction, with pedicle thrombosis and bleeding/hematoma as its leading causes.[1,32] Theoretically, antithrombotics may decrease the risk of pedicle thrombosis, consequently reducing the rate of flap failure. However, previous studies are inconclusive on whether antithrombotic use is beneficial.[3,4,33] Risk factors for pedicle thrombosis include vessel intima injury, suture technique error, vasospasm, external compression, vessel kinking, infection, hypercoagulable status, or history of thrombotic events.[34] The free-flap success rate may be affected by surgeons' technique, intraoperative course, postoperative care quality, and patients' overall condition, including any underlying disease, radiotherapy, smoking, age, and nutritional status.[35–38] Hence, inhibiting coagulation or platelet function alone by antithrombotics may be insufficient to reduce the risk of thrombus formation, pedicle

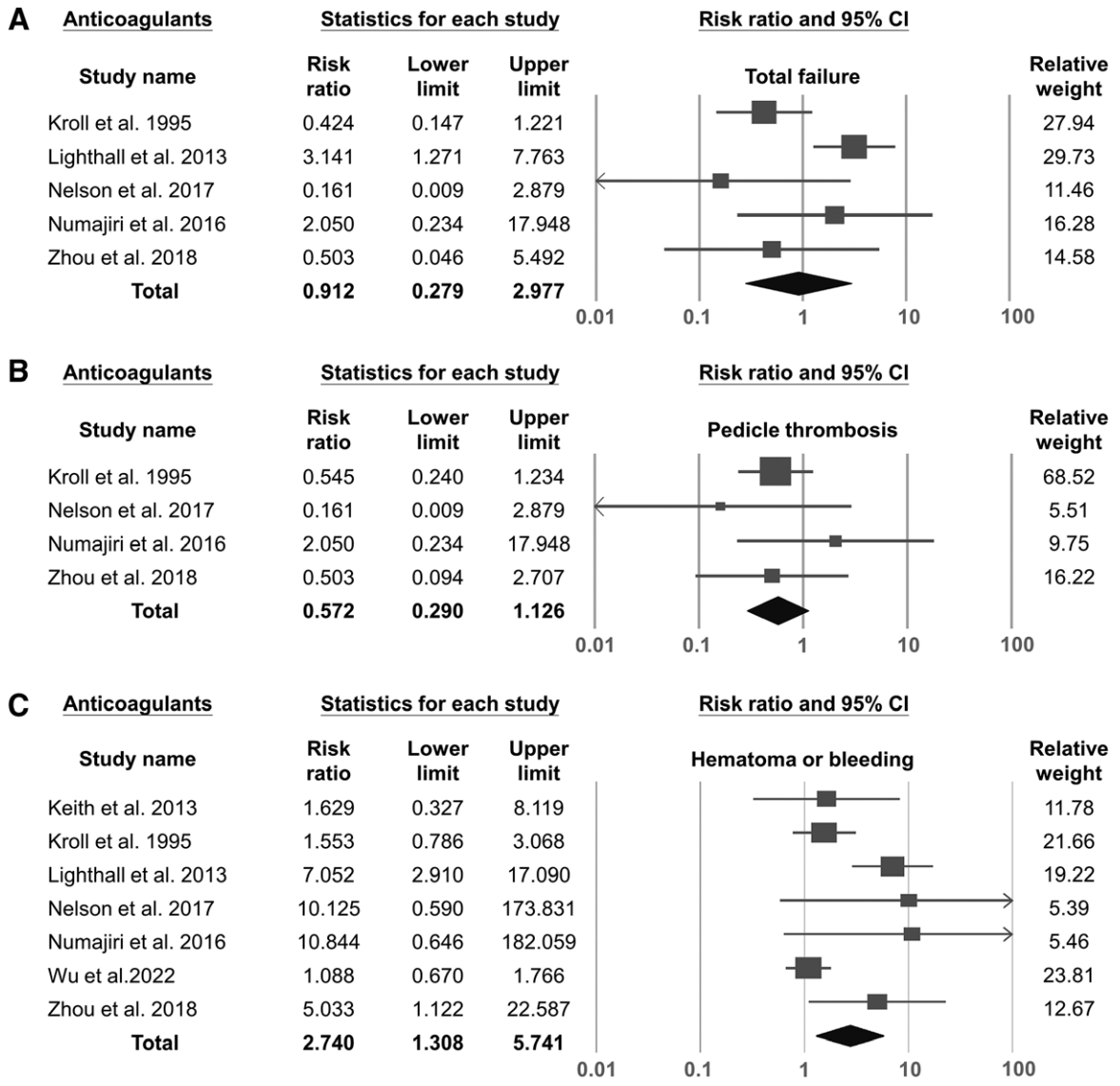

Fig. 5. Forest plot depicting patient outcomes after free flap surgery with or without postoperative anticoagulant use: total flap failure (A), pedicle thrombosis (B), and hematoma or bleeding (C).

thrombosis, or total flap failure. Our results suggested that, overall, post-free-flap surgery antithrombotic use may not reduce the rates of pedicle thrombosis and total flap failure (Fig. 3A–D).

Antithrombotic use increased bleeding rates in many studies.[7,11,15,17,20] In this meta-analysis, antiplatelets, and anticoagulants increased the pooled RR of bleeding/hematoma to 1.761 and 2.740, respectively (Fig. 4D, 5C). Numajiri et al reported that the rates of total flap failure and bleeding/hematoma were 3.3% and 8.3% in the heparin group, respectively, with both rates higher than those in the control group (1.6% and 0%).[17] A therapeutic dose of anticoagulants also increased the risk of total flap failure (**Supplemental Digital Content 3, http://links.lww.com/PRSGO/D207**), which may be because doctors tend to administer higher anticoagulant doses when there is vascular occlusion or a high risk of thrombosis during surgery. LMWH and dextran-40 combination was linked to a higher rate of bleeding/hematoma and total flap failure compared with LMWH alone for deep vein thrombosis prevention.[9,13] Therefore, surgeons should carefully consider whether the benefits of using antithrombotic agents outweigh the bleeding and complication risks.

In this meta-analysis, dextran-40 significantly reduced the risk of partial flap failure (Fig. 6D). Partial flap necrosis leads to wound dehiscence, inadequate soft tissue coverage for vital tissue, and potential complications including saliva leakage or deep neck infections. Patients may require a series of operations to reconstruct the area affected by the necrosis. The causes of partial flap failure include anastomosis insufficiency, bleeding/hematoma, embolism, thrombus, vessel kinking, vasospasms, and coagulopathies.[39–42] The distance between

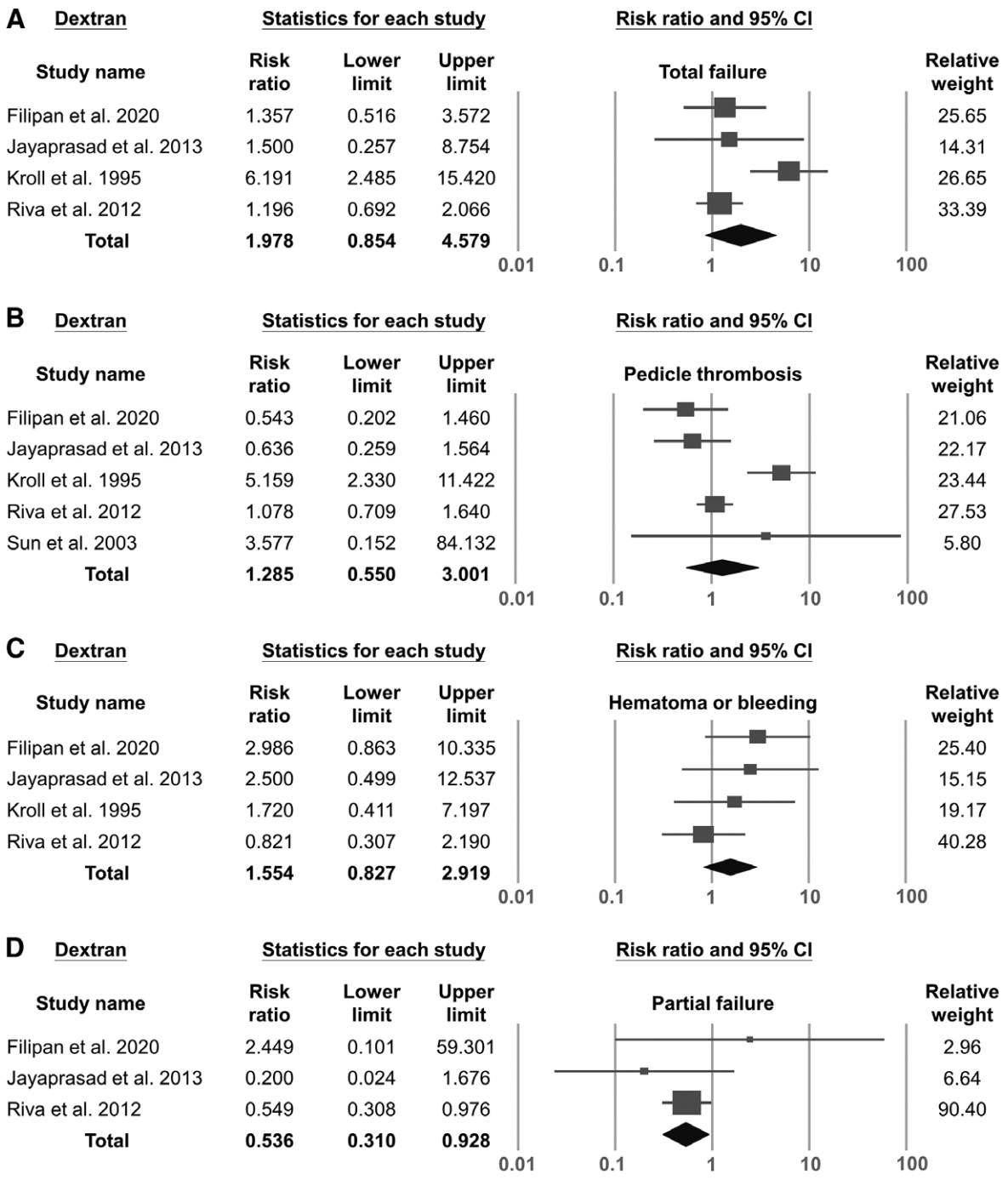

Fig. 6. Forest plot depicting patient outcomes after free flap surgery with or without postoperative dextran-40 use: total flap failure (A), pedicle thrombosis (B), hematoma or bleeding (C), and partial flap failure (D).

flap tissue and perforator is also positively correlated with the incidence of tissue necrosis, which increased from 10% to 22.9% when the distance extended from 8 cm to 12 cm.[43] Therefore, treatments enhancing intraflap blood flow may reduce the size and incidence of partial flap failure.

Dextran-40, a volume expander commonly used to treat shock, also exhibits antithrombotic functions, including hemodilution, enhancing fibrinolysis, reducing the platelet response to thrombin and decreasing the binding ability between platelets and fibrinogen.[13,31] It may improve local blood circulation and increase blood supply to the flap, reducing the risk of partial necrosis. All patients in the dextran-40 subgroup for partial flap failure analysis had undergone head and neck reconstruction, mostly due to cancer.[9,10,13] Cancer may affect the hypercoagulable state; thus, maintaining hemodilution may benefit this population.

PGE1 can enhance blood flow to the flap;[29,44] the maximal arterial blood flow within the postanastomosis vessel increased from 22.5 cm per second to 26.7 cm per second after 30 min of PGE1 administration.[44] However, limited studies have compared the effects of PGE1 on free flap outcomes, and the one included in this meta-analysis showed no impact of PGE1 on the rates of flap failure and pedicle thrombosis while demonstrating some augmenting effects on the risk of bleeding.[10] More studies comparing on the impact of increased blood flow on free flap outcomes are required to inform the clinical practice.

Although dextran-40 may reduce partial flap failure risk by approximately 46%, as estimated in this meta-analysis, its use is associated with the risk of severe complications, including atelectasis, pulmonary edema, adult respiratory distress syndrome, and anaphylaxis.[9,16,45,46] In a prospective randomized study on head and neck reconstruction, the incidence of cardiopulmonary complications was 29% and 51% after the administration of dextran-40 for 48 hours and 120 hours, respectively; the corresponding rate in the aspirin group was 7%.[16] Adult respiratory distress syndrome is a rare but very severe complication of dextran,[46] which can prolong the duration of mechanical ventilator use and intensive care unit stay, increasing the risk of death. Moreover, most previous studies failed to show any effects of dextran-40 on the rates of total flap failure and pedicle thrombosis.[9,10,13,21] In fact, patients treated with the combination of LMWH and dextran-40 had higher rates of bleeding/hematoma and total flap failure, compared with their counterparts treated with LMWH alone.[9,13] Consequently, although some evidence suggests that dextran-40 may help improve outcomes, its use requires a careful evaluation of risks and benefits, particularly the risk of pulmonary complications.

This study had some limitations. First, the number of eligible primary studies was relatively low, and many were small and retrospective and used diverse protocols. Comparing the outcomes of antithrombotic use is challenging, given the heterogeneity of doses and drug types and diversity of patients. Most patients had undergone head and neck free-flap reconstruction after cancer surgery, followed by breast reconstruction, and data on patients treated posttrauma or infection were insufficient. In contrast, despite the potential value of this analysis, we could not control for vein/interposition graft use due to the lack of data. These limitations preclude the creation of conclusive postoperative protocols. Further prospective studies on the effects of anticoagulants, antiplatelets, or treatments that increase the intraflap blood supply on partial flap failure are essential to achieve standardized approaches to antithrombotic therapies after free-flap surgery and future decision-making.

CONCLUSIONS

This meta-analysis demonstrated that postoperative antithrombotic use did not reduce the risk of total flap failure, partial flap failure, and pedicle thrombosis but increased that of bleeding/hematoma. In subgroup analysis, anticoagulant use (heparin, LMWH, and UFH) was associated with dose-related increases in the risk of bleeding or hematoma, compared with the risk of antiplatelet agent use (aspirin, PGE1, and ketorolac). Importantly, dextran-40 reduced the risk of partial flap failure. However, the risk of severe systemic complications associated with dextran-40, especially with long-term use, should be carefully considered. Further prospective studies are required to elucidate the effects of antithrombotics on free-flap surgery outcomes.

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DISCLOSURE

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