

summary, all 6 deaths were among the patients with del22q, either related or unrelated to their immunodeficiency. This association was statistically significant [6/15 vs 0/22, difference -0.4 , 95% CI -0.65 to -0.15 , $P = .002$].

In our experience microdeletion of chromosome 22q11.2 appears associated with poor overall outcome after surgical treatment of PA-VSD with MAPCAs. We believe that such a peculiarity, not necessarily related to special anatomic cardiac features associated with the syndrome itself, should justify the use of a protocol for preoperative assessment of immunologic status of patients with del22q undergoing surgery for PA-VSD with MAPCAs and the administration of a perioperative antifungal prophylaxis when necessitated by a depressed immunologic condition.

Within the population of patients with complex congenital heart lesions, the prevalence of genetic syndromes is relevant.⁹ Genetic syndromes may influence both clinical outcome and surgical results of treatment of congenital heart defects, both because of peculiar anatomic cardiac features and because of associated extracardiac abnormalities.^{9,10} This is the main reason that the possible association with a genetic syndrome should always be included among hypothetic risk factors within the analysis of postoperative outcome of congenital heart defects.

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References

1. Cho JM, Puga FJ, Danielson GK, Dearani JA, Mair DD, Hagler DJ, et al. Early and long term results of the surgical treatment of tetralogy of Fallot with pulmonary atresia, with or without major aortopulmonary collateral arteries. *J Thorac Cardiovasc Surg.* 2002;124:70-81.
2. Digilio MC, Marino B, Grazioli S, Agostino D, Giannotti A, Dallapiccola B. Comparison of occurrence of genetic syndromes in ventricular septal defect with pulmonic stenosis (classic tetralogy of Fallot) versus ventricular septal defect with pulmonary atresia. *Am J Cardiol.* 1996;77:1375-6.
3. Momma K, Kondo C, Matsuoka R. Tetralogy of Fallot with pulmonary atresia associated with chromosome 22q11 deletion. *J Am Coll Cardiol.* 1996;27:198-202.
4. Chessa M, Butera G, Bonhoeffer P, Iserin L, Kachaner J, Lyonnet S, et al. Relation of genotype 22q11 deletion to phenotype of pulmonary vessels in tetralogy of Fallot and pulmonary atresia-ventricular septal defect. *Heart.* 1998;79:186-90.
5. Hofbeck M, Rauch A, Buheitel G, Leipold G, von der Emde J, Pfeiffer R, et al. Monosomy 22q11 in patients with pulmonary atresia, ventricular septal defect, and major aortopulmonary collateral arteries. *Heart.* 1998;79:180-5.
6. Jedeke KB, Michels VV, Puga FJ, Feldt RH. Velocardiofacial syndrome associated with ventricular septal defect, pulmonary atresia and hypoplastic pulmonary arteries. *Pediatrics.* 1992;89:915-9.
7. Ackerman MJ, Wylam ME, Feldt RH, Porter CJ, Dewald G, Scanlon PD, et al. Pulmonary atresia with ventricular septal defect and persistent airway hyperresponsiveness. *J Thorac Cardiovasc Surg.* 2001;122:169-77.
8. Carotti A, Di Donato RM, Squitieri C, Guccione P, Catena G. Total repair of pulmonary atresia with ventricular septal defect and major aortopulmonary collaterals: an integrated approach. *J Thorac Cardiovasc Surg.* 1998;116:914-23.
9. Ferencz C, Loffredo CA, Correa-Villasenor A, Wilson PD. Genetic and environmental risk factors of major cardiovascular malformations: the Baltimore-Washington Infants Study, 1981-1989. Armonk (NY): Futura Publishing; 1997.
10. Marino B, Digilio MC. Congenital heart disease and genetic syndromes: specific correlation between cardiac phenotype and genotype. *Cardiovasc Pathol.* 2000;9:303-15. doi:10.1016/S0022-5223(03)01196-6

Caveat against the use of FEIBA in combination with recombinant factor VIIa

To the Editor:

We appreciate the recent report from Bui and colleagues¹ on a fatal thrombosis after administration of activated prothrombin complex concentrate (FEIBA) in a patient previously treated with recombinant activated factor VII (rFVIIa) for massive bleeding during extracorporeal membrane oxygenation. The activation of the coagulation system by FEIBA is a rare but known adverse reaction.² A fatal thrombosis after treatment with activated factor VIIa and FEIBA has been described previously.³

Despite this, the hemostatic treatment in this patients raises some further questions. As the authors stated, the extracorporeal

circulation (ECC) induces a disseminated intravascular coagulation-like state. A serum level of fibrin degradation products of 4 supports this theory and moreover indicates some degree of hyperfibrinolysis. Unfortunately, no information about the use of antifibrinolytic agents (aprotinin, tranexamic acid) in this patient were provided. We hypothesize that the use of antifibrinolytic agents might have attenuated the procoagulant condition in this patient.

Fibrinogen is extensively consumed in disseminated intravascular coagulation-like states.⁴ Because fibrinogen levels were not given for this patient, we have to speculate that fibrinogen levels in this patient were below the normal range because of profuse bleeding and elevated consumption, resulting in high levels of fibrin degradation products aggravating the bleeding condition. On the other hand, we can speculate that the substitution of 22 units of fresh-frozen plasma and, in particular, 30 units of cryoprecipitates may also have restored supernormal fibrinogen and factor VIII:c levels, which in this patient may have promoted a procoagulant potential possibly associated with the risk of thrombosis after administration of FEIBA.

Under conditions of profuse bleeding in association with a disseminated intravascular coagulation-like state, antithrombin activity is important. Antithrombin activity is decreased in ECC because of an elevated consumption,⁵ and thus the inhibitory potential of the plasmatic coagulation system may not have been preserved in this patient despite the substitution of 22 units of fresh-frozen plasma. Unfortunately, no information regarding antithrombin activity was provided. It is hypothesized that the substitution of antithrombin might have reconstituted the inhibitory potential of the plasmatic coagulation system, attenuating the procoagulant response to FEIBA.

Finally, we agree with the authors that the prothrombotic potential of rFVIIa is low, because this reflects our own observations.⁶ From in vitro results,⁷ we have to assume that the prothrombotic potential of FEIBA is higher. However, we disagree with the authors' conclusions on two points. First, despite the high safety profile of rFVIIa, the use of rFVIIa in cardiac and transplantation surgery needs further investigation before its use can be recommended, in particular for patients with prothrombotic risk factors.⁸ Second, the

initiation of heparin anticoagulation before treatment with factor concentrates in bleeding patients under ECC is controversial, because the effect of heparin is antithrombin dependent. We recommend the close monitoring and substitution of antithrombin in conditions with an ongoing activation of the hemostatic system. Although there is no evidence from the literature yet, inhibitor levels (in particular antithrombin) should be kept within the normal range before administration of factor concentrates to attenuate the procoagulant response, possibly resulting in thromboembolic complications.

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References

1. Bui JD, Despotis GD, Trulock EP, Patterson GA, Goodnough LT. Fatal thrombosis after administration of activated prothrombin complex concentrates in a patient supported by extracorporeal membrane oxygenation who had received activated recombinant factor VII. *J Thorac Cardiovasc Surg.* 2002;124:852-4.
2. Gruen DR, Winchester PH, Brill PW, Ramirez E. Magnetic resonance imaging of myocardial infarction during prothrombin complex concentrate therapy of hemophilia A. *Pediatr Radiol.* 1997;27:271-2.
3. Rosenfeld SB, Watkinson KK, Thompson BH, MacFarlane DE, Lentz DR. Pulmonary embolism after sequential use of recombinant factor VIIa and activated prothrombin complex concentrate in a factor VIII inhibitor patient. *Thromb Haemost.* 2002;87:925-6.
4. Horan JT, Francis CW. Fibrin degradation products, fibrin monomer and soluble fibrin in disseminated intravascular coagulation. *Semin Thromb Hemost.* 2001;27:657-66.
5. Noda A, Wada H, Kusiya F, Sakakura M, Onishi K, Nakatani K, et al. Plasma levels of heparin cofactor II (HCII) and thrombin-HCII complex in patients with disseminated intravascular coagulation. *Clin Appl Thromb Hemost.* 2002;8:265-71.
6. von Heymann C, Hotz H, Konertz W, Kox WJ, Spies C. Successful treatment of refractory bleeding with recombinant factor VIIa after redo coronary artery bypass graft surgery. *J Cardiothorac Vasc Anesth.* 2002;16:615-6.
7. Gallistl S, Cvirn G, Muntean W. Recombinant factor VIIa does not induce hypercoagulability in vitro. *Thromb Haemost.* 1999;81:245-9.
8. Dietrich W, Spannagl M. Caveat against the use of activated recombinant factor VII for intractable bleeding in cardiac surgery. *Anesth Analg.* 2002;94:1365-7. doi:10.1067/S0022-5223(03)01198-X

Is there an evidence in favor of off-pump coronary artery bypass?

To the Editor:

We read with interest the report of Mack and colleagues¹ that shows “improved outcome in coronary artery bypass grafting with beating-heart techniques.” In the era of evidence-based medicine and megatrials, class A level evidence will remain the standard tool that forces change of direction of currently applied surgical procedures, including coronary artery bypass grafting. We concede that in the absence of major prospective randomized trials^{2,3} retrospective studies such as this may contribute enough evidence to sway the balance in favor of or against off-pump coronary artery bypass grafting (OPCAB).

However, we wish to highlight two issues that could have a significant impact on the conclusions derived from the study. First, at one point the authors claimed that the conversion rate was 2.9% and stated that “these patients were analyzed with the on-pump group.” Later, however, they reported a conversion rate of 1.6% and suggested that the analysis was performed on an intent-to-treat basis (that conversions were analyzed with the OPCAB group). These conflicting statements require further clarification. Second, the need for a subgroup analysis of the cases converted from OPCAB to an on-pump procedure cannot be overemphasized. This analysis may provide the answer to a number of important questions regarding OPCAB, such as indications, timing, predictors, and, more importantly, the outcome of conversion in terms of mortality and morbidity.

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References

1. Mack M, Bachand D, Acuff T, Edgerton J, Prince S, Dewey T, et al. Improved outcomes in coronary artery bypass grafting with beating-heart techniques. *J Thorac Cardiovasc Surg.* 2002;124:598-607.
2. Yacoub M. Off-pump coronary bypass surgery: in search of an identity. *Circulation.* 2001;104:1743-5.
3. van Dijk D, Nierich AP, Jansen EW, Nathoe HM, Suyker WJ, Diephuis JC, et al. Early outcome after off-pump versus on-pump coronary bypass surgery: results from a randomized study. *Circulation.* 2001;104:1761-6. doi:10.1067/S0022-5223(03)01199-1

Short esophagi and a long career

To the Editor:

Professor J. Leigh Collis, a prominent surgeon, made several contributions to the development of the thoracic and cardiac surgery. However, he was immortalized and known worldwide for his work on gastroplasty, originally published in this Journal 46 years ago.¹

I contacted by letter the then-90-year-old Professor Collis, asking for data to be used in an article concerning the history of esophageal surgery. I was honored with a concerned and pleasant reply. After our last contact, however, I received the grievous notice that Professor Collis had died on February 4, 2003.

It is fitting to pay homage to this singular character in the history of the esophageal surgery in the same *Journal* that immortalized him.

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Reference

1. Collis JL. An operation for hiatus hernia with short esophagus. *J Thorac Surg.* 1957;14:768-73. doi:10.1067/S0022-5223(03)01199-1

Problems with complication rate analysis

To the Editor:

In a recent issue of this Journal, Grunkemeier and Wu¹ analyzed complication rates after bileaflet valve implantation by means of pooled data and regression anal-