

## A preoperative index of mortality for patients undergoing surgery for type A aortic dissection

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**Background.** The aim of this study was to identify and stratify the most important preoperative factors for in-hospital death after surgery for type A aortic dissection. **Methods.** From January 1985 to June 1998, 108 patients underwent surgery for type A aortic dissection. 89.9% of the patients had an acute type A dissection (AD), whereas 11.1% had a chronic dissection (CD). Cardiac tamponade and shock occurred in 22% and 14.8% of the patients, respectively. The location of the primary intimal tear was in the ascending aorta in 71.2% of the cases, in the arch in 16.6% and in the descending aorta in 7.4%. Univariate and multivariate analyses were conducted to identify non-embolic variables independently correlated to in-hospital death. A predictive model of in-hospital mortality was then constructed by means of a mathematical method with the variables selected from logistic regression analysis.

**Results.** The overall in-hospital mortality rate was 20.3% (22/108 patients), being 9% for CD and 21.6% for AD. Emergent procedures had an in-hospital mortality rate of 47.6%, whereas non-emergent operations had an in-hospital mortality rate of 13.7% ( $p < 0.01$ ). Univariate analysis revealed among 39 preoperative and operative variables, age (years), age  $> 70$  years, remote myocardial infarction, cerebrovascular dysfunction, diabetes, preoperative renal failure, shock, cardiopulmonary bypass time (minutes), emergency operation as factors associated to in-hospital death ( $p < 0.05$ ). Stepwise logistic regression analysis selected as independent predicting variables ( $p < 0.05$ ), remote myocardial infarction ( $p = 0.006$ ), preoperative renal failure ( $p = 0.032$ ), shock ( $p = 0.001$ ), age  $> 70$  years ( $p = 0.007$ ). Finally, a probability table of death risk was obtained with the logistic regression coefficients. The lower death probability (10.6%) was calculated in absence of risk variables; the higher one in presence of all of them (79.7%). Between these extremes, a total of 64 combinations of death risk were obtained.

**Conclusions.** Increasing age, shock, coronary artery disease and renal failure are variously associated to a high risk of

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in-hospital death after surgical correction of type A aortic dissection. This predictive model of death probability allows to collocate preoperatively patients with type A aortic dissection at different levels of risk for in-hospital death.

**KEY WORDS:** Aneurysm, dissecting - Risk factors - Follow-up studies - Mortality - Aortic aneurysm.

Although the surgical outcome in patients with type A aortic dissection has substantially improved over time, thanks to advances in diagnosis, surgical techniques, and perioperative management,<sup>1-4</sup> in-hospital mortality remains high, ranging from 10% to 30% in most reported experiences.<sup>5-9</sup>

Previous studies have focused on variables associated with early mortality after surgery for type A aortic dissection, in an attempt to identify patients at very high risk. An extensive review from the Stanford group,<sup>1</sup> has indicated earlier operative year, hypertension, cardiac tamponade, renal dysfunction, and older age as independent determinants of operative death. However, other variables, such as emergency operation, previous cardiac or aortic operation, visceral ischemia, involvement of the aortic arch and other coexistent medical problems have also been suggested according to the different experiences.<sup>3,8-10</sup>

The issue of a preoperative score index for mortality remains, however, unsolved, especially with regard to the identification of patients at very high risk or not eligible for surgery. We think that previous studies attempting to predict in-hospital death from peri-

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operative variables have been probably limited by two factors: a) both preoperative and postoperative variables are used, making difficult a prediction solely based on preoperative and operative variables; and b) the variables have not been examined in combination in a predictive model.

Accordingly, the goal of the present study was to address these limitations. In order to construct a predictive model of in-hospital mortality for patients undergoing surgery for type A aortic dissection, a multivariate analysis was conducted to determine preoperative individual factors and to examine these variables in combination.

## Materials and methods

### Patients

One-hundred and eight patients (73 men and 35 women) underwent surgery for spontaneous Stanford type A dissection of the aorta at Cardiologic Center "I. Monzino" Foundation between 1985 and 1998. The diagnosis of dissection was preoperatively confirmed with aortography, computed tomography, transesophageal echocardiography (TEE), magnetic resonance imaging. Since 1994, the preoperative or intraoperative diagnosis of aortic dissection has been made noninvasively by TEE.

The dissection was classified as acute if the diagnosis occurred within 14 days, and chronic if longer than 14 days. Type A aortic dissection was considered an indication for urgent surgery in all cases. Surgery was considered an emergency when the patients were operated on with hemodynamic instability, shock, tamponade or signs of progression of the dissection. All clinical data were obtained by retrospective review of hospital records by two of us (GP, MR).

Preoperative and operative clinical features of patients are reported in Table I. Briefly, 89.9% of patients had an acute type A aortic dissection, whereas only 11.1% had a chronic dissection. The mean age of all patients was 59±12 (range: 27-83 years). Hypertension was the most common predisposing medical disorder, occurring in more than 50% of the patients. Interestingly, a remote myocardial infarction was recognized in 11.1% of the population. Cardiac tamponade and shock occurred in 22% and 14.8% of the patients, respectively. 19.4% of patients were operated on with an acute renal dysfunction. The loca-

TABLE I.—Preoperative selected clinical variables of the study population (n=108).

Variables	No. (%)
Acute	96/108(89.9)
Chronic	12/108(11.1)
Emergency operation	20/108(18.5)
Age (years)	59±12
Age ≥60 years	56/108(51.8)
Age ≥70 years	17/108(15.7)
Female gender	35/108(32.4)
Body surface area (m <sup>2</sup> )	1.8±0.22
NYHA class	2.5±0.7
Marfan syndrome	9/108(8.3)
History of hypertension	59/108(54.6)
Remote myocardial infarction	12/108(11.1)
Diabetes insuline-dependent	20/108(18.5)
History of congestive heart failure	5/108(4.6)
Previous transient hischemic attack	13/108(12)
Chronic obstructive pulmonary disease	14/108(12.9)
Chronic renal dysfunction	7/108(6.4)
Redo operation	8/108(7.4)
Preoperative acute renal dysfunction	21/108(19.4)
Compromised visceral perfusion	3/108(2.7)
Cardiac tamponade	24/108(22.2)
Shock	16/108(14.8)
Aortic insufficiency	22/108(20.3)
Paraplegia	1/108(0.9)
<i>Site of primary intimal tear</i>	
—Ascending aorta	77/108(71.2)
—Aortic arch	18/108(16.6)
—Descending aorta	8/108(7.4)
—Unknown	5/108(4.6)

ID: insuline-dependent.

tion of the primary intimal tear was in the ascending aorta in the majority of patients (71.2%); in the arch in 16.6% and in the descending aorta in 7.4%.

### Operative techniques

Operative characteristics of patients are reported in Table II. A simple ascending aorta replacement with a tubular Dacron interposition graft was the preferred method whenever possible (50.9% of patients). Alternatively, an aortoplasty limited to the intimal tear site was performed in 11.1% of the cases. When indicated, an associated aortic valve replacement or resuspension was performed in 20.3% and 10.1% of cases, respectively. Alternatively, a modified Bentall was used for dissection involving the coronary sinuses and eventually the aortic valve or the coronary ostia (18.5% of the cases). The arch was usually but not systematically

TABLE II.—Operative selected clinical variables of the study population (n=108).

Variables	No. (%)
Cardiopulmonary bypass time (min)	158±72
Aortic cross-clamp time (min)	127±61
Deep hypothermic circulatory arrest	27/108(25)
Circulatory arrest time (min)	27±31
Aprotinine use	56/108(51.8)
<i>Type of surgery</i>	
— Ascending aorta replacement	55/108(50.9)
— Aortic valve plus ascend. aorta replacem.	22/108(20.3)
— Modified Bentall procedures	20/108(18.5)
— Aortoplasty	11/108(10.1)
<i>Concomitant procedures</i>	
— Coronary artery bypass grafting	9/108(8.3)
— Arch replacement	29/108(26.8)
— Aortic anastomosis wrapping	21/108(19.4)
— Aortic valve resuspension	12/108(11.1)

included in the repair (26.8% of the patients) when a) the intimal tear was in the transverse arch, b) the dissection extending from the ascending or descending aorta into the arch had ruptured in the arch portion, or c) the false channel in the arch was severely dilated.

Nonpulsatile hypothermic cardiopulmonary bypass with moderate hypothermia and multidose antegrade or retrograde (or both) cold crystalloid cardioplegia was used. In addition, deep hypothermia with circulatory arrest with antegrade or retrograde cerebral perfusion was employed in 25% of the patients when the aortic arch had to be replaced or when distal anastomosis was needed with the "open aorta" technique.<sup>10</sup>

Femoral artery and right atrium cannulation was usually performed. For emergency procedures, both arterial and venous femoral cannulation were performed before sawing the sternum.

Starting from 1989, glue, whether biologic (Tissucol; Immuno, Pisa, Italy) or resorcine (Colle biologique Gelatine/Resorcinol/Formol; Cardial, Saint Etienne, France) was placed in the false lumen to obliterate it.

#### Follow-up

Follow-up information, available for 94.5% of the hospital survivors, was obtained by examination or by correspondence with the patient, the referring physician, or both of them. The date of last injury was September 1998. The average duration of follow-up for hospital survivors was 47±22 months; 38 patients were followed for more than 5 years.

#### Statistical analysis

All continuous data are expressed as mean±SD; categorical variables are reported as a percentage; a commercial statistical software (SPSS for Windows, version 6.0, SPSS Chicago, USA) has been used for data analysis.

Univariate analysis was done to analyse the possible relationship between in-hospital mortality and the collected variables. Contingency table analysis for categorical data and "t"-test or Mann-Whitney "U"-test for continuous variables were used.

Covariates that have been found to be significant ( $p < 0.05$ ) have then been entered into a multiple stepwise logistic regression analysis, carried out with in-hospital death as dependent variable. Variables that achieved a  $p$  value of 0.05 or less were considered significant. Both preoperative and intraoperative variables on the considered event were entered in the logistic regression.

From the variables found significant in the multivariate analysis, a formula was produced, and the probability of stroke was calculated as a function of these variables, according to the following model:<sup>11</sup>

$$P = e^{a+bx+cx+\dots} / 1 + e^{a+bx+cx+\dots}$$

where  $P$  is the probability of death;  $a$  is the regression coefficient of the intercept (constant);  $b, c, \dots$  are the regression coefficients of the variables identified in the regression analysis;  $x, y, \dots$  are the variables in the equation, coded according to the presence ( $x=1$ ) or the absence ( $x=0$ ) of that variable.

## Results

#### In-hospital mortality

The overall in-hospital mortality rate was 20.3% (22/108). The mortality rate decreased over time, passing from 27.4% (14/51) in the period between 1985-1990, to 14% (8/57) in the period between 1991-1998. Emergency procedures had an in-hospital mortality rate of 47.6% (10/21), whereas non-emergency operations had an in-hospital mortality rate of 13.7% (12/87), ( $p < 0.01$ ). Chronic dissections had an operative mortality rate of 9% (1/11), and acute type A dissections had a mortality rate of 21.6% (21/97). Causes of in-hospital death are reported in Figure 1. Cardiac-related complications (mono-biventricular failure; myocardial infarction) were the most common caus-

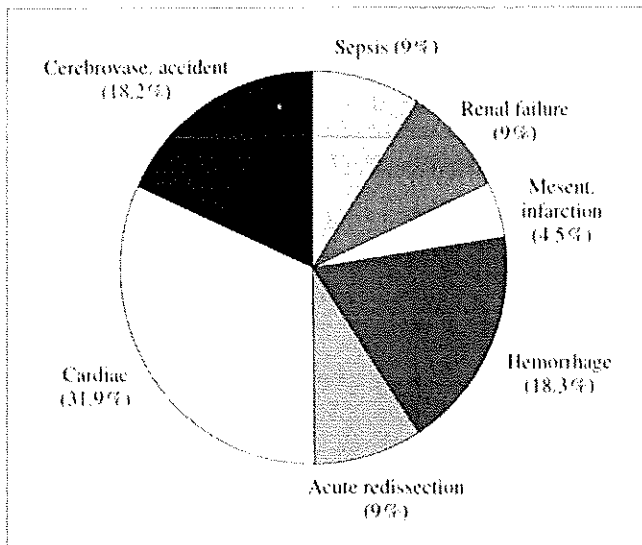


Fig. 1.—Causes of in-hospital death.

TABLE III.—Univariate analysis of risk factors for in-hospital death.

Variables	Patients discharged (86/108)	In-hospital death (22/108)	P
Age (years)	55.8±12	63.1±10	0.028
Age >70 years	8(9.3%)	9(40.9%)	0.0009
Remote MI	5(5.8%)	7(31.8%)	0.002
Previous TIA	7(8.1%)	6(27.2%)	0.03
Preoperative RF	12(13.9%)	9(40.9%)	0.01
Diabetes ID	12(13.9%)	8(36.3%)	0.03
Shock	7(8.1%)	9(40.9%)	0.0001
Emergency	12(13.9%)	9(36.3%)	0.03
CPB time (min)	123±41	173±69	0.02

MI=myocardial infarction, TIA=transient ischemic attack, RF=renal failure, ID=insuline-dependent, CPB=cardiopulmonary bypass.

es of postoperative death (31.9%). Stroke and hemorrhage both represented the cause of death in 18.3% of the cases. Other causes of mortality were acute redissection, renal dysfunction, sepsis (9%), and mesenteric infarction (4.5%).

#### Univariate analysis

Twenty-eight preoperative and 13 operative factors (Tables I and II) entered in the univariate analysis. The outcome variable, postoperative death, was coded with either 0 or 1 indicating the absence (0) or the presence (1) of postoperative death. Table III shows the factors that were significantly associated with death ( $p < 0.05$ ) at the univariate level: age (years);

TABLE IV.—Multivariable analysis of risk factors for in-hospital death.

Variables	p	OR
Emergency operation	ns	—
Remote myocardial infarction	0.006	1.981
Previous TIA	ns	—
CPB time (min)	ns	—
Preoperative renal insufficiency	0.032	0.885
Shock	0.001	3.128
Age >70 years	0.007	1.752
Diabetes ID	ns	—

OR=Odds Ratio; TIA=transient ischemic attack; CPB=cardiopulmonary bypass, ID=insuline-dependent.

APPENDIX I.—Combination of risk factors.

Age >75 years	Shock	MI	RD	Probability
0	0	0	0	0.1062
0	0	0	1	0.1907
0	0	1	0	0.2209
0	0	1	1	0.3600
0	1	0	0	0.2676
0	1	0	1	0.4202
0	1	1	0	0.4659
0	1	1	1	0.6337
1	0	0	0	0.2131
1	0	0	1	0.3495
1	0	1	0	0.3926
1	0	1	1	0.5619
1	1	0	0	0.4545
1	1	0	1	0.6230
1	1	1	0	0.6654
1	1	1	1	0.7978

Regression analysis coefficients:  $\alpha = -2.130$ , Age >70 years = 0.7339, Shock = 0.99, MI = 0.7155, RD = 0.7053

age >70 years; remote myocardial infarction, previous transient ischemic attack; insuline-dependent diabetes; preoperative renal dysfunction; shock; cardiopulmonary bypass time (minutes); emergency operation. These variables were entered in the multivariate analysis.

#### Logistic regression analysis

In this analysis, preoperative and operative variables were combined. As shown in Table IV, the factors statistically significant ( $p < 0.05$ ) were: remote myocardial infarction ( $p = 0.006$ ); preoperative renal dysfunction ( $p = 0.031$ ); shock ( $p = 0.001$ ); age >70 years ( $p = 0.007$ ).

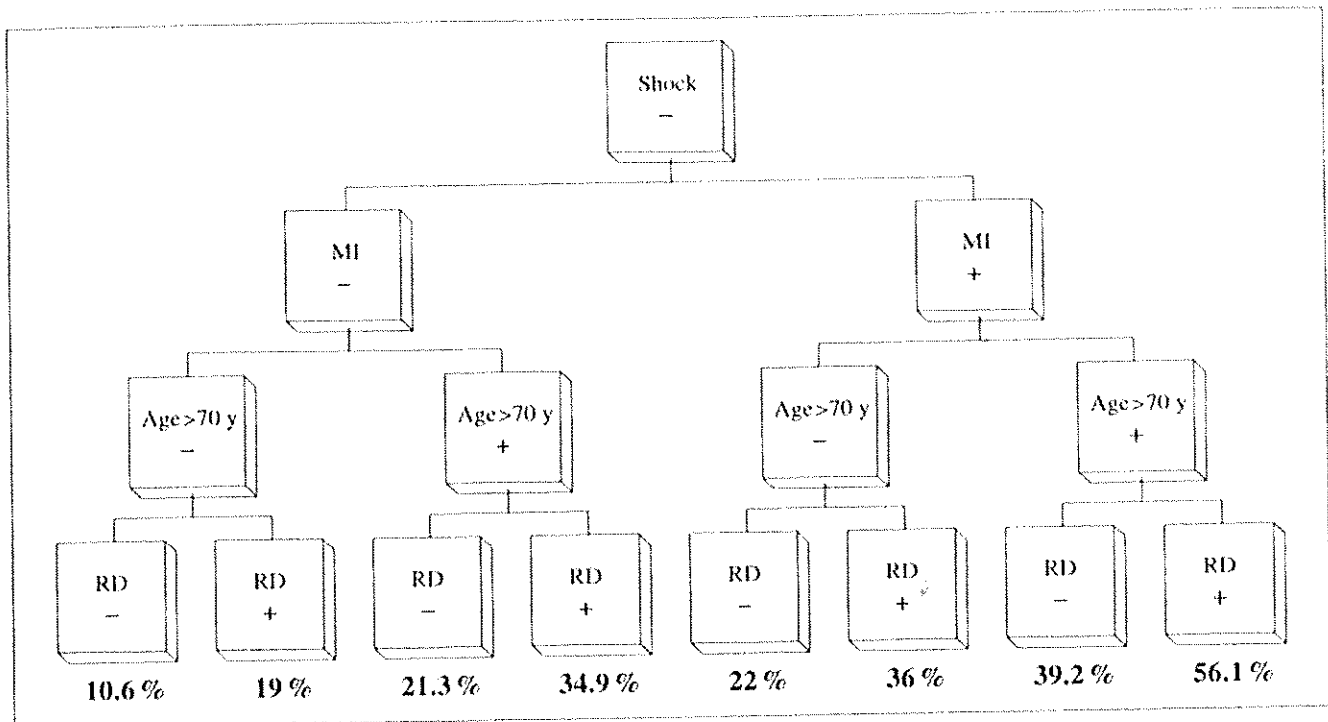


Fig. 2. — Calculated probability of in-hospital death.<sup>1</sup> MI: preoperative myocardial infarction; RD: preoperative renal dysfunction.

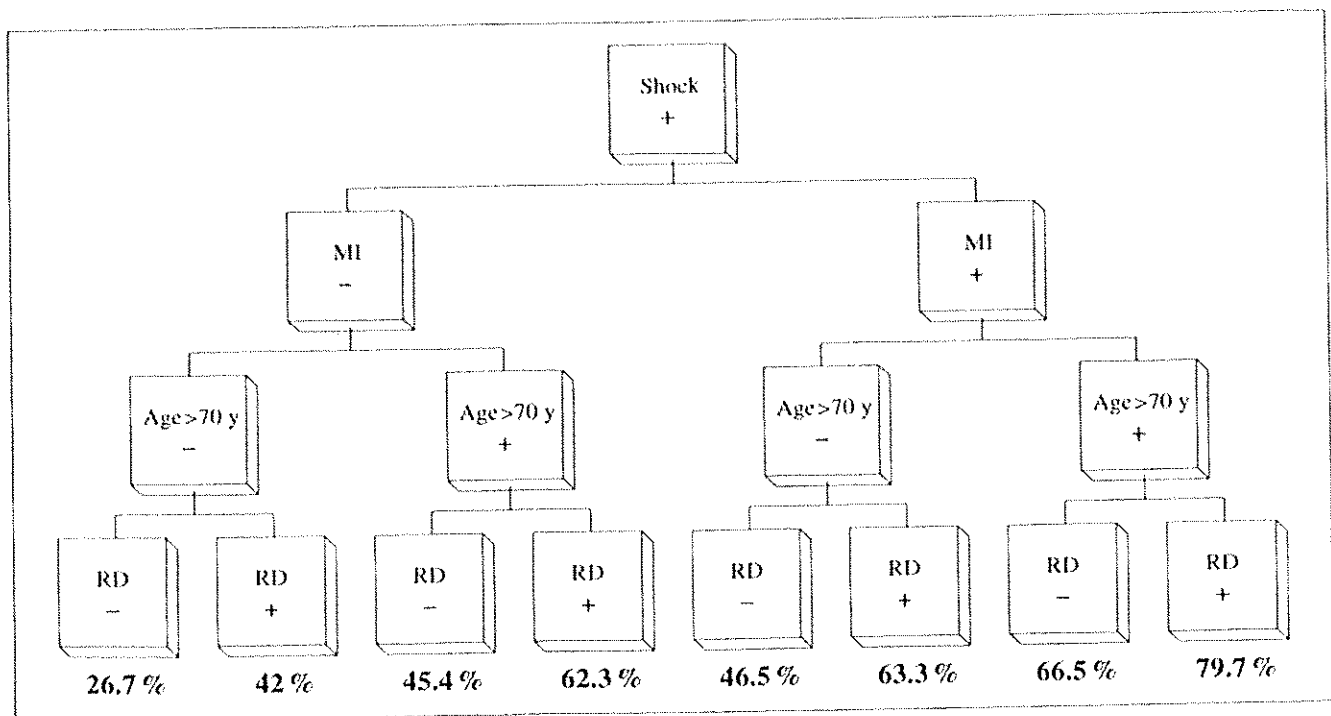


Fig. 3. — Calculated probability of in-hospital death.<sup>2</sup> MI: preoperative myocardial infarction; RD: preoperative renal dysfunction.

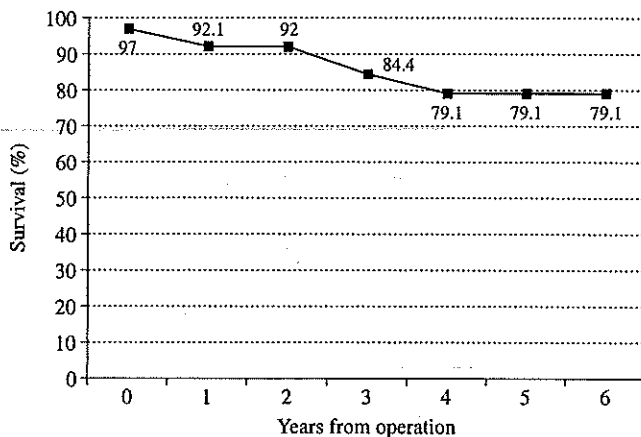


Fig. 4. — Actuarial survival curve for patients discharged.

#### Calculated probability of in-hospital death

Pooling together the variables found significant ( $p < 0.05$ ) in the logistic regression analysis, we obtained a probability table for each combination of variables (see Appendix 1).

The distribution of patients according to risk factor combination is shown as flow-charts in Figures 1 and 2. In this way the variables were estimated and represented in the flow-charts according to their importance. The lower death probability (10.6%) is calculated in the absence of risk variables; the higher one in the presence of all of them (79.7%). Intermediate levels of risk are easily constructed: for example, a patient older than 70 years of age with a preoperative renal dysfunction has a probability of in-hospital death of 34.9%. The same patient, operated on in shock increases twice as much his death probability (62.3%).

#### Follow-up

Among the 86 hospital survivors, 7 subsequently died during a mean follow-up of  $47 \pm 22$  months. Overall survival rate of hospital survivors was 79.1% 6 years postoperatively (Fig. 4).

#### Discussion and conclusions

This work has addressed the issue of constructing a preoperative in-hospital mortality index for patients candidate to surgical repair of type A aortic dissection.

From the variables independently associated with in-hospital death, a probability table was obtained. This aimed to stratify preoperatively the patients with type A aortic dissection at different level of surgical risk.

The overall operative mortality of 20.3% in the present series corresponds to a range of 5% to 39% reported by other groups in the surgical treatment of patients with type A dissection of the aorta.<sup>1-7 13-15</sup> Similarly, the reduction of operative mortality in the most recent part of this series (27% to 14%) corresponds to the improvements over time described by other groups.<sup>1 2 16 17</sup> Interestingly, our predicted non-risk adjusted probability of in-hospital death (10.6%) also falls within the aforementioned early death rates. This suggests that uncomplicated patients with type A aortic dissection clearly benefit from the modern policy of very early referral for operation and from advances in surgical techniques and strategy ("open aorta" anastomoses, use of biological glues, improved cerebral protection).

Previous studies attempted to identify factors related to early mortality. Miller *et al.*<sup>15</sup> in a multivariate analysis of 76 patients with type A aortic dissection identified renal dysfunction, cardiac tamponade, renal/visceral ischemia, and earlier operative period as variables associated independently with an increased risk of death. Similarly, Svensson *et al.*,<sup>2</sup> found as independent predictors of operative mortality, operation more than one day after symptoms, extension of the operation into the aortic arch, cardiac complications and earlier operative period. More recently, in a large review of 360 patients who underwent surgery for aortic dissection over a 30-year period, Fann *et al.* from Stanford<sup>1</sup> have indicated earlier operative year, hypertension, cardiac tamponade, renal dysfunction and older age as independent determinants of operative death. The variables found predictive of death in our series – age  $> 70$  years, remote myocardial infarction, renal dysfunction, shock – correlate well with the findings of the Stanford group. We didn't find in the multivariate analysis a time-dependent correlation with in-hospital death, although the mortality rate decreased over time in our thirteen-year experience. Moreover, remote myocardial infarction, instead of hypertension, emerged as predictive factor of death correlated with atherosclerosis.

Preoperative shock was the most important variable influencing in-hospital mortality, taking an isolated death probability of 26.7%. Other studies have indicated univariate<sup>15</sup> and multivariate<sup>1 8 9</sup> analysis fac-

tors associated with emergency procedures, like hypotension, cardiac tamponade, hemodynamic instability, as variables strongly correlated to an increased risk of operative mortality. We concur with Safi *et al.*<sup>9</sup> that also the modern supportive medical care does not appear able to affect patients with a severe shock at hospital admission. In this series, emergency procedures had a mortality rate of 47.6%.

The second factor influencing mortality is a remote myocardial infarction. The presence of chronic coronary artery disease remains a debated issue in patients who underwent surgery for type A aortic dissection. The prevalence of CAD in these patients varies. Rizzo *et al.*<sup>16</sup> found chronic CAD in 11% of type A dissection patients who had angiography. Rosenbloom *et al.*<sup>18</sup> found CAD in 33% of their 45 patients with acute dissection of the ascending aorta. In the present study, a remote myocardial infarction was found in 12 patients (11%). Seven of them died, 5 intraoperatively for causes related to the coronary disease. The isolated probability of death for patients with a remote myocardial infarction is 22%.

Although it has been reported that improved survival for patients with acute dissection can be achieved by the use of noninvasive diagnostic techniques such as transesophageal echocardiography,<sup>16</sup> it appears that coronary angiography may be considered in stable patients with a proved myocardial infarction. This approach seems to be shared by other groups.<sup>13 19</sup>

Another variable we found to influence in-hospital mortality is age  $\geq 70$  years. This subgroup included 17 patients; 9 of them died. The predicted isolated probability of death in patients aged  $\geq 70$  years is 21.3%. Yun *et al.*<sup>20</sup> reported a very high operative mortality (86%) for patients of 68 years of age or even older who underwent aortic arch repair for acute dissection (wondering if arch replacement should be performed for patients in this age group). More generally, other studies<sup>1 2 15 21</sup> have described the relationship between increasing age and operative mortality. We think that the problem of an advanced age in patients with aortic dissection should be framed in a wider evaluation of the clinical status of the patient. The presence of other ongoing systemic illnesses or other main risk factors in an aged patient can assist the physician in deciding not to proceed with surgical therapy.

Finally, renal dysfunction was the fourth predictive variable increasing death risk (isolated probability: 19%) found in this study. Most authors agree that the presence of preoperative renal dysfunction can be

considered as a sign of dissection-related complication.<sup>1-3 15 21</sup> In the present study, renal dysfunction represents together with preoperative shock, the only potentially modifiable preoperative variables, the incidence of which theoretically can be reduced by a very early diagnosis and surgical intervention.<sup>16</sup>

When taken all together in a predictive model of death risk, these variables allow a global view of in-hospital death probability for the patients with type A aortic dissection, not only for each individual independent determinant of risk, but, maybe more interestingly, to construct a different level of risk with the different combination of variables. A total of 64 combinations of death probability were obtained: the lower probability (10.6%) was calculated in the absence of those risk variables, the higher one in the presence of all of them (79.7%). Thus, a patient older than 70 (years of age), with a remote myocardial infarction, renal dysfunction at hospital admission, operated on in shock is very likely to die intraoperatively or within 30 days from operation, having no more than a 20% chance of survival. These results correspond well with the Stanford group experience,<sup>1</sup> who reported an overall salvage rate not exceeding 20% to 25% for patients with major dissection complications.

The obvious corollary is therefore to decide if the presence of all – or a detrimental combination – of these incremental risk factors should be considered as a contraindication to surgical intervention. We believe that in these cases an aggressive attitude towards surgical treatment is not completely justified, being comparable with the survival rates of medically treated patients.<sup>22 23</sup>

The possible limitation of the present study is that it has been obtained from a single-center series. A validation sample is obviously needed to evaluate the efficacy of this model in the clinical setting and from other surgical environments. We hope that this study can help the physician to predict patients referred to him with a complex disease as type A aortic dissection different levels of death risk after surgical correction.

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