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Four-factor Prothrombin Complex Concentrate During Liver Transplantation: A Retrospective Cohort Study

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Background. Four-factor prothrombin complex concentrate (PCC) is a plasma product that contains factors II, VII, IX, X, protein C, and protein S. PCC can be used off-label to treat coagulopathy during orthotopic liver transplantation (OLT). However, its use comes with safety concerns regarding thrombosis. The purpose of our study is to determine the safety of PCC in OLT. **Methods.** We conducted a retrospective cohort study of patients who received 4-factor PCC during OLT at our institution from January 1, 2018, to May 1, 2022, with a 1:1 match of 83 patients who received PCC and 83 patients who did not. We evaluated 30-d mortality, 1-y mortality, prevalence of thrombotic complications (portal vein thrombosis, deep venous thrombosis, myocardial infarction, and pulmonary embolus), and postoperative intensive care (ICU) length of stay (LOS). **Results.** There was no significant difference in 30-d mortality (odds ratio [OR] 5; 95% confidence interval [CI], 0.58-42.8; $P = 0.14$), 1-y mortality (OR 3; 95% CI, 0.61-14.86; $P = 0.18$), or ICU LOS (OR –13.8; 95% CI, –39.2 to 11.6; $P = 0.29$). There was no increased incidence of thrombotic complications among patients receiving PCC 90 d after surgery, including portal vein thrombosis (OR 1.5; 95% CI, 0.42-5.32; $P = 0.53$), pulmonary embolus (OR 1; 95% CI, 0.14-7.1; $P = 0.99$), deep venous thrombosis (OR 0.67; 95% CI, 0.11-3.99; $P = 0.66$), and myocardial infarction (OR 1.67; 95% CI, 0.4-6.97; $P = 0.48$). **Conclusions.** Although there was a statistically insignificant increase in mortality after PCC administration during OLT, we did not see a significant increase in perioperative complications, including thrombotic events and increased ICU LOS.

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Patients with end-stage liver disease (ESLD) pose a unique challenge because of their unpredictable procoagulant and anticoagulant hemostatic changes. The coagulopathy seen in this group may be multifactorial and results from platelet dysfunction and decreased synthesis of coagulation factors that may impact both pro- and antifibrinolytic proteins.[1] This complex dynamic predisposes these patients to complications from both hemorrhage and thrombosis. The unpredictable balance between hyper- and hypocoagulability is precarious, and several factors, such as infection, surgery, transfusion, blood loss, or hypothermia, can tip the balance toward life-threatening thrombosis or significant bleeding. Traditional laboratory testing, such as prothrombin time or international normalized ratio, may deceptively suggest a hypocoagulable state and may underestimate hypercoagulability because these tests are not sensitive to deficiencies of anticoagulant proteins.[2]

Orthotopic liver transplantation (OLT) is a high-risk surgery for patients with end-stage liver disease (ESLD) that commonly requires transfusion of blood products to achieve hemostasis without precipitating thrombosis. Transfusion of blood products during OLT is associated with higher mortality risk, reduced graft survival, and postoperative complications.[3] Accurately measuring the hemostatic balance during OLT and judicious correction of coagulopathy with transfusion of packed red blood cells, fresh frozen plasma, platelets, cryoprecipitate, and antifibrinolytics is paramount. Disadvantages of traditional blood product administration

include the need for collection, storage, risk of infection, potential for ABO incompatibility, transfusion-related lung injury, and transfusion-associated circulatory overload. In OLT, a major disadvantage to transfusion of these blood products is hypervolemia, especially given the high number of blood products that can be required during this operation. Transfusion-associated circulatory overload and hypervolemia are especially problematic in patients with cirrhosis as relative fluid overload in the splanchnic venous system may increase central venous and portal venous blood pressures and trigger portal and splanchnic hypertension, a known risk factor for bleeding during OLT.[4,5]

Four-factor prothrombin complex concentrate (PCC) is a plasma product containing 4 vitamin K–dependent factors (II, VII, IX, and X), protein C, and protein S in concentrations 25× greater than fresh frozen plasma.[1,6,7] Kcentra (CSL Behring, King of Prussia, PA) is the only Food and Drug Administration–approved 4-factor PCC in the United States and is currently Food and Drug Administration–approved for urgent reversal of acquired coagulopathy from vitamin K antagonism during major bleeding. This is not to be confused with the 1-factor factor VII (FVII) concentrate. These findings cannot be extrapolated to FVII, and we are not advocating its administration. However, PCC has also been used to treat coagulopathy intraoperatively during OLT in off-label use.[8] The advantage of PCC use is the reduction in volume administered to a patient compared with the volume of traditional products to achieve the same effect. However, the use of PCC has been associated with thrombotic complications in other settings and could theoretically result in venous thromboembolism (VTE), pulmonary embolism (PE), deep vein thrombosis (DVT), portal vein thrombosis (PVT), acute myocardial infarction (MI), and intracardiac thrombosis (ICT) during OLT.[6] As such, little evidence exists evaluating the safety of PCC during OLT.

As a busy liver transplant center that has successfully used PCC to treat perioperative hemorrhage, we hypothesized that 4-factor PCC is safe for reversing coagulopathy during OLT and is not associated with an increased risk of thrombotic complications or mortality. The primary aim of this study was to determine whether mortality significantly increased in patients who received PCC compared with patients who did not receive PCC during OLT. The secondary aim of this study was to compare the incidence of thrombotic complications, such as VTE, PE, DVT, PVT, MI, and ICT; need for reoperation within 72 h; and intensive care unit (ICU) length of stay (LOS) in patients receiving PCC during OLT versus those who did not.

MATERIALS AND METHODS

We conducted a retrospective cohort study to compare the mortality rate and complications of PCC in adult patients undergoing OLT who received PCC between 24 h before surgery and 24 h after surgery versus patients who did not receive PCC within that interval (see Figure 1). Although we do not have a formal protocol for PCC administration at our institution, we administer PCC in the setting of refractory bleeding after other products and reversals have been attempted as guided by traditional coagulation testing and thromboelastogram. It is used as salvage therapy and not as frontline treatment. It is administered in 500-unit increments at the discretion of the anesthesiologist until adequate hemostasis is achieved. We conducted a retrospective analysis of primary, single-organ liver transplant surgical data performed at our center between January 1, 2018, and May 1, 2022. Data were obtained from the hospital's electronic medical records (EMRs). Institutional review board approval was received.

Dependent Variables

A total of 11 different outcomes of interest were identified. The primary outcomes were 30-d and 1-y mortality. Secondary outcomes included ICU LOS, need for reexploration within 72 h, and new postoperative diagnoses of thromboembolic complications within 90 d after surgery. Thromboembolic complications included DVT, PE, PVT, VTE, ICT, and MI. Diagnosis codes (**Table S1, SDC,** http://links.lww.com/TXD/A651) retrieved all outcomes within 90 d of surgery. Information regarding ICU LOS was obtained from the EMR.

Independent Variables

Patient characteristics, such as age, sex, body mass index (BMI), and the last biologic model for ESLD (MELD) score recorded before surgery, were extracted from the EMR and used for matching. Patients' baseline intraoperative fibrinogen and hemoglobin levels were also included in the analysis. The primary independent variable in this study was the administration of 4-factor PCC on the day of OLT surgery coded as a binary variable (1 = administered, 0 = not administered). BMI and MELD were treated as continuous variables. Age was divided into 3 categories: younger than 50 y, 50–65 y, and older than 65. The first intraoperative fibrinogen levels were divided into 3 categories: <200 mg/dL (hypofibrinogenemia), 200–400 mg/dL (normal), and >400 mg/dL (hyperfibrinogenemia). Intraoperative hemoglobin results were also categorized into 3 categories: <12 g/dL (anemia), 12–17 g/dL (normal), and >17 g/dL (polycythemia). Patients who had a preoperative diagnosis of DVT, pulmonary embolism (PE), or PVT before surgery were combined to create a preoperative VTE variable, which was also included in the match. Patients who had a preoperative diagnosis of thromboembolic disease (VTE group) were excluded from analysis for the outcome of postoperative VTE, although these patients were propensity matched and their outcomes of ICU LOS and mortality were analyzed. An Elixhauser score,[9] which assesses multiple comorbidities in patients, was calculated and patients were categorized into 2 groups: those with a score >8 and those with a score <8.

Statistical Analysis

Patients who received PCC were matched with patients who did not receive PCC during surgery based on their Elixhauser score. The variables used for matching are summarized in Table 1. The matching algorithm used nearest neighbor matching (1:1) with a caliper width of 0.03 SDs of the logit of the propensity score. Standardized mean differences (SMDs) of <0.1 were used to determine the balance between the matched groups. After matching, conditional logistic regression was used to assess the association between PCC administration and postoperative complications, adjusting for covariates. Similarly, linear regression was used to determine the estimates of the numeric outcome variable (ICU LOS). A P value of <0.05 was used to determine statistically significant differences between the 2 groups. Based on the sample size of

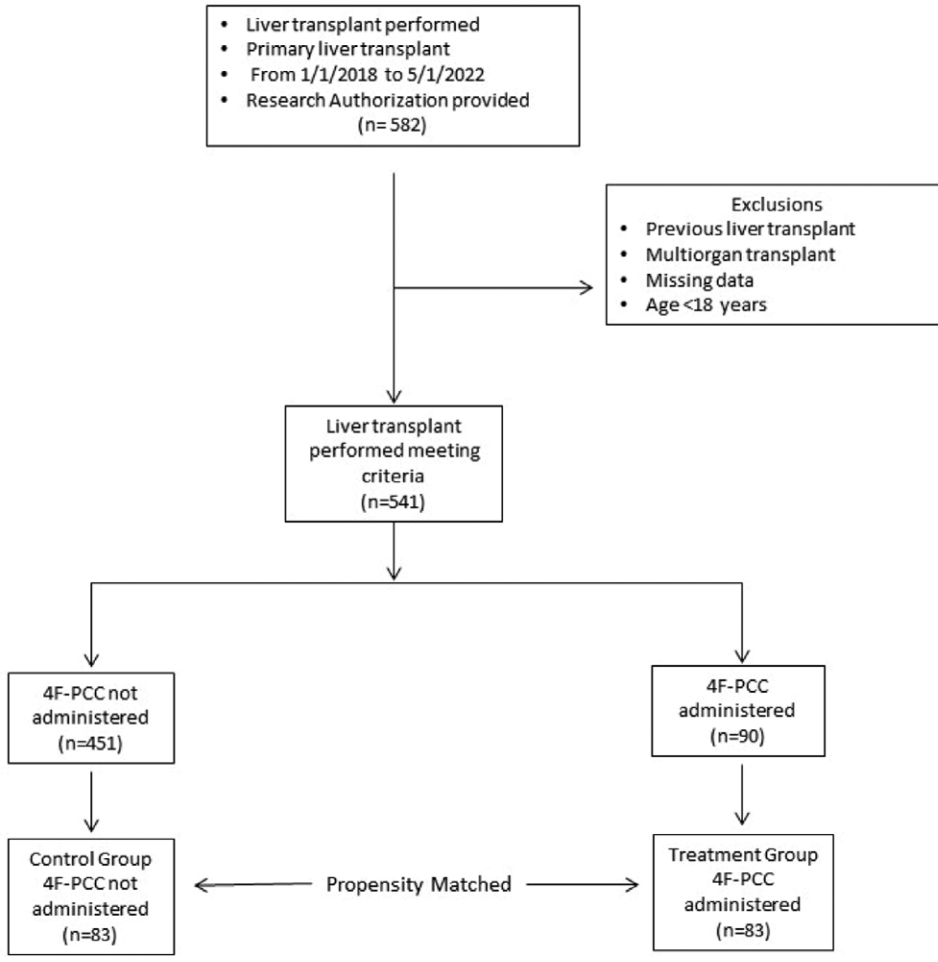

FIGURE 1. Selection of study population. 4F-PCC, 4-factor prothrombin complex concentrate.

83 in each group, we detected an effect size of 0.23 with an alpha of 0.05 and 80% power on a 2-tailed test. All analyses were conducted using R (version 4.1.0, R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

Table 1 summarizes the baseline characteristics of patients who received PCC and those who did not before the matching process. There are no significant differences in the BMI, age, sex, and MELD score between the 2 groups. However, there are significant differences in the distribution of fibrinogen levels between the 2 groups, with 67.8% (61/90) of those in the PCC group in fibrinogen levels <200 compared with 45.5% (205/451) of those in the control group ($P < 0.001$). Significant differences were also observed in the distribution of hemoglobin levels as the mean value in the PCC group was 9.4 ± 1.1 g/dL, compared with the control group with a mean value of 9.9 ± 1.4 g/dL ($P = 0.002$). Patients in the PCC group had a nonstatistically significant greater rate of higher comorbidities, with 68.9% of patients (62/90) having an Elixhauser score of >8 compared with 58.1% of patients (262/451) in the control group ($P = 0.056$). There were also significant differences in the number of patients who experienced previous VTE, with 37.8% of patients (34/90) in the PCC group compared with 21.3% of patients (96/451) in the control group. As shown in Table 2, the SMD value of 0.71 between the unmatched groups indicated a large imbalance before matching. However, after propensity score matching, the SMD shrank to 0.01, indicating that the matching successfully created 2 similar groups. The final population included 83 patients who received PCC and a control group of 83 patients who did not receive PCC.

Our matched results reveal that PCC does not carry an increased risk of 30-d mortality (odds ratio [OR] 5; 95% confidence interval [CI], 0.58-42.8; $P = 0.14$) or 1-y mortality (OR 3; 95% CI, 0.61-14.86; $P = 0.18$; see Figure 2). In the PCC group, there were 5 deaths within 30 d and 6 deaths within 1 y (3 died intraoperatively, 2 died postoperatively from bleeding or hypoxic respiratory failure, and 1 cause of death was unknown) compared with 1 death (intraoperative arrest) within 30 d and 2 deaths (unknown cause of death and intraoperative arrest) in 1 y in the control group. A Kaplan-Meier survival curve for 1-y postoperative survival analysis and a Cox proportional hazards model are supplied below (see Figure 3).

There was no increased incidence of thrombotic complications in 90 d after surgery in the group who received PCC compared with the group who did not receive PCC. These complications include PVT (OR 1.5; 95% CI, 0.42-5.32; $P = 0.53$), PE (OR 1; 95% CI, 0.14-7.1; $P = 0.99$), DVT (OR 0.67; 95% CI, 0.11-3.99; $P = 0.66$), and MI (OR 1.67; 95% CI, 0.4-6.97; $P = 0.48$). Of 83 patients, 6 (7.2%) in the PCC group experienced PVT compared with 4 (4.8%) in the control

TABLE 1.

Variables used for matching

Variables	Kcentra: no (N = 451)	Kcentra: yes (N = 90)	Total (N = 541)	*P*
BMI				0.172
Mean (SD)	29.2 (6.5)	30.2 (6.3)	29.4 (6.5)	
Range	12.0–54.5	20.7–47.6	12.0–54.5	
Age, y				0.168
<50	94 (20.8%)	11 (12.2%)	105 (19.4%)	
50–65	191 (42.4%)	42 (46.7%)	233 (43.1%)	
>65	166 (36.8%)	37 (41.1%)	203 (37.5%)	
Sex				0.327
Female	156 (34.6%)	36 (40.0%)	192 (35.5%)	
Male	295 (65.4%)	54 (60.0%)	349 (64.5%)	
Fibrinogen, g/L				<0.001
<200	205 (45.5%)	61 (67.8%)	266 (49.2%)	
200–400	213 (47.2%)	29 (32.2%)	242 (44.7%)	
>400	33 (7.3%)	0 (0.0%)	33 (6.1%)	
MELD score				0.108
Mean (SD)	25.1 (7.2)	26.5 (8.4)	25.3 (7.5)	
Range	6.0–50.0	8.0–40.0	6.0–50.0	
Hemoglobin, g/dL				0.002
Mean (SD)	9.9 (1.4)	9.4 (1.1)	9.8 (1.3)	
Range	6.8–14.8	7.4–11.8	6.8–14.8	
Elixhauser score				0.056
≤8	189 (41.9%)	28 (31.1%)	217 (40.1%)	
>8	262 (58.1%)	62 (68.9%)	324 (59.9%)	
Preoperative VTE				<0.001
No	355 (78.7%)	56 (62.2%)	411 (76.0%)	
Yes	96 (21.3%)	34 (37.8%)	130 (24.0%)	

Descriptive table of patient characteristics and laboratory values by PCC administration.
BMI, body mass index; MELD, model for end-stage liver disease; PCC, prothrombin complex concentrate; VTE, venous thromboembolism.

TABLE 2.

Match: nearest neighbor match with 0.03 caliper

	Unmatched: Kcentra (yes)	Unmatched: Kcentra (no)	Std. mean diff	Matched: Kcentra (yes)	Matched: Kcentra (no)	Standard mean difference
Distance	0.22	0.16	0.71	0.21	0.21	0.01
BMI	30.24	29.22	0.16	30.45	30.15	0.05
Age, y						
<50	0.12	0.21	–0.26	0.13	0.12	0.04
50–65	0.47	0.42	0.09	0.48	0.51	–0.05
>65	0.41	0.37	0.09	0.39	0.37	0.02
Sex						
Male	0.6	0.65	–0.11	0.63	0.67	–0.10
Female	0.4	0.35	0.11	0.37	0.33	0.10
Fibrinogen, g/L						
<200	0.68	0.45	0.48	0.65	0.69	–0.08
200–400	0.32	0.47	–0.32	0.35	0.31	0.08
>400	0.00	0.07	–0.31	0.00	0.00	0.00
MELD score	26.5	25.12	0.16	26.30	26.58	–0.03
Hemoglobin	9.43	9.90	–0.44	9.50	9.49	0.01
Elixhauser score						
≤8	0.31	0.42	–0.23	0.34	0.31	0.05
>8	0.69	0.58	0.23	0.66	0.69	–0.05
Preopeartive VTE						
No	0.62	0.79	–0.34	0.66	0.69	–0.05
Yes	0.38	0.21	0.34	0.34	0.31	0.05

BMI, body mass index; MELD, model for end-stage liver disease; VTE, venous thromboembolism.

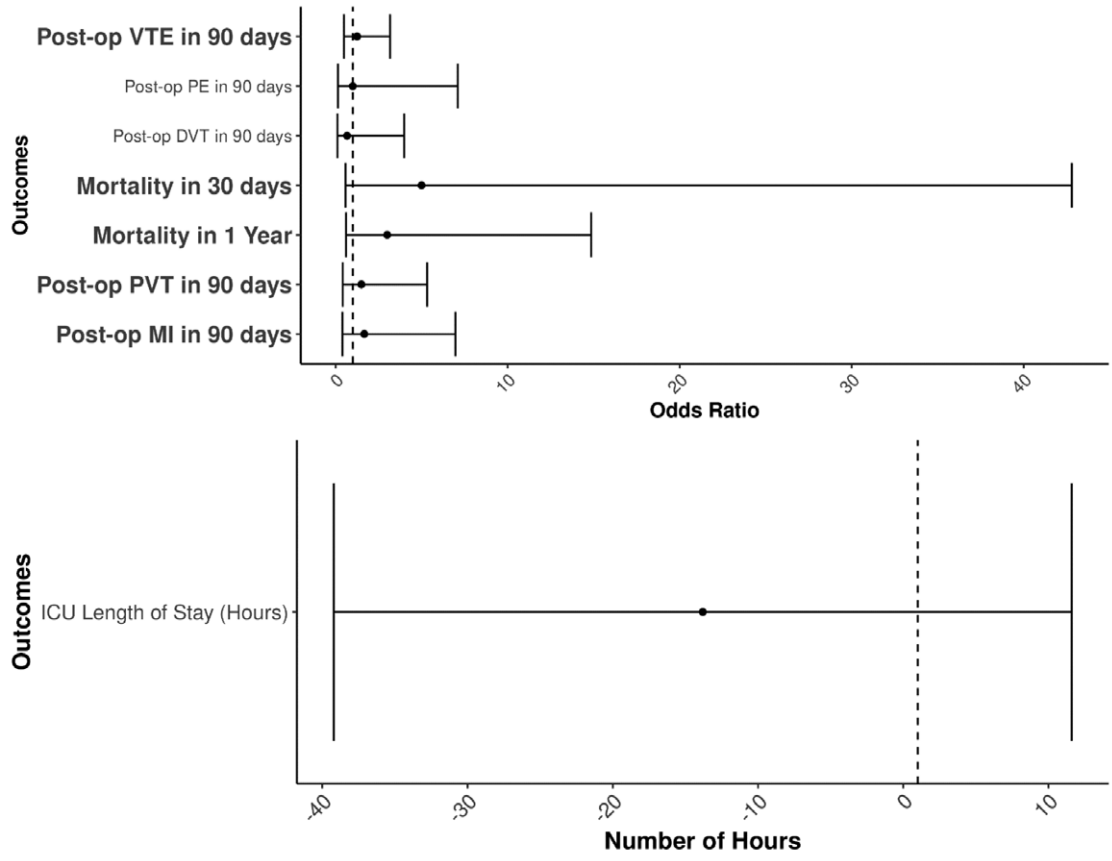

FIGURE 2. Forest plot of mortality, thrombotic complications, and ICU length of stay. DVT, deep vein thrombosis; ICU, intensive care unit; MI, myocardial infarction; PE, pulmonary embolism; Post-op, postoperative; PVT, portal vein thrombosis; VTE, venous thromboembolism.

group. Two patients (2.4%) in the PCC group experienced PE compared with 2 patients (2.4%) in the control group. Two patients (2.4%) in the PCC group experienced DVT compared with 3 (3.6%) in the control group. No patients in the PCC group experienced ICT compared with 1 patient (1.2%) in the control group. In the PCC group, 5 patients (6.0%) experienced MI compared with 3 (3.6%) in the control group. There was also no increased ICU LOS in the group who received PCC compared with the group who did not receive PCC (OR –13.8; 95% CI, –39.2 to 11.6; $P = 0.29$). The mean ICU LOS in the PCC group was 68.1 ± 61.2 h compared with 81.9 ± 55.9 h in the control group. Results are summarized in Table 3. An increase in mortality with PCC administration was observed but did not achieve statistical significance. The *P* value and ORs for reoperation within 72 h and ICT could not be calculated because there were no instances of reoperation in the control group and no instances of ICT in the PCC group. In 3 patients, PCC was used to reverse the severe bleeding that occurred after an intraoperative ICT had to be treated with heparin or tissue-type plasminogen activator (t-PA). These patients reported no further thrombotic complications after PCC was administered in these cases.

DISCUSSION

This retrospective cohort study demonstrated no significant increase in mortality, thromboembolism, and ICU LOS when PCCs are used during OLT compared with patients who did not receive PCC. PCC use has the advantage of rapidly reversing coagulopathy in this setting while decreasing exposure to allogeneic blood product administration and the associated complications.

Several studies have reported the safety of PCC in reducing international normalized ratio and reversing vitamin K antagonists; however,[10] the safety and efficacy of PCC in OLT has been highly contested with concerns of thromboembolic complications.[11-13] Among patients receiving PCCs, we found the incidence of PE to be 2.4%, which is comparable with previous reports.[10] Similarly, we found the incidence of PVT to be 7.2%, which also aligns with previous reports.[10] Interestingly, the rate of patients experiencing DVT after receiving PCC was 2.4% in our cohort, which is lower than previously reports.[10] Our group frequently implements "fast-track" anesthesia in the operating room, which consists of extubating the patient's trachea at the conclusion of the operation, transferring to the recovery room and ultimately bypassing the ICU altogether. This "fast-track" process with early ambulation may contribute to these improved outcomes with lower rates of DVT. Regardless of the type of thrombotic complication, PCC use did not significantly increase the risk of such events in our cohort.

PCC use has previously been investigated during OLT to varying degrees. An analysis of 35 randomized clinical trials in patients receiving recombinant FVII found that higher doses of this PCC were associated with a significantly increased risk of arterial thrombosis.[14] Similarly, a well-designed multicenter, randomized control trial also demonstrated no reduction in transfusion requirement when using FVII with a significantly

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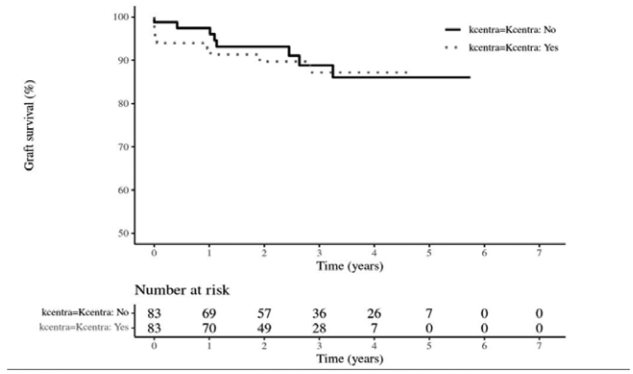

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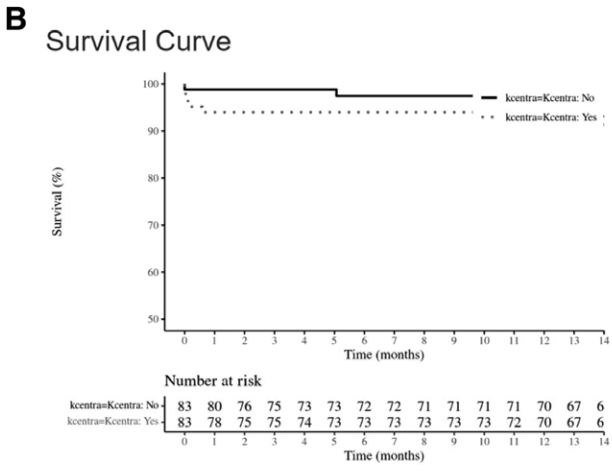

C

Characteristic	HR[1]	95% CI[1]	p-value
Kcentra Medication Administered			
Kcentra: No	—	—	
Kcentra: Yes	1.19	0.46, 3.09	0.7

[1] HR = Hazard Ratio, CI = Confidence Interval

FIGURE 3. 1 year post transplant survival curves. A, Kaplan-Meier overall survival curve. B, Survival curve up to 1 y. C, Cox proportional hazards model.

higher incidence of arterial thromboembolism.[15] Kirchner et al[13] demonstrated that rotational thromboelastometry–guided 4-factor PCC use did not result in a significant difference in the occurrence of thrombotic events between the coagulation factor concentrate (CFC) group and non-CFC group. For clarification, their CFC group included patients who received PCC or a fibrinogen concentrate. Fibrinogen was first corrected and then PCC was administered when the clotting time on EXTEM exceeded 71 s in the setting of refractory bleeding. However, in this study, the non-CFC group had a significantly lower MELD score than the CFC group. Similarly, Srivastava et al[7] found no difference in thrombosis with less bleeding when patients received 4-factor PCCs during OLT. Among patients receiving heart transplantation, Kantorovich et al[11] found the incidence of thrombosis to be 18% in patients receiving Profilnine SD (Grifols Biologicals Inc, Barcelona, Spain), a factor IX complex that contains factors II, VII, IX, and X.[12-18] Although our study and this effort both used factor IX-based PCCs, our lower rate of thrombosis may be because of the differences in ingredients between factor IX concentrates. Kcentra contains several antithrombotic agents, such as proteins C, protein S, and heparin whereas Profilnine SD does not. Given these findings, it

TABLE 3.

Summary of matched results

		Kcentra							
		No		Yes			Confidence interval		
Outcome	**Total**	**n**	**%**	**n**	**%**	**Odds ratio**	**Low**	**High**	***P***
Mortality in 1 y	83	2	2.4	6	7.2	3	0.61	14.86	0.18
Mortality in 30 d	83	1	1.2	5	6	5	0.58	42.8	0.14
Post-op DVT in 90 d	83	3	3.6	2	2.4	0.67	0.11	3.99	0.66
Post-op PE in 90 d	83	2	2.4	2	2.4	1	0.14	7.1	0.99
Post-op MI in 90 d	83	3	3.6	5	6	1.67	0.4	6.97	0.48
Post-op PVT in 90 d	83	4	4.8	6	7.2	1.5	0.42	5.32	0.53
Post-op VTE in 90 d	83	8	9.6	10	12	1.25	0.49	3.17	0.64
Post-op ICT in 90 d	83	1	1.2	0	0	NA	NA	NA	NA
OR bring back within 72 h	83	0	0	2	2.4	NA	NA	NA	NA
Outcome levels	**Total**	**Mean**	**SD**	**Mean**	**SD**	**Coefficient**	**Low**	**High**	***P***
ICU length of stay, h	83	81.9	55.9	68.1	61.2	−13.8	−39.2	11.6	0.29

The table displays the total number of patients in each group (total), the number of patients in each group who experienced different outcomes (N), the percentage of patients, the odds ratio and confidence interval, and *P* value for each outcome. The odds ratio could not be calculated for ICT in 90 d as no outcomes were observed in the treatment group.
DVT, deep vein thrombosis; ICT, intracardiac thrombosis; ICU, intensive care unit; MI, myocardial infarction; NA, not available; OR, operating room; PE, pulmonary embolism; Post-op, postoperative; PVT, portal vein thrombosis; VTE, venous thromboembolism.

appears the specific PCC used is critically important when trying to mitigate the risk of thrombosis.

Interestingly, 3 of 83 patients in the PCC group experienced intraoperative ICT before PCC administration. ICT is a rare complication with an incidence ranging between 1.2% and 6.2% during OLT and carrying a 40% risk of mortality.[6,16,17] In this small set of patients, PCC was used to reverse the severe bleeding after heparin or t-PA were given to treat the ICT and no instances of mortality were encountered. In these cases, the patient suffered no further thrombotic complications after PCC was administered, suggesting this is a viable option to treat the subsequent coagulopathy in high-risk patients and such efforts may prove to be lifesaving. However, PCC should be administered judiciously based on targeted needs guided by testing such as thromboelastogram, rotational thromboelastometry, coagulations, and not blindly. It is imperative to determine the specific requirement (eg, fibrinogen, platelets) necessary to achieve hemostasis. We do not currently advise PCC as frontline therapy. It should also be kept in mind that PCC is only effective when fibrinogen levels range between 2 and 2.5 g/L. PCC cannot be effective on its own and requires factors such as platelets and fibrinogen. Also, PCC may be more effective for heparin-induced bleeding because it contains factors II and X but is less effective for the treatment of t-PA-induced bleeding. In the setting of heparin reversal, PCC is used when protamine has been administered at an appropriate dose, but bleeding remains a problem. For further clarification, these results cannot be extrapolated to FVII, and the authors do not advocate for the administration of FVII.

This study has several limitations. This single-center study in an academic hospital commonly uses PCC, limiting external validity. Our results may depend on factors specific to our institutional practice and may not be generalizable to other settings. Aside from the risk of incomplete data from the EMR inherent to retrospective studies, our study is also limited by less control over the exposure factor and potential confounders. The nature of this study also gives little insight into the choice of dosage and timing of PCC because it was at the discretion of the anesthesiology team. However, our institution is a busy transplant center, with 144 transplants performed in 2022. These cases are covered by a group of anesthesia providers specialized in abdominal transplants—a feature that may add some standardization. We also do not report the dosage of PCC and treated exposure in a binary manner. Although the amount of PCC could theoretically impact the risk of thromboembolic complications, our institution has moved toward a fixed dosing regimen based on guidance from the American College of Cardiology.[18] Another limitation of our study is the relatively small sample of patients and the fact that our outcomes occur infrequently, limiting the statistical power to detect statistically significant differences between groups. Another limitation of the study is that hepatic artery thrombosis (HAT) was excluded from our study, given that surgical and graft factors are associated with the risk of developing HAT. Therefore, without exploring surgical/graft factors, the association between HAT and PCC administration could be misleading.

In conclusion, our study demonstrates that PCC may be a suitable alternative for reversing intraoperative coagulopathy during OLT, as its use did not demonstrate a significant increase in thrombotic complications and mortality. When compared with the risks associated with allogeneic blood product administration, the role of PCC in OLT may expand as evidence builds, demonstrating its relative safety. At our center, PCC was used as a rescue treatment for refractory bleeding after factors, protamine, tranexamic acid, etc had already been given, potentially leading to comparable survival rates as patients without severe bleeding. There is a paucity of robust literature investigating the role of PCC in this, and this effort is the largest cohort that has matched the cohort investigating PCC use in OLT. Although this retrospective effort provides insight into the relative viability of this clinical option, future prospective studies are certainly warranted.

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