Haemorrhagic risk of Marfan syndrome after cardiac surgery

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Marfan syndrome is a complex entity that affects one out of 5-10 thousands live births and is characterized by aortic and mitral abnormalities in 60 to 80% of adults. There is limited evidence that Marfan syndrome is also associated with grey platelet syndrome and tissue abnormalities that can lead to increased risk of bleeding, after cardiac surgery. The goal of this study was to test the hypothesis that in patients with Marfan syndrome that undergo cardiac surgery, blood loss is increased as compared to matched non-Marfan syndrome patients.

Methods

Patients were selected from the institutional registry of cardiac surgery in Bichat-Claude Bernard Hospital, Paris between January 2005 and June 2015. All patients with elective valvular surgery, associated or not to ascending aorta surgery, were included consecutively. Emergency surgery, aortic dissection and surgery with circulatory arrest were excluded. Patients with Marfan syndrome were matched to controls with a propensity score without replacement. The propensity score integrated demographic (age, sex), biologic, (hemoglobin, hemostasis) and surgery values : type of surgery, extra corporeal circulation (ECC), aortic cross clamping (ACC) and surgery durations; post operatives variables (24h blood loss, total blood loss intensive care, hospital length of stay and mortality. Results are expressed as median (IQR). The Student t-test was used to estimate differences between groups.

Results

From 2005 to 2015, one hundred and twenty one patients with Marfan syndrome were identified, out of 7718 cardiac surgery procedures. They were compared to 2504 « non-Marfan » patients. Before matching, Marfan patients were significantly younger, had longer ECC, ACC and surgery durations. The 24h and the total blood loss volumes were significantly higher in the Marfan group: 650mL (525-940) vs 420mL (310-580) $p<0.0001$ and 800mL (650-1012) vs 610mL (415-920) $p<0.0001$. After matching with the propensity score, fifty three Marfan patients were compared to 53 non-Marfan patient. The 24h and the total bleeding were still significantly higher in the Marfan group : 660mL (485-920) vs 480mL (330-780) $p=0.023$ and 800mL (650-1012,5) vs 610mL (415-920) $p=0.01$. Other variables did not differ between the two groups. Overall mortality was 2% in the Marfan group vs 3.6 % in the « non- Marfan » group ($p=0.44$). Hospital length of stay was not different between the groups: 9 days vs 10 days $p=0.94$.

	Before matching			After matching		
	Non Marfan (n=2505)	Marfan (n=121)	p value	Non Marfan (n=53)	Marfan (n=53)	p value
Patient sex: Female	1209 (48.3)	34 (28.1)	<0.0001	22 (41.5)	16 (30.2)	0.31
Patient sex: Male	1296 (51.7)	87 (71.9)		31 (58.5)	37 (69.8)	0.31
Age (years)	65 (53 to 75)	35 (27 to 46)	<0.0001	42 (37 to 56)	41 (28 to 53)	0.14
Preopérative biological values						
Creatinin (µmol/L)	86 (72 to 102)	77 (68.5 to 87)	<0.0001	76 (63 to 90)	78 (70 to 89)	0.51
Haemoglobin (g/dL)	13.4 (12.3 to 14.5)	14.4 (13.8 to 15.2)	<0.0001	13.9 (12.7 to 15.3)	14.4 (13.6 to 15.2)	0.14
Platelets (G/L)	219 (183 to 262)	233 (199.5 to 267)	0.013	228 (201 to 251)	225 (197 to 253)	0.73
Prothrombin time ratio(%)	93 (81 to 100)	99 (89 to 100)	0.00065	92 (82 to 100)	93 (85 to 100)	0.54
Euroscore II	6 (3 to 7)	4 (3 to 5)	<0.0001	5 (3 to 7)	4 (3 to 5)	0.04
Surgical procedures						
Group 1 : Bentall	13 (0.5)	41 (33.9)	<0.0001	7 (13.2)	5 (9.4)	0.66
Group 2 : valve surgery + ascending aorta surgery	2379 (95)	78 (64.5)		44 (83)	47 (88.7)	0.66
Group 3 : supra coronary tube surgery	113 (4.5)	2 (1.7)		2 (3.8)	1 (1.9)	0.66
CPB time (min)	63 (48 to 88)	128 (104 to 150)	<0.0001	134 (97 to 164)	121 (100 to 135)	0.21
Total duration of surgery (min)						
	160 (130 to 200)	240 (200 to 280)	<0.0001	250 (197.5 to 300)	215 (196.2 to 250)	0.11
Aortic cross clamping time (min)	47 (37 to 67)	114 (92 to 128)	<0.0001	113 (84 to 135)	107 (82 to 121)	0.39
Haemoglobin at start of CPB (g/dL)	12 (10.8 to 13.1)	13.1 (12.4 to 14)	<0.0001	12.5 (11.2 to 14.1)	13 (12.4 to 14)	0.11
24H Bleeding (mL)	420 (310 to 580)	650 (525 to 940)	<0.0001	480 (330 to 780)	660 (485 to 920)	0.023
Total Bleeding (mL)	515 (385 to 710)	800 (635 to 1115)	<0.0001	610 (415 to 920)	800 (650 to 1012.5)	0.01
Hospital stay (days)	10 (8 to 15)	10.5 (8 to 14)	0.93	9 (8 to 14)	10 (8 to 13.2)	0.94
ICU length of stay (days)	3 (2 to 5)	3 (2 to 5)	0.74	3 (2 to 4)	2 (2 to 4)	0.68
Death	91 (3.6)	2 (1.7)	0.44	2 (3.8)	0 (0)	0.5
Red cells units in ICU	0 (0 to 2)	0 (0 to 2)	0.15	0 (0 to 2)	0 (0 to 2)	0.24

After matching with the propensity score, fifty three Marfan patients were compared to 53 non-Marfan patient. The 24h and the total bleeding were still significantly higher in the Marfan group : 660mL (485-920) vs 480mL (330-780) $p=0.023$ and 800mL (650-1012,5) vs 610mL (415-920), $p=0.01$. Other variables did not differ between the two groups. Overall mortality was 2% in the Marfan group vs 3.6 % in the « non- Marfan » group ($p=0.44$). Hospital length of stay was not different between the groups: 9 days vs 10 days $p=0.94$

Conclusion

This study suggests that after matching, patients with Marfan syndrome had a small but statistically significant increase of blood loss after cardiac surgery. These results are an incentive to realize a prospective study to identify platelets and primary hemostasis abnormalities of patients with Marfan syndrome.