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**Background** Prompt reversal of anticoagulation by protamine administration could be a crucial therapeutic option to prevent major bleeding, hematoma or pseudoaneurysm from the puncture site. There are some controversy administering protamine after drug-eluting stent (DES) implantation for the possible risk of stent thrombosis. **Method** We retrospectively analyzed the patient's data in our hospital from 2014 to 2015 in 97 patients who received routine protamine (protamine group) and 112 patients who did not receive protamine (control group) after successful DES implantation. We compared the incidence of stent thrombosis, length of time to achieve hemostasis, and the frequency of complications in the two groups. **Result** Stent thrombosis did not occur in any protamine group and control group. Compared with control group, hemostasis was significantly shorter in the protamine group. ( $192 \pm 19.8$  vs.  $43 \pm 12.0$ ,  $p < 0.001$ ) No patients in the protamine group had adverse effects such as hypotension or vascular collapse during protamine administration. Pseudoaneurysm ( $n=3$ ) and major bleeding ( $n=2$ ) only occurred in the control group. **Conclusion** We conclude that routine protamine administration after DES implantation offers earlier sheath removal without any stent thrombosis and local complications..