clarify whether a multimodality approach could protect the patients against tumor recurrence.

The main problem of designing randomized trials with neoadjuvant treatment for patients with N1 NSCLC is how to obtain an accurate lymph node staging with the available diagnostic tools. Whereas cervical mediastinoscopy is highly sensitive and specific to exclude N2 as well as N3 status, computed tomographic scan of the chest does not allow detection of lymph node metastases in the stations 10 to 14 in most cases. The simultaneous combination of positron emission tomography and computed tomographic scan, as well as endoscopic ultrasonography, could afford further information about N1 nodes but are not yet considered for routine use. We agree with Margaritora and coauthors that is difficult to achieve the histologic or cytopathologic assessment of N1 disease and that more invasive diagnostic procedures (eg, video-assisted thoracoscopy or thoracotomy) are to be considered improper for routine clinical staging. Therefore, phase III studies on neoadjuvant chemotherapy or chemoradiotherapy in early stage NSCLC could actually be designed only by excluding patients with N2 and N3 disease and enrolling patients with true N1 and true N0 disease together.

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Influence of chromosome 22q11.2 microdeletion on surgical outcome after treatment of tetralogy of Fallot with pulmonary atresia

To the Editor:

We read with interest the important article by Cho and colleagues¹ recently published on the Journal. The article reported the huge surgical series of patients affected by pulmonary atresia with ventricular septal defect (PA-VSD) treated at the Mayo Clinic during the last 20 years. The analysis of follow-up data and risk factors related to surgery was extremely accurate, and the operative results were excellent. However, we noticed that the authors did not take into consideration the possible association with a genetic syndrome among the hypothetical risk factors for surgical mortality or morbidity.

The high prevalence of genetic abnormalities among patients with PA-VSD, particularly the chromosome 22q11.2 microdeletion (Di George or velocardiofacial syndrome) is well described in the literature,²⁻⁷ including important contributions from the Mayo Clinic.^{6,7} Chromosome 22q11.2 microdeletion (del22q) has been reported in about 40% of patients with PA-VSD,² particularly those with major aortopulmonary collateral arteries (MAPCAs)³ and complex loop morphology of the pulmonary arteries.^{4,5} The del22q abnormality has also been related to peculiar perioperative problems after surgery for PA-VSD, such as persistent airway hyperresponsiveness or increased prevalence of infectious complications.^{6,7}

Among the surgical series of 37 consecutive patients with PA-VSD and MAPCAs surgically treated at our institution between January 1994 and March 2002 (mean age 39 ± 48 months, range 22 days–13 years, 62% of patients 2 years old or younger), genetically diagnosed del22q (fluorescence in situ hybridization test) was present in 15 cases (40%, 95% confidence interval [CI] 24%–56%). Its occurrence did not relate to any peculiar anatomic phenotype with respect to either pulmonary vascular supply (mean number of MAPCAs 3.7 ± 1.3 for 15 patients with del22q, vs 3 ± 1.4 for 22 patients without del22q, *P* not significant), mean pulmonary arteries/collateral arteries lung segment perfusion ratio 1.5 ± 1.5 vs 2 ± 1.9 , *P* not significant) or prevalences of right aortic arch (53% [*n* = 8] among patients with del22q vs 36% [*n* = 8] among patients without del22q, *P* not significant) and infundibular atresia (53% [*n* = 8] among patients with del22q vs 50% [*n* = 11] among patients without del22q, *P* not significant).

Twenty-five patients underwent total unifocalization⁸ associated with successful either primary (*n* = 18) or secondary (*n* = 2) VSD closure in 80% of cases (20/25, 95% CI 64%–96%). The other 12 received an intermediate right ventricular outflow tract reconstruction with eventual second-stage unifocalization and repair in 11 cases, accounting for an overall reparability rate of the disease of 86% (31/36, 95% CI 74%–98%).

Mortality included 5 in-hospital deaths (15%, 95% CI 3%–27%), and 1 late death. Survival at 7-year follow-up was 81%. Two deaths occurred during the immediate postoperative course in 2 patients with del22q; pulmonary vascular disease was the cause in 1 case and no apparent cause was found at autopsy in the other. Postoperative hospital infections, including 2 fungal pneumonias, 1 fungal endocarditis, and 1 *Pseudomonas* pneumonia, occurred in 4 patients with del22q. Fungal infections were always related to a decreased CD4 lymphocyte count on peripheral blood samples and were responsible for 2 of 3 further in-hospital deaths. The last in-hospital death was that of a patient with del22q whose VSD was left open because of airway bleeding. Late death finally occurred in the case of a patient with del22q who had sudden airway bleeding early after successful second-stage closure of VSD. In

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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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