How much protamine is really needed in cardiac surgery?

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Objective Protamine is routinely administered to neutralize the anti-clotting effects of heparin, traditionally at a dose of 1 mg for every 100 IU of heparin – a 1:1 ratio – but this is based more on experience and practice than literature evidence. The use of Hemostasis Management System (HMS) allows an individualized heparin and protamine titration. This usually results in a decreased protamine dose, thus limiting its side effects, including paradox anticoagulation.

This study aimed at assessing how the use of HMS allows to reduce protamine administration while still meeting the target activated clotting time (ACT) in cardiac surgery.

Methods. We analyzed data from 42 consecutive patients undergoing cardiopulmonary bypass (CPB) for cardiac surgery. For all patients HMS tests were performed before and after CPB, to determine how much heparin was needed to reach target ACT and how much protamine was needed to revert it.

Results. At the end of surgery, 175±50 mg of protamine was sufficient to reverse heparin. The administered protamine was less than predicted by the standard 1:1 ratio approach, being 44% less than heparin total dose and 16% less than heparin initial dose.

Conclusion. A 1:1 initial heparin-to-protamine ratio is not needed to revert full anticoagulation.Additional protamine should be avoided to treat microvascular bleeding, since this is usually not related to heparin and could be worsened by protamine paradox anticoagulant effect. Protamine dosage should be titrated according to actual heparin levels and the use of HMS devices should be implemented to correctly manage anticoagulation for cardiopulmonary bypass.

Table 1. Heparin and Protamine Use

	Patients *n= 42*
Initial heparin dose, IU (mean±SD)	20,286±5,440
Initial heparin dose, IU/kg (mean±SD)	263±50
Need for additional heparin during CPB, IU (mean±SD)	10,674±5,490
Total heparin dose, IU (mean±SD)	31,095±9,567
Total heparin dose, IU/kg (mean±SD)	402±88
1:1 hypothetical protamine dose (total heparin), mg (mean±SD)	311±97
1:1 hypothetical protamine dose (initial heparin), mg (mean±SD)	203±54
HMS-driven administered protamine dose, mg (mean±SD)	170±59
Difference between hypothetical (initial heparin) and actual protamine dose, mg (median [IQR])	33±37
Difference between hypothetical (total heparin) and actual protamine dose, mg (median [IQR])	141±61
Basal ACT, s (mean±SD)	140±9
End-of-surgery ACT, s (mean±SD)	126±13

IU: International Units; SD: Standard Deviation; CPB: cardiopulmonary bypass; HMS: Hemostasis

Management System; IQR: Interquartile Range