otherwise. A correct analysis of data on cardiac valvular prostheses allows a better understanding of the results of such procedures and enables surgeons to choose the appropriate prostheses for their patients.

Nicola Vitale, MD
Luigi de Luca, MD
Istituto di Cardiochirurgia
Università d Bari
Piazza Giulio 11
70124 Bari, Italy

Maurizio Cotrufo, MD
Istituto di Cardiochirurgia
Seconda Università di Napoli
Ospedale V. Monaldi
Via L. Banchi 3
80100 Napoli, Italy

REFERENCES

1. de Luca L, Vitale N, Giannolo B, et al. Mid-term follow-up after heart valve replacement with Carbo-Medics bileaflet prostheses. J THORAC CARDIOVASC SURG 1993;106:1158-65.
2. Akins CW. Mechanical cardiac valvular prostheses. Ann Thorac Surg 1991;52:161-72.
3. BMDP Program 1L. BMDP statistical software manual. Vol 2. Los Angeles: University of California Press, 1990.
4. Colton T. Statistics in medicine. Boston: Little Brown, 1978.

12/8/65676

Tracheal sleeve pneumonectomy for bronchogenic carcinoma

To the Editor:

The January 1994 issue of this JOURNAL included our article, titled "Tracheal Sleeve Pneumonectomy for Bronchogenic Carcinoma" (J THORAC CARDIOVASC SURG 94; 107:13-8). The work reported our experience with 28 tracheal sleeve pneumonectomies (TSPs), 27 right TSPs and one left TSP. The very low operative mortality (only one death, which occurred on the thirtieth postoperative day as a result of myocardial infarction) and the absence of anastomotic complications (stenosis and dehiscence) seemed to impress the readers, as indicated by the many reprint requests and letters with specific questions on technical details of tracheobronchial anastomosis, on anesthesia modalities, and on preoperative and postoperative care.

High mortality rates are commonly reported in the literature (8% to 29%). The progress of ventilation techniques and of suture-performing modalities have allowed acceptance of TSP. Nevertheless, TSP is still carried out only in centers highly qualified to perform thoracic surgery.

From 1992 (when the period of observation ended) to date we have performed seven more right TSPs on patients with lung cancer involving the tracheobronchial angle. In this last group of patients we recorded two deaths caused by postoperative complications which, in our opinion, were due to inappropriate preoperative radiotherapy. In this letter we would like to stress the negative effects of high-dose radiotherapy in patients eligible for TSP.

Like other authors, we adopted preoperative radiation treatment to reduce the tumor size, so as to facilitate the anastomotic procedure. We chose the low-dose protocol introduced by Paulson and associates,[1] reserving it for large neoplasms that might be expected to benefit most from combined radiotherapeutic and surgical treatment. No radiotherapy is planned in small tumors.

In our series, of 35 patients subjected to TSP, 14 received a preoperative radiotherapy protocol consisting of 10 treatments of 30 Gy each. One patient had preoperative chemotherapy. Another patient had both radiotherapy and chemotherapy. Seventeen patients did not receive any preoperative treatment. Two patients had high-dose radiotherapy (60 Gy). Their clinical history and the reasons for the high-dose radiation treatment, which in our opinion caused the patients' deaths, are briefly described.

The first patient, a 67-year-old man, was counselled to receive radiotherapy in 30 Gy doses. We were unaware that his son, who is a physician, decided to subject the patient to 60 Gy doses. Evaluation after radiotherapy showed a good result and the patient was therefore subjected to TSP. The postoperative course was normal until the ninth postoperative day, when clinical and roentgenographic signs of bronchial fistula developed. A bronchoscopic examination showed a hyperemic anastomosis covered with fibrin and without any sign of tissue healing: the endoscopic picture closely resembled that of the immediate postoperative period. A small bronchial fistula was found on the right edge of the suture. A tracheostomy was done and the patient was intubated with the same tube (Sybilla's tube) that we used to carry out the anastomosis, by inflating the balloon distal to the anastomosis. The pleural cavity was drained. The patient had a number of complications, and he died on postoperative day 22 of a fatal hemorrhage from a gastric ulcer. Repeated bronchoscopic studies during the course had all failed to show granulation tissue or other signs of healing on the anastomosis.

The second patient was a 71-year-old man. Despite our prescription for preoperative radiation therapy in 30 Gy doses, his condition was judged inoperable by the radiotherapist who therefore subjected him to 60 Gy doses. This treatment yielded a remarkable reduction of the mass. Because we were not sure of the actual responsibility of excessive preoperative radiation in determining bronchial dehiscence in the previous case, and considering the good general conditions of this patient, we decided to perform TSP.

On the first postoperative day a conspicuous bronchorrhea developed that necessitated repeated bronchial suctions. The patient died on the eighth postoperative day of pulmonary edema. A bronchoscopic examination had revealed a normal tracheobronchial anastomosis.

Jensik and coworkers,[2] in an article published in 1982, had already stressed the fact that postoperative mortality

The Journal of Thoracic and
Cardiovascular Surgery
August 1995

was significantly greater in patients preoperatively treated with 5000 rad. In our global experience, no technical or clinical problems occurred in patients subjected to a preoperative dose of 30 Gy. After these last two failures, whenever reduction of the tumor size is needed to facilitate the procedure, we recommend that a preoperative radiation dose of no greater than 30 Gy be used.

Giancarlo Roviaro, MD, FCCP, FICS[a]
Federico Varoli, MD[a]
Carlo Rebuffat, MD[a]
Silvio Marco Scalambra, MD[a]
Contardo Vergani, MD[a]
E. Sibilla, MD[c]
L. Palmarini, MD[b]
Giuseppe Pezzuoli, MD, FCCP, FICS[d]
Departments of Surgery[a] *and Anesthesiology*[b]
S. Giuseppe Hospital
Department of Anesthesiology
Policlinico of Milan IRCCS[c]
Institute of Surgery
University of Milan[d]
Milan, Italy

REFERENCES

1. Paulson DL, Urschel HC, McNamara JJ, Shaw RR. Bronchoplastic procedures for bronchogenic carcinoma. J THORAC CARDIOVASC SURG 1970;59:38-48.
2. Jensik RJ, Faber LP, Kittle CF, Miley RW, Thatcher WC, El-Baz N. Survival in patients undergoing tracheal sleeve pneumonectomy for bronchogenic carcinoma. J THORAC CARDIOVASC SURG 1982;84:489-96.

12/8/64940

Topical use of aprotinin in cardiac surgery

To the Editor:

We read with great interest the letters concerning the topical effect of aprotinin by Edmunds[1] and by Tabuchi, de Haan, and van Oeveren.[2]

We[3] demonstrated the efficacy of topical aprotinin (1 million KIU) in the pericardial cavity in reducing postoperative blood loss in patients undergoing cardiac operations.[3] O'Regan and associates[4] recently reported that topical application of aprotinin in the pericardial cavity significantly reduced the postoperative blood loss after cardiac operations. The mechanism by which aprotinin exerts its effect topically differs from its systemic effect, wherein the mechanism of action is conservation of platelet function and inhibition of fibrinolysis.

de Haan and associates[5] reported an increased activity of tissue-plasminogen activator from the pericardium and proposed a fibrinolysis-related bleeding tendency after cardiopulmonary bypass. Of equal interest is a recent report by Tabuchi and associates,[6] who demonstrated enormous activation of fibrinolysis on the surgical wound during cardiopulmonary bypass. Tabuchi, de Haan, and van Oeveren[2] have recently reported a tremendous increase of fibrin degradation products in the blood of the surgical wound compared with systemic blood. Low-dose systemic aprotinin reduced fibrin degradation products in wound blood by half compared with that in a control group (17,900 ± 6,800 ng/ml versus 38,200 ± 9,300 ng/ml). The results of these studies,[2, 5, 6] combined with the results of Tatar,[3] and O'Regan,[4] and their colleagues, suggest that a local fibrinolytic state persists after closure of the thoracic cavity and contributes to the postoperative blood loss. Topical aprotinin seems to exert an antifibrinolytic action by which it stabilizes fibrin sealing of the surgical wound.

Systemic absorption and effect of the topically applied aprotinin is a concern. The plasma aprotinin levels were measured in eight patients in our original study, and aprotinin could not be detected in any. However, this was a small number from which to reach a conclusion. Therefore we measured systemic drug concentrations in 30 of 150 patients in whom we used aprotinin topically (1 million KIU) in the pericardial cavity immediately after our original study at the GATA Department of Cardiovascular Surgery. Systemic aprotinin levels were determined by means of the sandwich-enzyme-linked immunosorbent assay technique at the first hour after the chest tubes were unclamped. Aprotinin could not be detected in any patient's blood. The exposure time to topical aprotinin was 11.4 minutes on average. Although aprotinin is a small molecule (about 7000 daltons), short exposure time and low topical dose limit systemic absorption. Our data once again confirm that the drug remains restricted to the pericardial space and the effect is completely due to topical action.

Although aprotinin has been reported as safe in earlier studies, a number of adverse reactions including renal impairment, graft occlusion, anaphylaxis after reuse, and disseminated intravascular coagulation after profound hypothermic bypass have begun to accumulate with increasing systemic use of aprotinin. The topical use of aprotinin will completely abolish most of the complications and eliminate the need for prophylactic use. We have used topical aprotinin extensively since 1991 with no adverse actions or intolerance. Another important consideration is treatment cost, which may be reduced by approximately 80% with the topical use of the drug.

We agree that "nothing is ever simple in the enzymatic stew of coagulation"[1] but believe that a simple approach to the problems sometimes brings better solutions. In our opinion, topical use of aprotinin will be established as a therapeutic option to reduce postoperative blood loss. It can at least be combined with systemic use to reduce the high intravenous doses. We also emphasize that careful surgical hemostasis is the key in reducing postoperative blood loss and that pharmacologic agents should be used not as an alternative but a supplement to surgical hemostasis.

Sertaç Çiçek, MD
Texas Heart Institute
Cardiovascular Surgery
P.O. Box 20345
Houston, TX 77225-0345
Harun Tatar, MD
Ufuk Demirkılıç, MD
Erkan Kuralay, MD
Department of Cardiovascular Surgery
GATA, Gülhane School of Medicine
Etlik, Ankara, Turkey