Title: Platelet Nadir and Postoperative Delirium after Cardiac Surgery with Cardiopulmonary Bypass

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Background

Cardiac surgery with cardiopulmonary bypass (CPB) has one of the highest rates of postoperative delirium when compared to other surgery types; with an estimated incidence of 26-52% when using well-validated diagnostic standards.[1] Risk factors, pathophysiology, and treatment of delirium is still not fully understood.[2] Similar mechanisms that have been proposed to explain the development of postoperative delirium have been implicated in CPB-associated platelet activation and decline.[3-7] In addition, platelet activation following CPB has been associated with postoperative consequences such as acute kidney injury (AKI), stroke, and mortality.[8-10] In this study we hypothesize that nadir platelet counts cardiac surgery with cardiopulmonary bypass will be associated with incidence of delirium.

Methods

The study design is a multi-site retrospective cohort of cardiac surgery patients (n = 2,455) at an academic medical hospital and community hospital with cardiac surgery programs. The study was approved by the Colorado Multiple Institution Review Board #17-2455. For normally distributed continuous variables, we used a two-tailed t test. For non-normally distributed variables we used a Wilcoxon signed rank test. For categorical variables we used a chi squared test. We performed a multivariate logistic regression to develop a prediction model for delirium within 7 days of intensive care unit admission. We also performed a sensitivity analysis to compare the full model, a parsimonious model, and a univariate model using Akaike information criterion. Our primary exposure of interest was platelet nadir, and our secondary exposures of interest were platelet nadir time in minutes and age.

Results

The patient cohort characteristics are listed in table 1. In an unadjusted univariate analysis, patients experiencing delirium compared to those who did not have a lower platelet nadir, later platelet nadir time, and were older (table 1).

In a multivariable model age, sex, diabetes, platelet nadir, and platelet nadir time were independently associated with the incidence of delirium (table 2). The AUC ROC for the model was 0.685. A parsimonious model containing age, sex, platelet nadir, and platelet nadir time carried 98.7% of the cumulative model weight with an AUC ROC of 0.638. A univariate model with platelet nadir carried 96.9% of the full model weight with an AUC ROC of 0.601 (table 3). The optimal cutoff value for platelet nadir was 83 x 10^9/L using Youden's J statistic.

Conclusion

Platelet count after cardiac surgery with cardiopulmonary bypass may be a pragmatic indicator for predicting the incidence of delirium in the cardiothoracic intensive care unit.

Tables

Table 1. cohort characteristics and comparison between patients with and without a diagnosis of delirium in the first 7 days after cardiac surgery in a univariate analysis.

Patient demographics	
Age	62.7 ± 12.9
Sex, male	1724/2433 (71%)
Race, white	1889/2455
Institution, academic	1769/2433 (73%)
Pre-operative characteristics	
Heart failure	804/2433 (33%)
Diabetes	572/2433 (24%)
Obstructive sleep apnea	225/2433 (91%)
Carotid stenosis	195/2433 (8%)
Cognitive impairment	4/2433 (0.2%)
Procedure	
Aortic Procedures	453/2419 (19%)
AVR	532/2419 (22%)
CABG	983/2419 (41%)
Off pump CABG	3/2419 (0.1%)
PVR	26/2419 (1%)
TVR	18/2419 (1%)
Outcomes	
Post-operative Delirium	293/2433 (12%)
Post-operative Death	78/2433 (3%)

Univariate analysis	All n = 2,433	No delirium 2140/2,433	Delirium 293/2,433	P value
Platelet nadir (x10^9/L)	106 ± 42	107 ± 42	94 ± 41	<0.0001
Platelet nadir time (minutes)	3,612±1,763	3551 ± 1694	4028 ± 2,133	0.003
Age (years)	62.7 ± 12.9	62.2 ± 12.9	66.1 ± 12.3	<0.0001

Table 2. Multivariable regression of the full model and ROC curve.

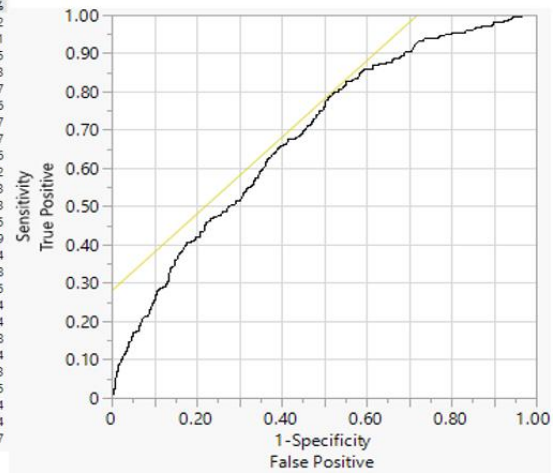| Term		Estimate	Std Error	ChiSquare	Prob>ChiSq	Lower 95%	Upper 95%
Intercept	Unstable	-8.6708014	13397.717	0.00	0.9995	-26267.714	26250.3722
age		0.02631976	0.0057674	20.83	<.0001*	0.01518339	0.03780571
gender[Female]		0.29765393	0.0689055	18.66	<.0001*	0.16190199	0.43222425
race[American Indian and Alaska Native]		0.85482514	0.5688468	2.26	0.1329	-0.3486086	1.93480533
race[Asian]		-0.7739371	0.5006746	2.39	0.1222	-1.8771928	0.14182537
race[Black]		-0.1742016	0.3125581	0.31	0.5773	-0.786112	0.46449866
race[Hawaiian or Pacific Islander]		0.43644888	1.0531073	0.17	0.6786	-2.2305965	2.25034217
race[Multiracial]		-0.2701662	0.3776751	0.51	0.4744	-1.0419111	0.46690257
race[Other]		0.00769463	0.2793165	0.00	0.9780	-0.5261659	0.59660866
facility_location[MHC HOSPITAL]	Unstable	6.04219588	13397.717	0.00	0.9996	-26253.001	26265.0852
facility_location[UCH HOSPITAL]	Unstable	6.98630692	13397.717	0.00	0.9996	-26252.057	26266.0293
death[False]		0.1057218	0.1631633	0.42	0.5170	-0.201656	0.44140683
HF[False]		-0.004967	0.0711892	0.00	0.9444	-0.143345	0.13597455
DM[False]		-0.1849295	0.0793816	5.43	0.0198*	-0.3391204	-0.0275819
OSA[False]		0.07506766	0.1166501	0.41	0.5199	-0.1448092	0.31416284
carotid_stenosis[False]		-0.0513175	0.1223284	0.18	0.6748	-0.2823115	0.19922428
cog_impair[False]		-1.1021224	0.5377273	4.20	0.0404*	-2.2359631	0.00987925
plt_nadir		-0.0057334	0.00181	10.03	0.0015*	-0.009356	-0.0022614
Platelet nadir time (minutes)		6.8168e-5	3.6927e-5	3.41	0.0649	-5.0607e-6	0.00013984
Redo[No]		0.10525633	0.2151759	0.24	0.6247	-0.2874498	0.56800038
Procedure[Aortic]		0.0194415	0.259836	0.01	0.9404	-0.4802233	0.57733404
Procedure[AVR]		-0.504086	0.2615987	3.71	0.0540	-1.0081978	0.05590943
Procedure[CABG]		-0.3557173	0.2518905	1.99	0.1579	-0.8391071	0.19003975
Procedure[MVR]		-0.3931198	0.2695738	2.13	0.1448	-0.9140303	0.17897854
Procedure[OFF PUMP CABG]		1.30433323	1.1213201	1.35	0.2447	-1.4070301	3.49358944
Procedure[PVR]		-0.1029323	0.5855568	0.03	0.8605	-1.4179659	0.95482317

Table 3. Sensitivity analysis of a parsimonious multivariable model and univariate model.

Term	Estimate	Std Error	ChiSquare	Prob>ChiSq	Lower 95%	Upper 95%
Intercept	-2.8757515	0.4518502	40.51	<.0001*	-3.7746027	-2.0025015
plt_nadir	-0.0061465	0.0017529	12.30	0.0005*	-0.0096458	-0.0027754
Platelet nadir time (minutes)	6.16115e-5	3.5453e-5	3.02	0.0822	-8.8767e-6	0.00013024
age	0.02133933	0.0053953	15.64	<.0001*	0.01093733	0.03209807
gender[Female]	0.27864991	0.0651193	18.31	<.0001*	0.15020265	0.40568354

Term	Estimate	Std Error	ChiSquare	Prob>ChiSq
Intercept	-1.1357805	0.1732359	42.98	<.0001*
plt_nadir	-0.0085045	0.0016939	25.21	<.0001*
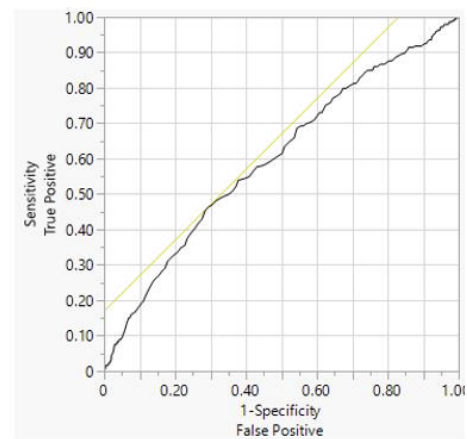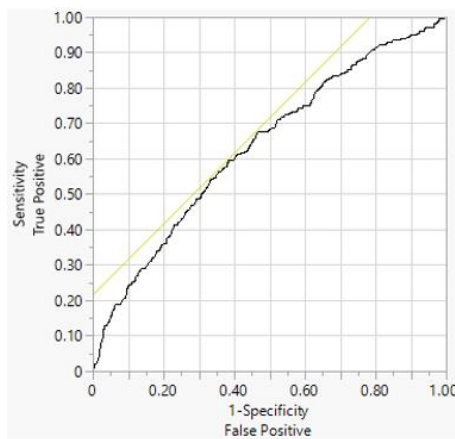
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