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Prothrombin complex concentrate use in durable and short term LVAD implantation

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Introduction

Durable LVAD's therapy is used in advanced heart failure (HF) patients as either a bridge to transplantation or as a destination therapy while short term LVAD's are used to treat cardiogenic shock or as a bridge to decision. Regardless of the LVAD type, implantation is associated with a high risk of bleeding with up to 30% of patients returning to the operating room for surgical bleeding (1,2).

PCC is used for emergency reversal of oral anticoagulation therapy (3), despite its efficacy, a serious concern with the use of PCC is thromboembolism, which is greater in LVAD patients, with pump thrombosis being the most threatening complication. Thus, although some trials have shown promise in the use of PCC to control bleeding complications in cardiac surgery (4), there is still limited data on the use of PCC in LVAD patients. Since VAD thrombosis is a major adverse event we investigated the safety of low dose PCC use in the management of bleeding post LVAD implantation comparing durable to short term LVAD's.

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Referenced paragraph

Left Ventricular Assist Device (LVAD) implantation is associated with a high risk of procedural bleeding, prothrombin complex concentrates (PCC) may be used to mitigate this risk, however it has been associated with thrombotic complications. Since VAD thrombosis is a serious complication we investigated the safety of low dose PCC (~ 1000 U) use in the management of bleeding post VAD implantation. Of the 27 cases who received PCC, 21 were implanted with a durable LVAD and 6 implanted with a short-term LVAD. No durable LVAD patients suffered from PCC related complications, However, out of the short term LVAD cohort, 5 complication events were recorded.

Methods

Study protocol

Following Institutional Review Board (IRB) approval, a retrospective chart review of the patients who had undergone LVAD implantation from January 2014 to June 2017 was performed. Adults >18 who had received Profilnine®/Kcentra® for bleeding in the up to 12 hours post-OP were included. Postoperative variables included thrombotic complications e.g. CVA, DVT, PE as well as pump thrombosis. Patient charts were reviewed from admission till 1-year post discharge. Categorical variables were compared with each other using a chi-squared test and continuous variables were compared with the Wilcoxon rank-sum test.

Post CPB Transfusion Algorithm

In case of refractory bleeding after discontinuation of CPB and reversal of heparin with protamine, the chest was packed and coagulopathy was corrected in accordance with the institutional perioperative cardiovascular transfusion algorithm (Figure 1) If bleeding persisted despite aggressive transfusion, PCC was administered at a dose of 10–15 U/kg.

Results

Patient demographics

530 patients undergone LVAD implantation (435 Durable LVADs) at our institution between January 2014 and June 2017 and were retrospectively analyzed. PCC was used in 27 cases. Low dose PCC was either given at the end of the operation or upon arrival to the ICU (Table 1).

Adverse events

We monitored the patients for short and long-term survival as well as development of pump thrombosis, CVA and PE up to one year post the surgery and found a statistically significant difference between the groups. Of the 21 patients treated with Durable LVADs and PCCs there was no pump thrombosis in none of the LVAD pumps, there was however a pump thrombosis in one of the RVAD's in these patients. No PE or CVA was detected in any of these patients. 17 out of 21 patients of this group survived beyond 90d. However, of the patients treated with short term LVADs and PCCs, 3 patients had pump thrombosis events which required extracorporeal pump replacements, 2 patients developed a PE and none suffered from CVA while being treated with heparin and having a therapeutic PTT the majority of the time; 3 out of 6 patients survived beyond 90d.

Discussion

Following previous work that showed the safety of vitamin K antagonism reversal and the use of PCC in bleeding LVAD patients (5) we set out to examine whether the risk of thrombosis, following PCC administration, was dependent on the type of LVAD in use and the time of use e.g. immediately post implantation. We were able to demonstrate a statistical difference in pump thrombosis incidence between the cohort groups; while durable LVAD

patients suffered no sequela following the use of PCC post implantation this was not the case in short term LVAD's, with patients suffering from both pump thrombosis as well as PE.

Bleeding post LVAD implantation is a well-known adverse event and is contributed to several factors, ranging from liver dysfunction e.g. synthesis of coagulation factors due to right ventricle overload, anticoagulation treatment as well and acquired Von-Willibrand syndrome due to mechanical sheer stress similar to Heyde syndrome (6). Thus, novel tools to address post implantation bleeding are constantly being evaluated. PCC is considered superior to FFP (2,3), for numerous reasons but also due to the fact that it requires considerably lower volumes than FFP to achieve its effect, which may prevent right ventricular overload. Thus, PCC might prove to be especially suitable to use in LVAD patients, who are at increased risk of right ventricle failure (1).

Our study agrees with previous findings on PCC safety of use in cases where warfarin reversal was needed or use due to excessive post-OP bleeding (7–9). However, in our cohort the patient population that was supported by a short term LVAD was different, they were younger and usually supported due to an acute event thus making them an INTERMACS 1 profile type of patient; while age was not shown to be a risk factor for thrombosis in the literature, INTERMACS 1 patient profile was (10). Thus, the combination of the above-mentioned patient profile, short-term LVAD and PCC use should be used with caution, pending publications of larger series.

To the best of our knowledge, no study thus far examined the use of PCC in short term LVAD's nor the use of PCC at the time of implantation of Heartware or HMIII. We conclude that in our patient population the use of low dose PCC did not induce pump thrombosis, CVA or PE in the durable LVAD cohort; However, we cannot conclude whether the PCC was responsible for the short term LVAD cohort reported thrombotic complications in the short term LVAD cohort due to the lack of a control group. Future prospective trials with a larger treatment groups, are warranted in order to further validate the findings of this study.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

References:

1. Kirklin JK, Pagani FD, Kormos RL, et al. Eighth annual INTERMACS report: Special focus on framing the impact of adverse events. *J Heart Lung Transplant*. 2017 10;36(10):1080–1086. [PubMed: 28942782]
2. John R, Lee S The biological basis of thrombosis and bleeding in patients with ventricular assist devices. *J Cardiovasc Transl Res*. 2009 3;2(1):63–70. [PubMed: 20559970]
3. Leissinger CA1, Blatt PM, Hoots WK, Ewenstein B. Role of prothrombin complex concentrates in reversing warfarin anticoagulation: a review of the literature. *Am J Hematol*. 2008 2;83(2):137–43. [PubMed: 17729241]
4. Song HK, Tibayan FA, Kahl EA, Sera VA, Slater MS, Deloughery TG, Scanlan MM. Safety and efficacy of prothrombin complex concentrates for the treatment of coagulopathy after cardiac surgery. *J Thorac Cardiovasc Surg*. 2014 3;147(3):1036–40. [PubMed: 24365268]

5. Jennings DL, Jacob M, Chopra A, Nemerovski CW, Morgan JA, Lanfear DE. Safety of anticoagulation reversal in patients supported with continuous-flow left ventricular assist devices. *ASAIO J.* 2014 Jul-Aug;60(4):381–4. [PubMed: 24658518]
6. Makris M, Greaves M, Phillips WS, Kitchen S, Rosendaal FR, Preston EF. Emergency oral anticoagulant reversal: the relative efficacy of infusions of fresh frozen plasma and clotting factor concentrate on correction of the coagulopathy. *Thromb Haemost* 1997 3;77(3):477–80. [PubMed: 9065997]
7. Brown CS, Zemrak WR, Dyer KJ, Rolfe S. Low-Dose Prothrombin Complex Concentrate in Patients with Left Ventricular Assist Devices. *ASAIO J.* 2018 3 20.
8. Rimsans J, Levesque A, Lyons E, Sylvester K, Givertz MM, Mehra MR, Stewart GC, Connors JM. Four factor prothrombin complex concentrate for warfarin reversal in patients with left ventricular assist devices. *J Thromb Thrombolysis.* 2018 5 21.
9. Bradford CD, Stahovich MJ, Dembitsky WP, Adamson RM, Engelbert JJ, Perreiter AS. Safety of Prothrombin Complex Concentrate to Control Excess Bleeding During Continuous Flow LVAD Insertion. *ASAIO J.* 2015 Sep-Oct;61(5):509–13. [PubMed: 26102176]
10. Kirklin JK, Pagani FD, Kormos RL, Stevenson LW, Blume ED, Myers SL, Miller MA, Baldwin JT, Young JB, Naftel DC. Eighth annual INTERMACS report: Special focus on framing the impact of adverse events. *J Heart Lung Transplant.* 2017 10;36(10):1080–1086. [PubMed: 28942782]
11. Ghadimi K, Levy JH, Welsby IJ. Perioperative management of the bleeding patient. *Br J Anaesth.* 2016 12;117(suppl 3).

Figure 1:
The Duke Cardiac Surgical Intraoperative Transfusion Algorithm; *Figure modified from the British Journal of Anesthesia – Supp. 1 (11).*

Table 1:

Demographic data and patient characteristics

	Durable LVAD N (%), mean $\pm$ SD	Short term LVAD N (%), mean $\pm$ SD	p -value
Age	62.5 $\pm$ 14.65	34.5 $\pm$ 18.34	0.003
Female	3 (14%)	1 (17%)	0.885
LVAD type:	21 (100%)	6 (100%)	
HMII	12 (57%)		
HMIII	1 (5%)		
Heartware	8 (38%)		
Short term LVAD		6 (100%)	
+RVAD	6 (29%)	5 (83%)	
HF etiology:			0.001
ICM	13 (62%)	0 (0%)	
NICM	8 (38%)	3 (50%)	
Other		3 (50%)	
Redo OP	11 (52%)	0 (0%)	0.001
Concomitant procedure	8 (38%)	3 (50%)	0.601
Albumin	2.78 $\pm$ 0.53	2.68 $\pm$ 0.31	0.537
CR	1.55 $\pm$ 0.54	1.85 $\pm$ 1.4	0.55
Survival >90d	17 (81%)	3 (50%)	0.127
Pump thrombosis	1 (5%) – RVAD	3 (50%)	0.001
PE	-	2 (33%)	
CVA	-	-	