

Subclavian Needle Versus Cutdown? Consider the Risk To the Editor:

At least two procedures of which I am aware
Are done with risk to patients and suboptimal care:
Pacemaker insertion and Port-A-Caths* too;
Cessation of subclavian sticks for these is long overdue.

I doubt that there is any surgeon in the USA
Who cannot do a cutdown of the cephalic vein.
Iatrogenic complications should be nil.
Cutdowns of the cephalic vein require minimal skill.

I've heard it so often it makes me sad,
"This is the first pneumothorax I've ever had."
Why do surgeons who use needles persist?
Don't they realize that there's an extra risk?

Sure, it's true the risk is relatively small;
Two to five percent doesn't seem large at all.
Look again at Table 1; just give it a glance,
How many of our patients want to take that chance?

Philosophically, all surgeons will agree that to take a totally unnecessary risk on a patient is wrong. And yet, many surgeons, if not most, use the subclavian vein catheterization approach to insert a pacemaker or Port-A-Cath. This is unnecessary and not in patients' best interests. Complications (Table 1) of subclavian vein catheterization have been described in the literature for 30 years. Justification for the procedure has been that it facilitates placing catheters in the central venous circulation. In the setting of pacemaker or Port-A-Cath insertion there is little justification in that the central venous circulation is easily and safely reached by cephalic vein or, if need be, external jugular vein cutdown. The skin incision has to be made in any instance.

Furthermore, the subclavian stick even without a complication is more expensive. A cutdown on the cephalic vein requires a couple of ligatures, whereas the subclavian catheterization apparatus costs at least \$50 per case, double this if two leads are required. Multiply \$50 by the number of pacemakers placed in

Table 1. Reported Complications From Subclavian Vein Catheterization

1. Pneumothorax
2. Hemothorax
3. Arterial injury
4. Thoracic duct injury
5. Venous air embolism
6. Subclavian vein thrombosis, acute or delayed
7. Lead or catheter fracture/shear
8. Local bleeding
9. Unrecognized intrapleural placement of catheter
10. Arteriovenous fistula
11. Brachial plexus injury
12. Osteomyelitis and septic arthritis

* Port-A-Cath (SIMS-Deltec, Inc, St. Paul, MN): A totally implantable central venous port.

each year in this country, and the cephalic vein approach becomes even more attractive.

Subclavian vein catheterization does have its place, but not in pacemaker or Port-A-Cath insertion when performed by skilled surgeons.

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Aprotinin in Staged Heart Transplantation: Anaphylactic Potential of Repeated Exposure To the Editor:

The recent article by Goldstein and colleagues [1] is an excellent review of a multicentric experience of left ventricular assist device implantation, focused on the use of aprotinin to facilitate hemostasis. We agree with Goldstein and colleagues that limiting the requirement of packed red cells and blood products during the insertion of a mechanical assist device for staged heart transplantation is of utmost importance to preserve pulmonary function and prevent right heart failure. The drug seems to be essentially safe, as demonstrated by its relatively long-standing extensive use in cardiac surgery [2]. Among the adverse events listed in the article, a case of hypotension at the time of transplantation is reported but the incidence of anaphylaxis was zero. However, in the discussion Dr Loebe refers to a patient who died as a consequence of a severe allergic reaction to aprotinin. Because aprotinin is a polypeptide derived from bovine organs, there is always the possibility of a sensitization to the agent with an anaphylactic reaction after a second administration; the incidence of this in the literature is reported to be between 0.22% and 10% of cases [3, 4].

In our institution we routinely use aprotinin in general cardiac operations and in thoracic organ transplantation as well as during implantation of mechanical assist devices, according to a modified Royston protocol (2,000,000 KIU [280 mg] before cardiopulmonary bypass, 2,000,000 KIU [280 mg] in the priming and 600,000 KIU [84 mg] in continuous perfusion for 6 hours after cardiopulmonary bypass).

Even if in our experience the introduction of aprotinin in clinical practice was of tremendous benefit, an anaphylactic reaction with fatal consequences that occurred at the moment of transplantation in a patient supported with a left ventricular assist device prompted us to reexamine our protocols and to be more cautious. A 56-year-old patient with dilated cardiomyopathy underwent LVAD implantation (Novacor N100P; Baxter Healthcare Corp, Oakland, CA) because of refractory cardiac failure despite intraaortic counterpulsation. During the operation aprotinin was administered according to our standard protocol. The immediate postoperative course was complicated by dynamic subocclusion of the colon, hemorrhagic gastritis, and respiratory insufficiency, which required prolonged ventilation. On day 30 he underwent mediastinal debridement and sternal reapproximation for complete sternal dehiscence complicated by local and systemic enterococcal infection. Because of diffuse bleeding in the surgical field 600,000 KIU (84 mg) of aprotinin was administered; shortly thereafter bronchospasm developed, which was immediately treated with injection of solbutamol and hydrocortisone. An allergic reaction to aprotinin was suspected, and a thorough laboratory evaluation and immunologic profile was carried out. Total immunoglobulin E level was 271 KU/L (normal value, <250 KU/L). The concentration of tryptase, a mediator released by mast cells, normally undetectable, was 8 U/L, and this is the only test that could probably support the

thesis of an allergic reaction to aprotinin. The anti-aprotinin immunoglobulin E antibody radioallergoadsorbent test was not performed because of the unavailability of the proper kit.

The patient recovered rapidly and, fully rehabilitated, was allowed short out-of-hospital stays. Elective heart transplantation was performed 77 days after left ventricular assist device implantation and 47 days after the second exposure to aprotinin. The routine test dose of 10,000 KIU (1.4 mg) of aprotinin administered before CPB caused immediate hypotension with loss of peripheral vascular tone, unresponsive to pharmacologic treatment (epinephrine and norepinephrine up to $0.5 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$) and high-flow cardiopulmonary bypass. The operation was completed, but the patient died on day 15 of multiorgan failure directly related to the perioperative shock.

This dramatic experience raises some considerations regarding the appropriate use of this very effective drug in staged cardiac transplantation, where two consecutive major operations are necessary: (1) Because any drug or blood product can cause anaphylaxis in the case of repeated exposure to aprotinin, it is advisable to follow the recommendations proposed by Levy [4], first performing the prick test, then the intradermal test followed by an intravenous test dose. (2) Due to the risk of repeated administration, even if the extension of the potentially bleeding surface and the stiffness of the adhesions can complicate hemostasis at the removal of the device, we prefer to reserve the use of aprotinin to the implantation phase, in which limited bleeding can significantly contribute to preserve the pulmonary function and right heart hemodynamics. (3) Because some biological glues contain aprotinin, one must be aware of the possibility of concealed causes of sensitization.

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References

1. Goldstein DJ, Seldomridge A, Chen JM, et al. Use of aprotinin in LVAD recipients reduces blood loss, blood use, and perioperative mortality. *Ann Thorac Surg* 1995;59:1063-8.
2. Westaby S Aprotinin in perspective. *Ann Thorac Surg* 1993;55:1033-41.
3. Wuthrich B, Schmid P, Tornic M. IgE-mediated anaphylactic reaction to aprotinin during anesthesia. *Lancet* 1992;340:173-4.
4. Levy JH. Antibody formation after drug administration during cardiac surgery: parameters for aprotinin use. *J Heart Lung Transplant* 1993;12:S26-32.

Reply

To the Editor:

I have reviewed the letter by Martinelli and associates regarding the risk of anaphylactic reactions to repeat aprotinin use. In the case reported, the anaphylactic reaction causing death occurred after the third administration of the drug in a short period. Because aprotinin is an animal protein, the incidence of hypersensitivity reactions would be expected to increase with each reexposure. Because hypersensitivity-type reactions can range from mild symptoms like pruritis, dyspnea, and tachycardia to sometimes fatal anaphylactic shock, the potential ramifications should not be underestimated.

My colleagues and I routinely use aprotinin both at the time of long-term left ventricular assist device insertion and at the time of heart transplantation several months later. Of the 33 patients undergoing both procedures (device insertion and subsequent heart transplantation) we have had one episode of anaphylactic shock resulting from the readministration of aprotinin. In this patient, we rapidly exposed and cannulated the femoral artery and vein and achieved cardiopulmonary bypass with excellent flows although our systemic pressures remained at approximately 20 mm Hg. After stopping the aprotinin administration and administering appropriate high-level vasoconstricting agents, we were able to achieve a reasonable blood pressure within 10 minutes, and the patient subsequently survived the transplantation and was neurologically intact. Since this episode, we have routinely exposed the aorta or femoral artery before administering the repeat dose of aprotinin. We recognize that we lose the antiinflammatory and antifibrinolytic benefits of the drug during the initial skin incision and sternotomy; however, this provides us an extra level of safety in the event of an unexpected anaphylactic reaction.

With this policy, we have been able to administer the drug with confidence. In the event of circulatory collapse, we would be able to rapidly achieve cardiopulmonary bypass and resuscitate the patient. In addition, we obtain the benefits of less bleeding and less blood product requirements with less right-sided circulatory failure. Surgeons should be aware that although the incidence of anaphylaxis is extremely small at the time of initial aprotinin administration, the incidence of anaphylaxis during readministration may be as high as 5% [1]. The technique we offer will provide a buffer in this group of patients.

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Reference

1. Schulze K, Graeter T, Schaps D, Hausen B. Severe anaphylactic shock due to repeated application of aprotinin in patients following intrathoracic aortic replacement. *Eur J Cardiothorac Surg* 1993;7:495-6.

Experimental Retrograde Cerebral Perfusion via Bilateral Maxillary Vein in Dogs

To the Editor:

Boeckstaens and Flameng [1] recently reported their results regarding cerebral blood flow and venovenous shunting during retrograde cerebral perfusion (RCP) in baboons. They are to be congratulated on their results. They measured the cerebral blood flow using the colored microsphere method, brain and rectal temperature, blood gas during RCP, and histologic findings of the brain tissue after administration of circulatory arrest and RCP. They analyzed those data in great detail and concluded that RCP did not perfuse the brain in their experimental model. The experimental model they used perfused blood in both jugular veins, and the return through the caval vein was measured using an electromagnetic flow probe during RCP. During retrograde perfusion, the aorta was clamped at the distal arch. In their experiment, the largest fraction of perfusion volume during RCP returned through the inferior caval vein (IVC) due to venovenous shunting.