

## Comparison between complications of vascular surgery procedures with and without aPTT assessment and protamine sulfate reversal

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### Abstract

**Background:** Thrombosis will occur due to contact of blood with unepithelialized surfaces after vascular clamping and also blood stasis during vascular surgery. Heparin is administered to prevent thrombosis. The aPTT test is used for assurance of the anticoagulative effect of heparin. At the end of the operation heparin is neutralized by protamine sulfate in some centers. In this study we assessed the necessity of aPTT and the use of protamine during vascular surgery.

**Methods:** In this case-control survey 154 cases of vascular surgery were divided into two groups, while the groups were matched regarding age, underlying disease and for vascular complications during the first postoperative 24 hours. In group A (62 cases), aPTT was determined after 2 minutes of heparin administration but heparin was not neutralized by protamine at the end of the operation. In group B (92 cases), aPTT was not determined after heparin administration but heparin was neutralized by an appropriate dose of protamine at the end of the operation.

**Results:** Complications were seen in 4 cases of vascular surgery (2.6%): right leg embolus in 1 case (0.65%), spinal ischemia in 1 case (0.65%), neuropathy in 1 case (0.6%) and hypotension due to protamine in 1 case (0.65%). 3 cases were from group A and 1 case was from group B, but differences were not statistically significant although the power is high enough (power=70%).

**Conclusion:** According to our findings it seems with appropriate techniques and accomplishing surgical principles, there is no need for aPTT assessment and protamine administration. This can reduce the cost and duration of operation, its complications, and prevent adverse reactions to protamine.

**Keywords:** Vascular surgery, Complications, aPTT, Heparin, Protamine.

### Introduction

Thrombosis occurs during vascular surgery following clamping for hemostasis on nonendothelialized surfaces. Heparin is

used to prevent vascular thrombosis. It is often administered as a single dose and is neutralized with protamine sulfate after at least 20 minutes or at most 80 minutes [1,2].

Heparin, which is a complex glycosamino-

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glycan, has long been used for its temporary anticoagulant effect during cardiovascular surgery. The aPTT test is used for assurance of proper anticoagulation during the operation and before clamping the arteries.

Performing an aPTT test is based on reducing thrombosis due to clamping by gaining assurance of the anticoagulant effect of heparin before clamping. While bleeding complications due to heparin were seen in 10-15% [3], it can also rarely lead to chronic complications such as alopecia and skeletal defects [4].

To prevent and control the former, protamine sulfate is often used at the end of the operation to neutralize heparin [1,3,5,8].

Protamine is an alkaline polypeptide which can cause complications dividable in to 3 groups: systemic hypotension, anaphylactoid reaction and catastrophic pulmonary vasoconstriction [6,9,10]. New methods are used to minimize the dose of protamine needed for neutralizing heparin and its complications [7,11,14].

In this study, we tried to clarify the necessity of the aPTT test and the use of protamine during vascular surgery.

### Methods

This study is a case-control study and the groups are matched regarding age and underlying disease. The samples were selected conveniently, not randomly. Our vascular surgery patients were divided in to two groups.

In group A, patients received standard I.V injection doses of heparin (50- 100 IU/kg [15,16] or 5000-7000 IU) [10].

Clamping was started after 2 minutes if the aPTT level was up to 1.5 times of control value [10], otherwise heparin administration was repeated. No protamine neutralization was done in this group at the end of

the operation if there was no abnormal bleeding in the surgical field [10,15,16].

In the second group of patients (B), clamping the arteries was done after 2 minutes following IV injection of standard doses (50 - 100 IU/kg [15,16] or 5000 – 7000 IU[10]) of heparin without measuring aPTT. In all patients of this group the possible remaining portion of injected heparin was neutralized with protamine at the end of surgery [10,15,16] according to the duration of operation and the half-life of heparin.

Data about complications of vascular surgery during the first 24 hours after operation was gathered in all patients from Nagoya University Hospital in Japan, from Dec 2001 through May 2002 (group A) and Stadt Klink Baden-Baden, affiliated with Heidelberg University in Germany, from Feb-Jul 2003 (group B).

The data were analyzed descriptively and analytically (mean, frequency,  $\chi^2$ , t-test) using SPSS14.

### Results

In this research, 154 patients who had vascular surgery, were assessed with a mean age of 68.29 years (SD = 10.94), 86 cases (55.8%) being 70 years old or more; 118 cases were men and (76.6%) 36 cases were women (23.4%).

The first group consisted of 62 cases (40.3% total) with aPTT examination and without receiving protamine at the end of the operation.

The second group was composed of 92 cases (56.7% total) without aPTT examination and receiving protamine at the end of the operation.

Bypass of lower limb arteries in 33 cases was the most common procedure (21.4%) followed by abdominal aortic aneurysm surgery in 29 cases (18.8%). Other proce-

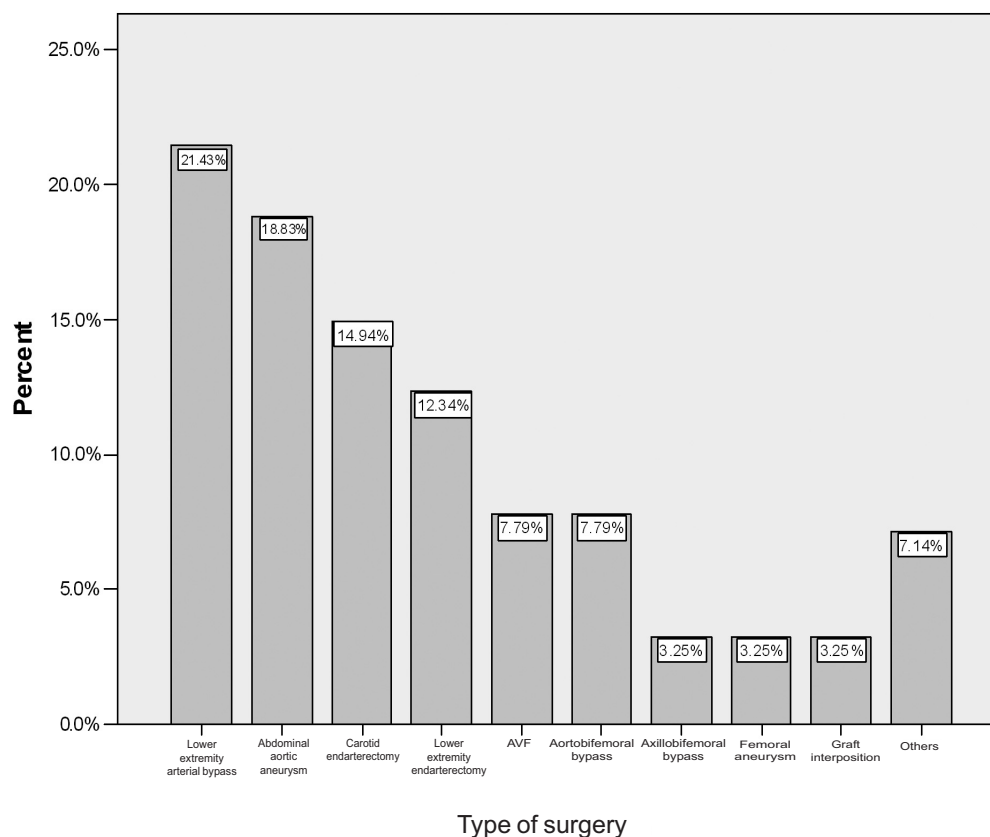


Fig.1. Type of vascular surgery in studied cases.

dures are mentioned in Fig.1

Out of 154 patients, the following complications occurred during the first 24 hours after operation in 4 (2.6%): 1 case (0.65%) right leg embolus, 1 case (0.6%) neuropathy, 1 case (0.65%) spinal cord ischemia and 1 case (0.65%) of hypotension due to protamine administration. 3 cases (4.8%) from the first group showed vascular complications while complications were not seen in the second group, but the difference was not statistically significant ( $p$  value = 0.065).

1 case (1.1%) from the second group developed protamine complication but the difference was not statistically significant ( $p$  value = 1).

Age and sex variables and also type of surgery showed no relation with vascular surgery complications (Table I).

### Conclusion

In this study 154 patients who were candidates for vascular surgery were studied in two groups regarding vascular surgery complications during the first 24 hours.

Only 4 cases of nonmortal complications occurred due to vascular surgery during the first postoperative 24 hours; 3 in group A and 1 in group B, without significant statistical difference.

These include: one case of limb embolism, 1 case of limb neuropathy, and 1 case of spinal cord ischemia were in group

| Variables                             | Vascular surgery complication |                  | Total            | P value       |       |
|---------------------------------------|-------------------------------|------------------|------------------|---------------|-------|
|                                       | Positive                      | Negative         |                  |               |       |
| <b>Mean age (Standard Difference)</b> | 65.25<br>(10.5)               | 68.37<br>(10.52) | 68.29<br>(10.49) | 0.559         |       |
| <b>Age</b>                            | 70=<<br>(%)                   | 2<br>(2.3%)      | 84<br>(97.7%)    | 86<br>(100%)  | 1     |
|                                       | 70><br>(%)                    | 2<br>(2.9%)      | 66<br>(97.1%)    | 68<br>(100%)  |       |
| <b>Gender</b>                         | Male<br>(%)                   | 2<br>(1.7%)      | 116<br>(98.3%)   | 118<br>(100%) | 0.233 |
|                                       | Female<br>(%)                 | 2<br>(5.6%)      | 34<br>(94.4%)    | 36<br>(100%)  |       |
| <b>Therapeutic Group</b>              | aPTT(+)<br>(%)                | 3<br>(4.8%)      | 59<br>(95.2%)    | 62<br>(100%)  | 0.065 |
|                                       | aPTT(-)<br>(%)                | 0<br>(0%)        | 92<br>(100%)     | 92<br>(100%)  |       |
|                                       | Total<br>(%)                  | 3<br>(100%)      | 151<br>(100%)    | 154<br>(100%) |       |
| <b>Therapeutic Group</b>              | Protamine(+)<br>(%)           | 1<br>(1.1%)      | 91<br>(98.9%)    | 92<br>(100%)  | 1     |
|                                       | Protamine(-)<br>(%)           | 0<br>(0%)        | 59<br>(100%)     | 59<br>(100%)  |       |
|                                       | Total<br>(%)                  | 1<br>(100%)      | 150<br>(100%)    | 151<br>(100%) |       |

Table 1. Comparison of age, sex and surgical groups of cases by complications

A and one case of hypotension due to protamine administration occurred in group B. Although the number of patients was different in two groups (62 cases vs. 92 cases), the complications showed no significant statistical difference.

Regarding the above results we conclude that performing an aPTT test before placing a vascular clamp and also neutralization of heparin with protamine at the end of surgery shows no effect on vascular surgery complications during the first postoperative 24 hours.

It is important to say that the studied samples of the two groups were from different university vascular surgery centers in Japan and Germany and the surgical team and techniques were not the same for all patients. Thus bias should be considered. However according to the results of

different studies on decreasing the neutralizing dose of protamine (to reduce its complications), complications of surgery will change or might even decrease [1,7,10,14,17,19]. Also the probable potential and dangerous complications of protamine might decrease.

Our findings show that by observing basic principles of vascular surgery and the 2 minute interval between heparin injection and clamping there is no need to perform an aPTT test before placing the clamp and to use protamine, given no abnormal bleeding occurs in the surgical field at the end of surgery. Thus the duration, risks, complications and expenses of surgery can be reduced.

Generalization of our findings needs more extensive studies in this context.

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