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REVIEW

Safety and efficacy of prothrombin complex concentrate (PCC) for anticoagulation reversal in patients undergoing urgent neurosurgical procedures: a systematic review and metaanalysis

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Abstract

Anticoagulant therapy poses a significant risk for patients undergoing emergency neurosurgery procedures, necessitating reversal with prothrombin complex concentrate (PCC) or fresh frozen plasma (FFP). Data on PCC efficacy lack consistency in this setting. This systematic review and metaanalysis aimed to evaluate efficacy and safety of PCC for anticoagulation reversal in the context of urgent neurosurgery. Articles from PubMed, Embase, and Cochrane databases were screened according to the PRISMA checklist. Adult patients receiving anticoagulation reversal with PCC for emergency neurosurgical procedures were included. When available, patients who received FFP were included as a comparison group. Pooled estimates of observational studies were calculated for efficacy and safety outcomes via random-effects modeling. Initial search returned 4505 articles, of which 15 studies met the inclusion criteria. Anticoagulants used included warfarin (83%), rivaroxaban (6.8%), phenprocoumon (6.1%), apixaban (2.2%), and dabigatran (1.5%). The mean International Normalized Ratio (INR) prePCC administration ranged from 2.3 to 11.7, while postPCC administration from 1.1 to 1.4. All-cause mortality at 30 days was 27% (95%CI 21, 34%; $I^2 = 44.6\%$; p-heterogeneity = 0.03) and incidence of thromboembolic events was 6.00% among patients treated with PCC (95%CI 4.00, 10.0%; $I^2 = 0\%$; p-heterogeneity = 0.83). Results comparing PCC and FFP demonstrated no statistically significant differences in INR reversal, mortality, or incidence of thromboembolic events. This metaanalysis demonstrated adequate safety and efficacy for PCC in the reversal of anticoagulation for urgent neurosurgical procedures. There was no significant difference between PCC and FFP, though further trials would be useful in demonstrating the safety and efficacy of PCC in this setting.

Keywords Prothrombin complex concentrate (PCC) · Neurosurgery · Neurosurgical procedures · Metaanalysis

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Introduction

Anticoagulant therapy is commonly used for the prevention of thromboembolic events including venous thromboembolism [18] and in the setting of atrial fibrillation [21]. Warfarin has historically been the mainstay of this treatment; however, in recent years, novel oral anticoagulants (NOACs) have become increasingly popular for many indications [26]. Anticoagulation introduces a substantial risk of major bleeding complications and also poses a challenge during surgical procedures [5]. Prior to elective surgical procedures, parenteral bridging therapies are used to normalize coagulation. In the setting of emergency, however, a more rapid reversal of anticoagulation is critical. This is particularly true for emergency neurosurgical procedures given the life-threatening consequences of intracranial hemorrhage (ICH).

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Reversal of oral anticoagulation may be achieved with several agents, including fresh frozen plasma (FFP), prothrombin concentrate complex (PCC), and recombinant factor VIIa [20]. FFP has been the historical standard; however, it is associated with a range of complications including allergic reactions, transfusion-related acute lung injury [29], transfusion-transmitted diseases [39], and transfusion-associated circulatory overload. PCC is a more recent alternative that is prepared from pooled plasma and exists as several different preparations, including 3F-PCC (containing coagulation factors II, IX, and X) and 4F-PCC (containing coagulation factors II, VII, IX, and X). Although PCC is more expensive than FFP, PCC has several practical advantages, including more rapid administration and action, no requirement for ABO compatibility, and lower administration volume resulting in lower risk of volume overload. Randomized controlled trials have demonstrated noninferiority and superiority of PCC over FFP in achieving rapid correction of the international normalized ratio (INR), including in the setting of major bleeding [44] and urgent general surgical procedures [24]. Neurosurgery, however, represents a uniquely sensitive context in which even minor differences in time or mass effect can have significant impacts. It therefore warrants separate consideration of anticoagulation protocols.

Studies examining PCC in neurosurgical populations have focused largely on anticoagulation-related ICH irrespective of the treatment modality and have established the efficacy of PCC in this setting [27, 31, 37, 40, 49, 54]. However, the data are less consistent for patients undergoing emergency neurosurgery. This metaanalysis was performed to assess the efficacy and safety of PCC in patients undergoing urgent neurosurgical procedures.

Methods

Comprehensive search

The study was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) extension statement for the reporting of systematic reviews [28]. This search was performed using Cochrane, Embase, and PubMed databases from inception through November 2019. Title and abstract screening and full text screening were performed using Covidence [52].

Study selection

Studies were selected according to predefined inclusion and exclusion criteria. Inclusion criteria captured studies reporting outcomes for patients aged > 18 years who received PCC for the reversal of anticoagulation prior to urgent neurosurgical procedures. Exclusion criteria included nonEnglish language papers, case reports, conference abstracts, nonurgent neurosurgical procedures such as elective tumor resection, nonneurosurgical procedures, and the use of additional reversal agents such as idarucizumab and andexanet alfa. The included anticoagulant agents were either vitamin K antagonists (warfarin and phenprocoumon) or direct factor Xa inhibitors (apixaban, rivaroxaban, and dabigatran).

Data extraction

Abstract and full text screening, data extraction, and study quality grading were performed by two independent authors for each paper, with disputes resolved either by discussion or by a senior author (RAM, AB). The extracted data included demographic data, indications for surgery and anticoagulants used, magnitude of INR reversal achieved by intervention, 30-day mortality, and incidence of thromboembolic complications. Additional planned outcome measures such as length-of-stay, duration of hemostasis, and the time for INR reversal could not be extracted or pooled due to inconsistent reporting.

Risk of bias assessment

Study quality was assessed based on the study design. Case series were graded based on factors such as a clear study objective, well defined protocols, explicit inclusion/exclusion criteria, specified time interval for patient recruitment, consecutive patient enrollment, clinically relevant outcomes, prospective outcomes for data collection, and follow-up rate [16]. The Newcastle Ottawa scale was used to rate the quality of comparative observational studies. Case-control studies were assessed based on case definitions, representative cases, selection of controls, comparability of case and control, ascertainment of exposure, and nonresponse rate [47]. Cohort studies were scored based on representation of exposed cohort, selection of exposed cohort, ascertainment of exposure, comparability of cohort based on study designs or analysis, assessment of outcome, and the adequacy of follow-up of cohorts [47].

Data analysis

Pooled incidence was calculated for each outcome with random effects modeling to observe both between and within study variances. When available, difference in means comparing PCC and FFP were pooled. The DerSimonian and Laird approach was utilized to estimate variances between studies [19]. For heterogeneity present among studies, Cochrane Q statistics were calculated using the chi-square test, with p-values of < 0.10 indicating significant heterogeneity [25]. I squared values were calculated to show the percentage of between-study heterogeneity, with values > 50% indicating a

high statistical heterogeneity. For the magnitude of INR reversal achieved by PCC, subgroup analysis by anticoagulant type (warfarin vs. phenprocoumon) was conducted. Publication bias was assessed by using a funnel plot for visual determination of asymmetry and by using Begg's and Egger's tests for statistical significance [4, 45, 50]. Statistical analysis was conducted using the Comprehensive Meta-Analysis V3 (copyright 1998–2018, Biostat, Inc.) software.

Results

The initial search returned a total of 4505 articles. After removal of duplicates, abstract screening, and full text screening, 18 studies [1–3, 6–10, 12–14, 17, 33, 35, 41, 53, 55, 56] remained eligible for inclusion in this metaanalysis (Fig. 1). Common reasons for exclusion were nonurgent neurosurgical procedures such as elective tumor resections, results not stratified by intervention, case reports, and nonEnglish language articles. Of the included studies, 13 were case series, 3 were cohort studies, and 2 were case control studies. A total of 565 patients were included, comprising 435 (77%) patients treated with PCC and 130 (23%) with FFP. The mean number of included patients per study was 33 (range 5 to 128), and the median gender distribution was 60% male. The mean study quality was 6 for case series (range 3 to 8) and 8.5 for case control and cohort studies (range 8 to 9). Extractable data on the type of anticoagulant used were available for 454 patients, with prescribed anticoagulants including warfarin ($n = 378$), phenprocoumon ($n = 28$), apixaban ($n = 10$), rivaroxaban ($n = 31$), and dabigatran ($n = 7$). Indications for therapy included atrial fibrillation, prosthetic heart valves, deep vein thrombosis, cardiomyopathy, and arteriovenous fistulas. Emergency procedures included decompressive craniectomy, intracranial hematoma evacuation, external ventricular drain placement or replacement, and urgent tumor resection. The numbers of patients for each indication and procedure were not extractable (Table 1).

INR

Fourteen studies [1, 3, 6–8, 12–14, 17, 33, 35, 41, 53, 55] (266 patients) reported INR data before and after PCC administration. The mean INR prior to intervention ranged from 2.3 to 11.7. Following PCC administration, the INR value dropped and ranged from 1.1 to 1.4. Comparative INR data for both PCC- and FFP-administered patients were reported by 3 studies [1, 13, 14] (195 patients). The pooled mean INR reduction following anticoagulation reversal was greater by 0.11 in the FFP group than the PCC group (95% CI −0.02, 0.25; $I^2 = 0\%$; p-heterogeneity = 0.70), although this difference was not statistically significant ($p = 0.11$) (Fig. 2). Patients treated with PCC were further stratified by anticoagulant agent, with a greater reduction in INR observed in patients treated with warfarin (mean reduction −1.83; 95% CI-2.46, −1.20; $I^2 = 97.0\%$; p-heterogeneity < 0.01) than in patients treated with phenprocoumon (mean reduction −1.61; 95% CI −2.91, −0.32; $I^2 = 58.2\%$; p-heterogeneity = 0.12). Nevertheless, this difference between warfarin and phenprocoumon was not statistically significant (p-interaction = 0.77) (Fig. 3). Subgroup data for NOAC anticoagulants were not extractable.

Mortality

Seventeen studies [1–3, 6–10, 12–14, 17, 33, 35, 41, 53, 56] (412 patients) reported mortality data for PCC patients, with a pooled mortality incidence of 27.0% (95% CI 21.0, 34.0%; $I^2 = 44.6\%$; p-heterogeneity = 0.03). The mortality incidence reported by individual studies ranged from 5 to 57% for patients treated with PCC. Only two studies (124 patients) reported mortality for patients treated with FFP, giving a pooled mortality rate of 21.0% (95% CI 15.0, 29.0%; $I^2 = 0\%$; p-heterogeneity = 0.51). The difference in mortality incidence comparing patients treated with PCC to those treated with FFP was not statistically significant (p-interaction = 0.26) (Fig. 4).

Thromboembolic events

Data on thromboembolic complications were reported for PCC patients in 15 studies [1–3, 6–8, 10, 12, 13, 17, 33, 35, 41, 53, 56] (283 patients) and for FFP patients in 2 studies [1, 13] (124 patients). The pooled incidence of thromboembolic events among patients treated with PCC was 6.00% (95% CI 4.00, 10.0%; $I^2 = 0\%$; p-heterogeneity = 0.83). The incidence reported by individual studies ranged from 1.00 to 14.0%. Among patients treated with FFP, the pooled incidence of thromboembolic events was 1.00% (95% CI 0.00, 6.00%; $I^2 = 0\%$; p-heterogeneity = 0.65). The difference between the PCC and FFP groups was not statistically significant (p-interaction = 0.054) (Fig. 5).

PCC protocols

The protocols for PCC administration are presented in Table 2. Thirteen studies [2, 6–10, 13, 33, 35, 41, 53, 55, 56] used 4F-PCC and 3 [3, 12, 17] used 3F-FFP. Three studies [12, 14, 53] calculated PCC dosing base on body weight; 2 studies [33, 35] based on body weight and initial INR; 3 studies [6–8] based on body weight, initial INR, and target INR; 1 study [41] based on initial INR alone; 2 studies [9, 10] based on the treating doctor's discretion; and 4 studies [2, 3, 13, 56] used a fixed PCC dose.

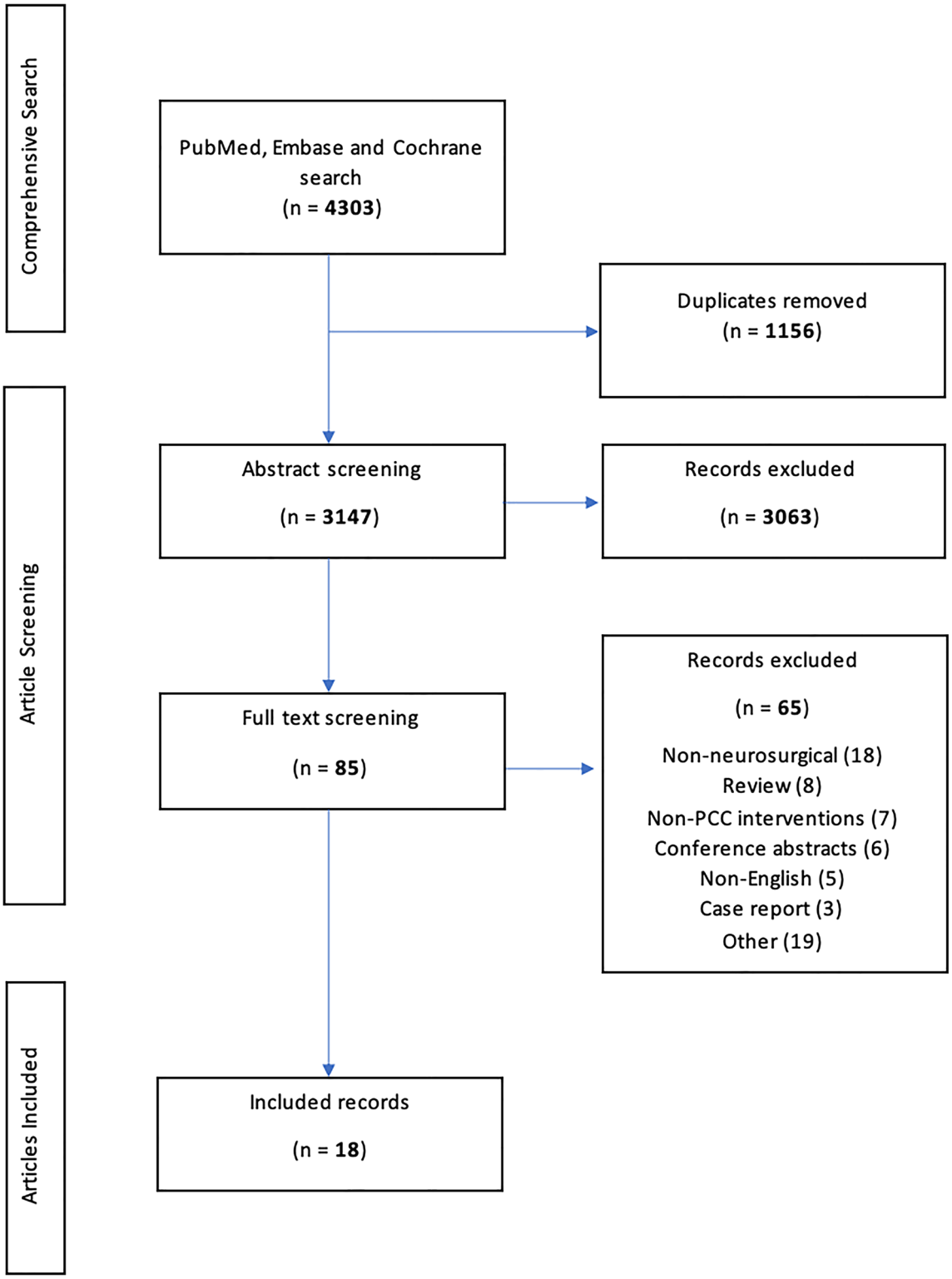

Fig. 1 PRISMA flow-chart for systematic review identifying articles reporting the use of PCC for anticoagulation reversal prior to urgent neurosurgical procedures

Discussion

This metaanalysis demonstrated no significant differences in INR reversal, mortality, and incidence of thromboembolic complications between PCC and FFP for the reversal of anticoagulation in patients undergoing emergency neurosurgery procedures. To the best of our knowledge, this is the first metaanalysis of PCC in neurosurgical patients requiring

Table 1 Characteristics of the included studies

Study	Study design and timing	Intervention (number of patients)	Mean age (years)	Male %	Anticoagulant type	Indications for surgery	Study quality[1]
Comparative observational studies: cohorts ($n = 3$)							
Beynon, 2019 [10]	Retrospective, cohort	PCC (128)	Not specified	76	Warfarin, apixaban, rivaroxaban, dabigatran, endoxaban	ICH	9
Agarwal, 2018 [1]	Retrospective, cohort	PCC (28) FFP (35)	67.3	62	Warfarin	ICH	9
Rizos, 2010 [40]	Prospective, Cohort	PCC (5)	77	50	Phenoprocoumon	ICH	9
Comparative observational studies: case controls ($n = 2$)							
Carothers, 2018 [13]	Retrospective, case-control	PCC (31) FFP (89)	77	61	Warfarin	ICH, traumatic brain injury	8
Cartmill, 2000 [14]	Prospective, case-control	PCC (6) FFP (6)	65	50	Warfarin	ICH	8
Noncomparative observational studies: case series ($n = 13$)							
Beynon, 2019 [10]	Retrospective, case series	PCC (10)	80	50	Apixaban, rivaroxaban, endoxaban	Spinal tumor, spinal empyema, spinal hematoma	6
Allison, 2018 [2]	Retrospective, case-series	PCC (31)	73	46	Rivaroxaban, apixaban	ICH, traumatic brain injury	7
Mačiukaitiene, 2018 [34]	Retrospective, case-series	PCC (35)	67.5	49	Warfarin	ICH	7
Yoshimura, 2017 [54]	Prospective, case-series	PCC (10)	72.5	60	Rivaroxaban, apixaban, dabigatran, edoxaban	ICH	6
Beynon, 2015 [8]	Retrospective, case-series	PCC (5)	70.6	60	Phenoprocoumon	Brain tumor	7
Beynon, 2015 [7]	Retrospective, case-series	PCC (9)	65.5	11	Phenoprocoumon	Aneurysmal ICH	7
Beynon, 2014 [6]	Retrospective, case-series	PC (18)	76.2	61	Phenoprocoumon	Spinal tumor, spinal hematoma	7
Yanamadala, 2014 [53]	Prospective, case series	PCC (5)	NA	Not specified	Warfarin	ICH, hydrocephalus	3
Cabral, 2013 [12]	Retrospective, case-series	PCC (8)	72.8	63	Warfarin	ICH, hydrocephalus	8
Barillari, 2012 [3]	Retrospective, case series	PCC (23)	23	96	Warfarin, acenocoumarol	ICH	5
Chong, 2010 [17]	Retrospective, case-series	PCC (7)	62.2	57	Warfarin	ICH	3
Vigué, 2007 [51]	Prospective, case-series	PCC (18)	71	Not specified	Not specified	ICH, hydrocephalus	6
Lankiewicz, 2006 [32]	Retrospective, case-series	PCC (58)	67.2	Not specified	Warfarin	ICH, hydrocephalus	7

[1] Case series were graded using a scale developed by Chan and Bhandari [16], based on factors such as a clear study objective, well defined protocols, explicit inclusion/exclusion criteria, specified time interval for patient recruitment, consecutive patient enrollment, clinically relevant outcomes, prospective outcomes for data collection and follow-up rate. The Newcastle Ottawa scale was used to rate the quality of comparative observational studies. Case-control studies were assessed based on case definitions, representative cases, selection of controls, comparability of case and control, ascertainment of exposure, and non-response rate [45]. Cohort studies were scored based on representation of exposed cohort, selection of exposed cohort, ascertainment of exposure, comparability of cohort based on study designs or analysis, assessment of outcome, and the adequacy of follow up of cohorts [45]

FFP Fresh frozen plasma; *ICH* intracranial hemorrhage; *PCC* prothrombin complex concentrate

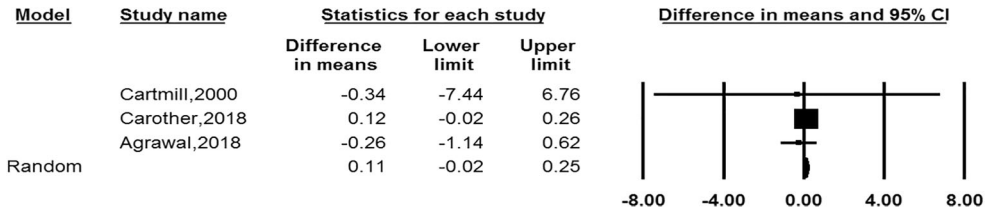

Fig. 2 Comparison of mean INR reduction following PCC and FFP administration prior to urgent neurosurgery, with the mean INR reduction being greater by 0.11 for patients treated with PCC than those treated with FFP

urgent surgical procedures. PCC was associated with adequate INR reversal and safety profile underscoring its value in neurosurgical procedures and supporting common practice. In nonneurosurgical contexts, the use of PCC is supported by robust evidence demonstrating decreased mortality [15, 49], increased hemostasis rates [44], and more rapid INR correction [15, 44, 49, 54] when compared with FFP. In the setting of trauma-associated bleeding, for example, the European Critical Care Guidelines have a grade 1A recommendation (strong recommendation based on highest quality evidence) for the use of PCC in the reversal of anticoagulation [46]. Similarly, for ICH associated with oral anticoagulation, the Neurocritical Care Society and Society of Critical Care Medicine guidelines recommend the use of PCC over FFP based on moderate quality evidence [23]. In the context of urgent neurosurgery, the advantages of PCC, particularly its rapid administration, rapid INR correction, and lower administration volume, may provide substantial benefits given the sensitivity and urgency of neurosurgical presentations. The reduced time to INR correction achieved with PCC is a particularly important factor in emergency, time-critical neurosurgery. Data on the timing of anticoagulation reversal could not be systematically analyzed in this paper due to inconsistent reporting in the included studies; however, the rapid onset of PCC's therapeutic effect is well established [15, 54]. PCC also has a more favorable safety profile than FFP, due to a lack of blood group specificity and a viral inactivation process that minimizes infectious disease transmission [34]. Further, when accounting for administration times and subsequent blood product requirement, several models have found PCC to be cost-effective relative to FFP [24, 30]. The incidence of thromboembolic complications among patients treated with PCC in our metaanalysis (6.1%) was consistent with the existing literature on anticoagulation reversal in nonneurosurgical contexts. The reported incidence of thromboembolic events following PCC administration range from 1.4 to 10.4% [18, 22, 36, 38, 43, 51], with the variability related in large part to differences in study methodology. For example, in their large metaanalysis, Dentali et al. [18] reported thromboembolic complications in just 12 of 1032 patients (1.4%), with all reported thromboembolic events occurring within 4 days of PCC treatment. In their study of 4F-PCC, Santibanez et al. [43] reported thromboembolism in 10.4% of patients (and in 17% of patients undergoing urgent surgery), however included events occurring up to 14 days following PCC administration. The studies included in our metaanalysis demonstrated similar variability, with reported thromboembolic event incidence ranging from 1.5 to 14.3%. The low incidence of venous thromboembolic complications among FFP patients in our study (0.9%) may be an artifact related to the relatively small number of included FFP studies and patients and was not consistent with rates reported in the broader literature. For example, in a large systematic review, the rate of venous thromboembolic complications among patients treated with FFP was 4.8% [15] (similar to the 4.2% rate observed in the PCC group). In a study specifically designed to detect venous thromboembolic complications with active surveillance, the rate of such complications following FFP was 20.2% [57]. Mortality rates are highly cause-specific, and the 26% mortality incidence reported for urgent neurosurgical patients in our metaanalysis cannot be meaningfully compared with literature in other areas. Additional clinical

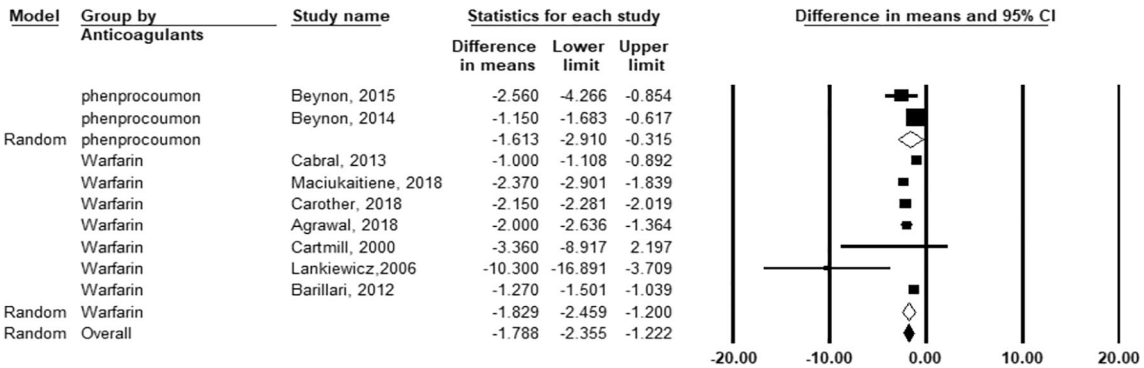

Fig. 3 Comparison of the mean INR reduction following PCC administration prior to urgent neurosurgery, stratified by anticoagulant, with no statistically significant difference between warfarin and phenprocoumon

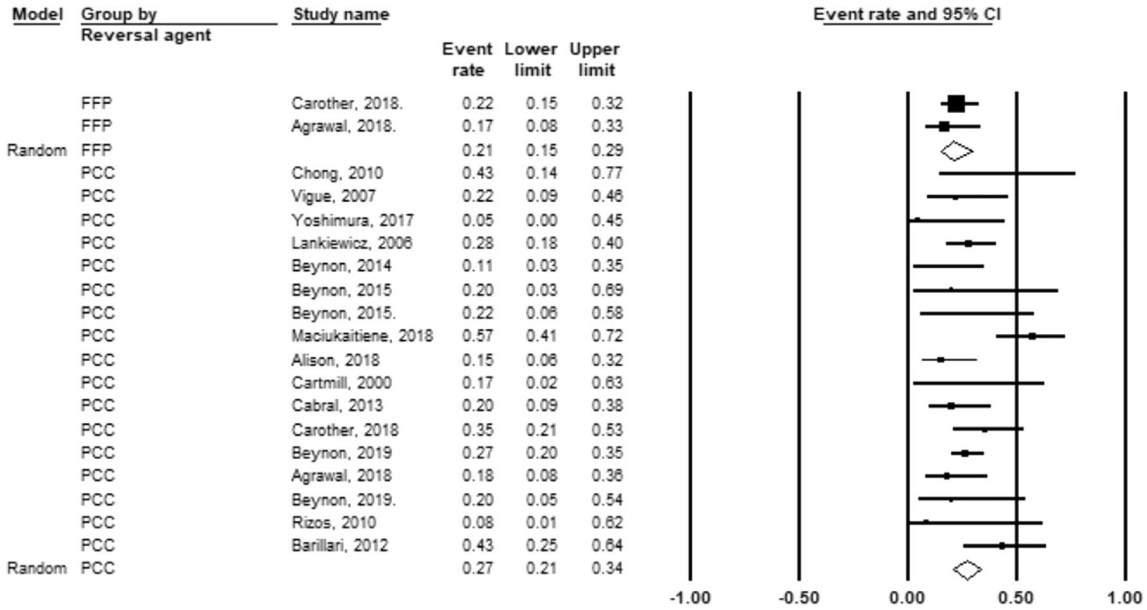

Fig. 4 Comparison of 30-day all-cause mortality following PCC and FFP administration prior to urgent neurosurgery

or radiological outcome variables were reported sporadically and inconsistently in the included studies and, therefore, could not be systematically analyzed. However, reported mortality rates demonstrated the high risk of poor outcome in anticoagulated patients with neurosurgical pathology [42, 48], even with the use of PCC or FFP to achieve anticoagulation reversal and therefore expedited surgical treatment. Therefore, careful prognostication of neurosurgical patients is warranted, and the risks and benefits of such intervention should be carefully weighed. Although subgroup analysis based on the type of anticoagulant was not possible, our metaanalysis included at least 48 patients treated with NOACs. While several in vivo and in vitro studies have suggested efficacy of PCC in the reversal of NOACs [11], data remain limited. Moreover, other specific reversal agents have recently been approved, e.g., idarucizumab (for dabigatran), andexanet alfa (for factor Xa inhibitors), or are under investigation, e.g., aripazine (universal); however, the widespread use of such agents is limited by high cost and inconsistent availability. Our study suggested that in the absence of specific NOAC antidotes, PCC may be a viable and accessible alternative for the reversal of emergency NOAC anticoagulation. Further studies of NOAC populations and subgroup analysis of individual NOACs should be considered to provide more specific data. Importantly, INR may not reflect the true extent of the anticoagulation effect produced by NOACs, and future studies should include analysis of additional parameters such as antiXa assays. Our review found wide a variation in PCC administration protocols, which might have a substantial impact on a range of outcomes,

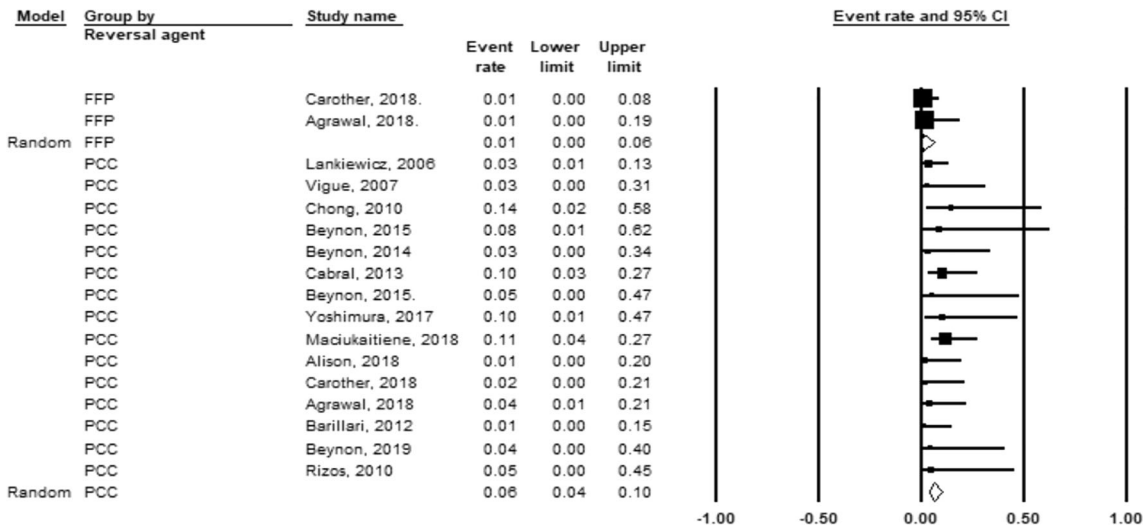

Fig. 5 Comparison of thromboembolic event incidence following PCC and FFP administration prior to urgent neurosurgery

Table 2 PCC administrating and dosing protocols in the included studies

Study	3F-PCC or 4F-PCC	Protocol dose	Dosing strategy
Comparative observational studies: cohorts ($n = 3$)			
Beynon, 2019 [9]	4F-PCC	Not reported	Doctor's discretion
Agarwal, 2018 [1]	Not reported	Not reported	Not reported
Rizos, 2010 [40]	4F-PCC	500 IU if INR 1.5–2.0 1000 IU if INR > 2.0	Initial INR
Comparative observational studies: case controls ($n = 2$)			
Carothers, 2018 [13]	4F-PCC	1000 IU	Fixed dose
Cartmill, 2000 [14]	Not reported	50 IU/kg	Body weight
Noncomparative observational studies: case series ($n = 13$)			
Beynon, 2019 [10]	4F-PCC	Not reported	Doctor's discretion
Allison, 2018 [2]	4F-PCC	35 IU/kg	Fixed dose
Mačiukaitiene, 2018 [34]	4F-PCC	23 IU/kg–3000 IU	Body weight and initial INR
Yoshimura, 2017 [56]	4F-PCC	1000 IU	Fixed dose
Beynon, 2015 [8]	4F-PCC	25–50 IU/kg	Body weight and initial INR and target INR
Beynon, 2015 [7]	4F-PCC	25–50 IU/kg	Body weight and initial INR and target INR
Beynon, 2014 [6]	4F-PCC	25–50 IU/kg	Body weight and initial INR and target INR
Yanamadale, 2014 [55]	4F-PCC	1500–200 IU	Not reported
Cabral, 2013 [12]	3F-PCC	Mean 28.3 IU/kg	Body weight
Barillari, 2012 [3]	3F-PCC	500 IU	Fixed dose
Chong, 2010 [17]	3F-PCC	1000-3000 IU	Not reported
Vigué, 2007 [53]	4F-PCC	20 IU/kg	Body weight
Lankiewicz, 2006 [33]	4F-PCC	25–50 IU/kg	Body weight and initial INR

INR International normalized ration; *IU* international units; *PCC* prothrombin complex concentrate

including the speed and efficacy of INR reversal and the risk of thromboembolism and hemorrhage. A lack of standardized terminology and definitions precluded further quantitative analysis of protocol efficacy, as it had in previous studies. In a large 2016 systematic review of PCC administration, Khorsand et al. [32] found similar and favorable results with a range of predefined dosing protocols, including fixed dosing and dosing based on bodyweight; bodyweight and initial INR; and bodyweight, initial INR and target INR. Poorer INR outcomes were observed with dosing according to doctors' discretion. Further, standardized research would be useful in clarifying this area of ongoing debate. The differences between PCC and FFP found in our study are likely related in large part to differences in the study populations, given that only 3 studies allowed direct comparison between PCC and FFP. Of those studies, one demonstrated similar rates of thrombotic complications between the PCC and FFP groups [1], and another demonstrated similar rates of mortality and thromboembolic complications, but more rapid and more effective INR reversal in patients treated with PCC [13]. Cartmil et al. [14] similarly demonstrated a more rapid INR reversal among PCC patients, though there was insufficient data to assess INR reversal times in our metaanalysis. The small number of studies reporting outcomes for both PCC and FFP is a significant limitation of this metaanalysis, likely resulting in differences in study protocol, baseline population characteristics, and nature or severity of the presenting neurological illnesses. In addition, the small number of studies reporting FFP outcomes and the relatively small number of FFP patients are an important limitation of the comparative results. Particularly in cases of time-sensitive neurosurgical pathology, local differences in practice may result in a variety of biases that could impact external validity and comparability. Another important limitation is the lack of randomized studies, which prevented balanced comparisons of PCC and FFP in the setting of emergent neurosurgical procedures. Finally, the inability to stratify results by the indication for surgery may be an important limitation. Nuances in the underlying pathology and purpose of anticoagulation reversal may impact the outcomes of PCC or FFP administration. For example, in the setting of ICH, anticoagulation reversal is essential in limiting hematoma expansion, whereas in the setting of ischemic stroke, anticoagulation reversal prior to decompressive surgery may contribute to the underlying thrombosis and exacerbate ischemia. Although our results suggested that the efficacy and safety profile of PCC and FFP were similar in the setting of urgent neurosurgical procedures, further randomized studies would help address the limitations of this study and provide comparative data in this high-risk population.

Conclusion

This metaanalysis demonstrated acceptable INR reversal, 30-day mortality, and thromboembolic event incidence among patients receiving PCC prior to urgent neurosurgical procedures, with no statistically significant differences in outcomes between PCC and FFP. Randomized evidence is required to better understand the optimal management of anticoagulation in this sensitive context.

Data availability Not applicable.

Compliance with ethical standards

Conflict of interest The authors report no disclosures or conflicts of interest.

Conflict of interest The authors declare that they have no conflict of interest.

Ethics approval Ethics committee approval was not sought as this study analyzed published data.

Consent to participate Not applicable.

Consent for publication Not applicable.

Code availability Not applicable.

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