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Is Continuing Anticoagulation or Antiplatelet Therapy Safe Prior to Kidney Transplantation?

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Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
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Background: Patients undergoing kidney transplantation are often placed on anticoagulation or antiplatelet therapy, and their perioperative management is often challenging. This study aimed to determine the safety of continuing anticoagulation or antiplatelet therapy prior to kidney transplantation. The primary outcome was bleeding after transplantation.

Material/Methods: Patients who underwent kidney transplantation between January 2017 and July 2019 were included and divided into 3 groups: pretransplant anticoagulation with warfarin (WARF; n=23); pretransplant antiplatelet therapy with clopidogrel/aspirin (ASA/CLOP; n=32); and control (CTL; n=197). Patients received kidneys from live or deceased donors. Preoperative INRs and platelet counts were compared to ensure therapeutic anticoagulation in the warfarin group and no significant platelet count variation among groups. The primary outcome was graft exploration for bleeding at 3 and 6 months after transplantation. Secondary outcomes included perioperative transfusion requirements, prolonged length of stay (>7 days), and outcomes at 3 and 6 months after transplantation, including hemodialysis and rejection rates and creatinine levels.

Results: Pretransplant INR was significantly greater in the warfarin group (CTL 1.1, WARF 2.2, ASA/CLOP 1.2; $P<0.01$). There were no differences in pretransplant platelet count (CTL 202×10^3, WARF 186×10^3, ASA/CLOP 194×10^3; $P=0.31$), graft exploration for bleeding at 3 (CTL 3%, WARF 0%, ASA/CLOP 3%; $P=0.69$) and 6 months after transplantation (CTL 1%, WARF 4%, ASA/CLOP 0%; $P=0.12$), or perioperative blood transfusion requirements (CTL 4%, WARF 4%, ASA/CLOP 14%; $P=0.13$). Prolonged length of stay was similar (CTL 24%, WARF 26%, ASA/CLOP 44%; $P=0.08$). There were no significant differences among groups at 3 months in dialysis (CTL 2%, WARF 0%, ASA/CLOP 0%; $P=0.71$), creatinine (CTL 1.5 mg/dL, WARF 1.7 mg/dL, ASA/CLOP 1.7; $P=0.13$), or rejection (CTL 6%, WARF 0%, ASA/CLOP 0%) or at 6 months in dialysis (CTL 3%, WARF 0%, ASA/CLOP 0%; $P=0.49$), creatinine (CTL 1.5 mg/dL, WARF 1.7 mg/dL, ASA/CLOP 1.5; $P=0.49$), or rejection (CTL 1%, WARF 0%, ASA/CLOP 3%).

Conclusions: Continuing anticoagulation or antiplatelet was safe in not increasing bleeding complications or perioperative transfusion requirements. Outcomes were similar at 3 and 6 months among groups. This strategy avoids exposing patients to risk of thrombosis if treatment is held and simplifies proceeding to transplantation.

Keywords: Anticoagulants • Kidney Transplantation • Platelet Aggregation Inhibitors

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Background

There is currently a lack of anticoagulation and antiplatelet management guidelines in kidney transplantation. Some clinicians believe that reversing, bridging, or interrupting anticoagulation or antiplatelet therapy can prevent bleeding complications. Experience at out center has shown that, apart from being logistically challenging, these procedures inevitably increases the risk of thromboembolic events or bleeding, depending on the strategy. Additionally, they often result in delays to transplantation. This issue triggered our interest in evaluating whether uninterrupted perioperative anticoagulation and antiplatelet therapy (clopidogrel/aspirin) in the setting of kidney transplantation is safe. To the best of our knowledge, there are currently only a few case reports and small case series that describe uninterrupted anticoagulation in the setting of kidney transplantation [1-3].

Material and Methods

The study included all patients who underwent live-donor and deceased-donor kidney transplantation between January 2017 and July 2019. Patients were divided into 3 groups: (1) a control group who were off anticoagulation/antiplatelet therapy (n=197); (2) patients receiving perioperative anticoagulation with warfarin only (n=23), and (3) patients receiving perioperative antiplatelet therapy with clopidogrel/aspirin (n=32). Recipient demographic data, including age, sex, and indication for transplantation, were evaluated prior to comparing perioperative variables. Indications for anticoagulation included a history of deep vein thrombosis/pulmonary embolism, atrial fibrillation, and prosthetic heart valves. Indications for antiplatelet therapy included a history of coronary artery disease, peripheral vascular disease, and stroke. We analyzed recipient pretransplant international normalized ratios (INRs) and platelet counts to ensure there were therapeutic anticoagulation levels in the warfarin group and no significant variation in the platelet counts, which could act as a cofounding variable. The primary outcome of interest was graft exploration for bleeding at 3 months and 6 months after transplantation. Secondary outcomes included perioperative transfusion requirements, prolonged length of stay (>7 days), and outcomes at 3 months and 6 months after transplantation, including hemodialysis and rejection rates and creatinine levels. Statistical analysis was conducted using the chi-squared and Kruskall-Wallis tests. Adverse effects from anticoagulation or antiplatelet use were not encountered in our series and were therefore not analyzed.

Results

Recipient demographic data showed a significantly higher proportion of female patients and patients with basiliximab induction immunosuppression in the warfarin group. There was a statistically significant difference in recipient age; however, this difference was deemed not clinically relevant. Otherwise, there were no significant differences in indication for transplantation and maintenance immunosuppression (**Table 1**).

The pretransplant INR was significantly higher in the warfarin group. No difference among pretransplant platelet count was found (**Table 2**). The pretransplant INR was clearly in the therapeutic range in the warfarin group, compared to that of the control and antiplatelet groups. There was no significant difference in platelet count in the warfarin group.

There was no statistically significant difference in graft exploration for bleeding or perioperative blood transfusion requirements (**Table 3**). Prolonged length of stay was similar among the groups. There were no statistically significant differences among the groups at 3 months and 6 months after transplantation in rates dialysis and rejection and creatinine levels.

Discussion

Prospective kidney transplant recipients are at higher risk of bleeding complications because of their baseline platelet dysfunction. Transplantation is also a procedure with a high risk of bleeding because it involves the creation of vascular anastomoses. Nonetheless, our study showed that uninterrupted anticoagulation and antiplatelet therapy has no significant impact on perioperative bleeding complications or kidney transplant outcomes. This is highly significant as it can minimize the risk of thromboembolic events before and after transplantation in patients with ventricular assist devices, mechanical heart valves, venous thromboembolism, and coronary artery disease and history of stroke.

Some clinicians advocate the use of bridging anticoagulation or antiplatelet reversal prior to transplantation. These strategies have been recommended for some surgical procedures; however, there is currently no data to support their use in kidney transplantation [4]. Large randomized trials have actually shown higher rates of perioperative bleeding when bridging anticoagulation is employed in a non-transplant setting [5-8]. Our data further demonstrated that neither bridging anticoagulation nor antiplatelet reversal should be considered. The risk of interrupting anticoagulation or antiplatelet therapy to avoid bleeding complications is not justified in our view. Therefore, we could not draw a direct comparison of thromboembolic rates between interrupted or bridged therapy and uninterrupted therapy. Differences in recipient age and indication for transplantation were neither clinically nor statistically significant. Donor differences in sex are unlikely to have an impact on the perioperative variables and outcomes analyzed.

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Table 1. Recipient demographics, indication for transplantation, induction, and maintenance immunosuppression.

	WARF (n=23)	ASA/CLOP (n=32)	CTL (n=197)	p Value
Gender (M: F)	6: 17	21: 12	118: 79	0.01
Mean age (y)	60	62	55	0.01
Kidney disease (%)			0.54	
DM	39%	44%	29%	
HTN	17%	25%	17%	
Glomerulonephritis	13%	13%	14%	
PCKD	9%	6%	12%	
Other*	22%	12%	28%	
Induction Immunosuppression			0.01	
Thymoglobulin	70%	72%	88%	
Basiliximab	30%	16%	10%	
Other	0%	13%	3%	
Maintenance Immunosuppression				
Tacrolimus	91%	91%	93%	0.94
Cyclosporine	3%	4%	2%	
Other**	6%	4%	5%	

* Includes IgA nephritis, lupus nephritis, Alport Syndrome, obstructive uropathy, drug-induced nephritis, cardiorenal syndrome, hepatorenal syndrome; ** includes belatacept, rapamycin, and solumedrol only.

Table 2. Pretransplant variables at time of admission.

	CTL	WARF	ASA/CLOP	p Value
INR	1.1	2.2	1.2	<0.01
Platelet count (×10^3/mcL)	202	186	194	0.37

Table 3. Perioperative bleeding complications, prolonged length of stay, and 3-month and 6-month outcomes.

	CTL	WARF	ASA/CLOP	p Value
3-Month graft exploration	3%	0%	3%	0.69
6-Month graft exploration	1%	4%	0%	0.12
Perioperative blood transfusion	4%	4%	13%	0.13
3-Month outcomes				
Prolonged LOS (>7 days)	24%	26%	44%	0.08
Hemodialysis	5%	13%	6%	0.71
Creatinine (mg/dL)	1.6	1.5	1.6	0.49
Rejection	9%	4%	6%	0.32
6-month outcomes				
Prolonged LOS (>7 days)	24%	26%	44%	0.08
Hemodialysis	5%	13%	6%	0.71
Creatinine (mg/dL)	1.6	1.5	1.6	0.49
Rejection	9%	4%	6%	0.32

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Recommendations for preoperative antiplatelet reversal are even less clear. Multiple observational studies have not demonstrated a benefit in reducing bleeding complications in non-transplant procedures [6-11]. Furthermore, the risk of adverse cardiovascular events has been linked with the interruption of antiplatelet therapy prior to surgery. As mentioned before, it is our view that interrupting antiplatelet therapy to avoid bleeding complications is not justified. Our study supports the continuation of antiplatelet agents, avoiding the risk of cardiovascular events in patients with recently placed coronary stents, which most of the patients in the antiplatelet group in our study had [11].

Conclusions

Kidney transplantation can be performed safely without interrupting perioperative anticoagulation and antiplatelet therapy. Our single-center retrospective study demonstrated that bridging anticoagulation or antiplatelet reversal strategies were not necessary. The lack of interruption avoided the added risk of thromboembolic events or any delay in kidney transplantation.

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