Multicenter Registry of Acute Aortic Dissection. The RADAR Study. Preliminary Results.

CLAUDIO HIGA[MTSAC], JAVIER GUETTA[†], RAÚL A. BORRACCI[MTSAC], RAÚL MERIBILHAA, MARÍA PÍA MARTURANO[†], RICARDO MARENCHINO, MARIANO BENZADÓN, PABLO COMIGNANI, FERNANDO BOTTO[MTSAC], JUAN JOSÉ FUSELLI[MTSAC], On Behalf of the Investigators of the RADAR Study. Research Area and Council on Cardiovascular Emergency Care, Argentine Society of Cardiology

Received: 06/19/2009
Accepted: 08/04/2009

Address for reprints:
Dr. Claudio Higa
Sociedad Argentina
de Cardiología
Azcuénaga 980
(1115) Buenos Aires, Argentina

SUMMARY

Background
Acute aortic syndrome (AAS) still represents one of the most severe cardiovascular conditions due to its high mortality and morbidity; for this reason, it is extremely important to perform an early diagnosis of the disease.

Objectives
The *Registro de la Sociedad Argentina de Cardiología de Disecciones AóRticas Agudas* (RADAR registry) was designed to analyze the modalities of clinical presentation, diagnosis, treatment and mortality of AAS through a continuous registry of this not very prevalent disease.

Material and Methods
From February 2007 to April 2009, 95 patients consecutively admitted to 12 centers with a diagnosis of AAS were enrolled; basal clinical characteristics, complementary studies, type of treatment and clinical outcomes were obtained.

Results
Most patients were men (68%), mean age was 58.8±13.9 years, 78% were type A aortic dissections and 22% were type B. Eighty four percent of patients had hypertension, 28% were current smokers and 24% had dyslipemia. Chest pain or dorsal pain was present in 85.1% of cases. Global median time interval from onset of symptoms to intervention was 18 hours (12-72). Surgery was performed in 89% of type A and in 15% of type B dissections. Beta blockers were used in 64.7% of cases, sodium nitroprusside in 47.4%, aspirin in 15.8%, oral anticoagulant agents in 3.2% and thrombolytic drugs in 3.2%. Global mortality was 32.6%. Mortality rate of type A dissection was 37.8% (31% in patients undergoing surgery versus 87.5% in absence of surgical treatment; p=0.01). Dissection type B had mortality rates of 14% versus 12%, respectively (p=ns). A pattern of circadian variation regarding onset of symptoms was observed, with a peak in the morning hours. Logistic regression analysis showed that the independent variables associated with in-hospital mortality were age >70 years and the presence of hypotension or shock at admission.

Conclusions
Mortality from AAS is still high despite technical progress. Physicians should be alert to detect this condition in order to perform early diagnosis and treatment. This type of continuous and multicenter registry allows a more real approach to the problem related to this severe disease in our environment in order to optimize diagnostic and therapeutic strategies.

Rev Argent Cardiol 2009;77:354-360.

Key words > Aorta - Aortic Dissection - Registry - Mortality - Cardiovascular Surgery

Abbreviations >

ECG	Electrocardiogram	**BP**	Blood pressure
AAS	Acute aortic syndrome		

[MTSAC] Full Member of the Argentine Society of Cardiology
[†]To apply as full member of the Argentine Society of Cardiology

BACKGROUND

Acute aortic syndrome (AAS) refers to a variety of conditions of the aortic wall and represents one of the most severe and potentially life-threatening cardiovascular emergencies. Mortality rate reaches 50% in the first 48 hours without treatment (1) and 15% to 30% with surgical treatment, according to the different series. (2, 3) The syndrome includes three entities: aortic dissection, intramural hematoma and penetrating atherosclerotic ulcer. (4) The incidence of AAS is approximately 20-40 cases per 100 000 person-years; (5, 6) about 80% are aortic dissections, 15% intramural hematomas and 5% penetrating atherosclerotic ulcers.

Despite the better comprehension of the physiopathology of AAS and the availability of novel diagnostic imaging techniques and therapeutic options, the mortality of this syndrome still remains high due to the severity of the disease and the delayed diagnosis.

Recently, several groups have published information about the preoperative risks and the prognosis of the disease. (3, 7-14) However, most of these data come from retrospective studies based on a small number of patients included over short periods and without making any difference between type A and type B dissections. (9-12) Occasionally, studies were based on large patient series but with data collected over a long period of time (15 to 20 years) and thus the results are not comparable. On the contrary, other multicenter studies are biased as they have been performed at referral centers (3, 7, 8) and the results cannot be extrapolated to the real world.

The RADAR registry (Registro de Disecciones Aórticas Agudas) was designed to analyze the modalities of clinical presentation, diagnosis, treatment and mortality of AAS through a continuous registry performed at cardiovascular surgery centers of the Autonomous City of Buenos Aires.

MATERIAL AND METHODS

This prospective and continuous registry was conducted from February 2007 to April 2009 at 12 centers in the city of Buenos Aires and included patients > 18 years with diagnosis of aortic dissection or ASS lasting not more than 14 days. The diagnosis was made based on clinical data collected from the medical record, on the results of image tests (chest X-ray, aortogram, computed tomography, magnetic resonance imaging and echocardiography), or on post mortem findings. Patients with traumatic aortic dissection were excluded. The continuous nature of the registry was chosen due to the low incidence of aortic dissections and the centers were periodically surveyed. The registry was coordinated by the Research Area in conjunction with the Council on Cardiovascular Emergency Care of the Argentine Society of Cardiology. The protocol was approved by the Committee on Bioethics of the Argentine Society of Cardiology and by the authorities of each participant center. An informed consent form was signed by the patients and/or relatives before the inclusion in the registry. Data were collected from hospital medical charts and recorded in a standardized form containing 104 variables including demographics, history, physical findings, imaging studies and clinical outcomes. Hypertensive emergency was defined as blood pressure (BP) > 180/120 mm Hg, complicated with end-organ dysfunction that required immediate BP lowering to prevent or limit organ damage. Hypotension/shock was defined as systolic BP < 90 mmHg or urinary output < 0.5 ml/kg/h. Syncope was defined as a sudden and temporary loss of consciousness and of postural tone due to global hypoperfusion of the brain that recovered spontaneously. Finally, acute kidney failure was defined as an increase of > 50% in basal creatinine levels (for previously abnormal values), serum creatinine > 2 mg/dl for normal basal values or hemodialysis requirement.

Statistical analysis

Qualitative variables were expressed as percentages and quantitative variables as means ± standard deviations or medians and their corresponding 25-75% interquartile ranges according to the type of distribution. Normality of distribution of the latter variables was assessed using the goodness of fit test. Mortality was compared with the chi-square test. Logistic regression analysis was performed considering in-hospital mortality a dependent variable. A fitted curve was constructed for the chronobiological analysis of the time of symptom onset of the aortic dissection. The analysis of circadian rhythmicity was performed on hourly data. A p value < 0.05 was considered statistically significant. Statistical analysis was performed using SPSS 13.0 statistical package software (Chicago, Illinois).

RESULTS

From February 2007 to April 2009 95 patients with diagnosis of AAS were included. Mean age was 58.8 ± 13.9 years and 68% were men (64 patients). Type A dissection was identified in 78% of patients (74 cases) and type B in 22% (21 cases). The clinical characteristics of patients according to type of dissection are described in Table 1. Among smokers, 59% (31 cases) were current smokers and 31% (15 cases) had given up the habit. Pathological examination revealed syphilitic aortitis in one case (1.2%) and Marfan syndrome in 5 cases (5.3%). Aortic dissection was related with previous surgery in one patient and a iatrogenic lesion caused

Table 1. Clinical characteristics of patients according to type of acute aortic dissection

	Type A dissections n = 74	Type B dissections n = 21
Age (years), median (interquartile range)	58 (47-69)	61 (49-70)
Men, n (%)	51 (68.9)	13 (61.9)
Hypertension, n (%)	62 (83.9)	17 (81.0)
Diabetes, n (%)	6 (8,0)	0 (0)
Hipercolesterolemia, n (%)	23 (31.1)	6 (28.6)
Current smoking, n (%)	17 (23)	9 (42.9)
Prior surgery, n (%)	3 (4.1)	1 (4.8)
Chest pain, n (%)	65 (87.8)	15 (71.4)

by angiography was detected in another patient. A total of 40 patients (42%) had been referred from medical centers lacking diagnostic and therapeutic services to manage the disease.

Presenting symptoms and radiological and electrocardiographic features

The majority of patients complained of chest pain or pain in the back (85%, 80 cases); migratory pain was present in 30% of patients (28 cases). Syncope was the presenting symptom in 4.2% of patients (4 cases). Hypertensive emergency at initial presentation occurred in 10.5% of patients (10 cases), and 11.6% (11 cases) were admitted with hypotension or shock. Other clinical presentations were cardiac tamponade (7.4%, 7 cases); kidney failure (7.4%, 7 cases); coma (9.5%, 9 cases); absence of pulse or pulse deficit (6.3%, 6 cases); peripheral ischemia (7.4%, 7 cases); spinal cord ischemia (6.3%, 6 cases), and stroke (3.2%, 3 cases).
Chest radiography at admission showed mediastinal widening in 67% (65 cases) of patients (67.6% -50 cases- in type A dissections versus 75% –15 cases– in type B dissections).

The 12-lead electrocardiogram was normal or showed nonspecific abnormalities in 82% (77 cases) of patients; there were signs of ischemia or myocardial infarction in 10.5% (8 cases) (10.8% –10 cases– in type A dissections and 10% –2 cases– in type B dissections).

Diagnostic Imaging

A transthoracic echocardiogram was performed in 69% of patients (66 cases); the result was positive for AAS 66% of patients (43 cases) and negative in 6% (4 cases), while a diagnosis of suspected AAS was made in 28% (19 cases). Transesophageal echocardiography was performed in 60% (57 cases) of patients and was positive for AAS in 96% (55 cases), negative in 1.7% (1 case) and in 1.7% (1 case) of patients a diagnosis of suspected dissection was made. A total of 64 patients (67%) underwent chest computed tomography; the diagnosis was positive in 85% (55 cases), negative in 1.5% (1 case), and a diagnosis of suspected dissection was made in 12% (8 cases). Magnetic resonance imaging was used in only 8.4% (8 cases) of patients, and the diagnosis was positive in 85% of cases (7 cases). Coronary angiography was used in 13% (14 cases) of patients; a positive diagnosis was made in 92% (13 cases). In total, 40% (38 patients) of patients underwent a single study, while 52% (49 cases) needed two studies. Transthoracic echocardiography and computed tomography were used together in 26% (24 cases) of patients and this test combination was the most frequent, followed by transthoracic and transesophageal echocardiography (21%, 20 cases). Transesophageal echocardiography and computed tomography were used together in 13% (12 cases) of patients and the result was positive in both tests. Table 2 shows the percentage of positive results for each test according to the type of dissection.

Moderate to severe aortic regurgitation was present in 48.9% (36 cases) of type A aortic dissections versus a 5% of type B dissections. In 29.7% (22 cases) of type A dissections, the aortic diameter was > 6 cm versus 5% in type B dissections (1 case). A patent false lumen was present in 58% (64 cases) of type A dissections and in 25% (5 cases) of type B dissections. Partial thrombosis of the false lumen occurred in 14.9% of type A dissections (11 cases) and in 20% of type B dissections (4 cases). Total false lumen thrombosis was present in 4.1% (3 cases) of type A dissections and in 30% of type B dissections (6 cases). Penetrating atherosclerotic ulcers were found in 1.4% (1 case) of type A dissections and in 10% (2 cases) of type B dissections. Intramural hematoma was present in 9.5% (7 cases) of type A dissections and in 30% (6 cases) of type B dissections.

Table 2. Positive results for each test according to the type of dissection

	Type A dissections n = 74	Type B dissections n = 21
Positive transthoracic echocardiography, n (%)	40 (54.1)	3 (14.3)
Positive transesophageal echocardiography, n (%)	49 (66.2)	6 (28.6)
Positive computed echocardiography, n (%)	38 (51.4)	17 (81.0)
Positive magnetic resonance imaging, n (%)	3 (4.1)	4 (19.0)
Positive angiography, n (%)	10 (13.5)	3 (14.3)

Chronobiology and time interval from symptoms onset to diagnosis

Figure 1 shows the circadian variation in onset of AAD. The information about the time of symptom onset was available in 75% of patients (72/95) and was reported by the patient, relatives, or witnesses. These patients were included in the analysis of circadian rhythmicity performed on hourly data after categorization into 24 one-hour increments. The information about the time interval from symptoms onset to the beginning of the intervention was available in 70% of the population and was of 14 hours (4-48) for all dissections. This time interval was of 12 hours (4-48) for type A dissections and of 16 hours (6-56) for type B dissections.

Management and treatment

In total, 71 patients (74%) underwent surgical treatment. Surgical procedures (89%, 66 cases) for type A dissections included replacement of the ascending aorta (92.6%, 61 cases), aortic arch (21.8%, 17 patients), descending aorta (10.6%, 7 cases) and elephant trunk procedure (6.1%, 4 cases). Surgical therapy for asso-

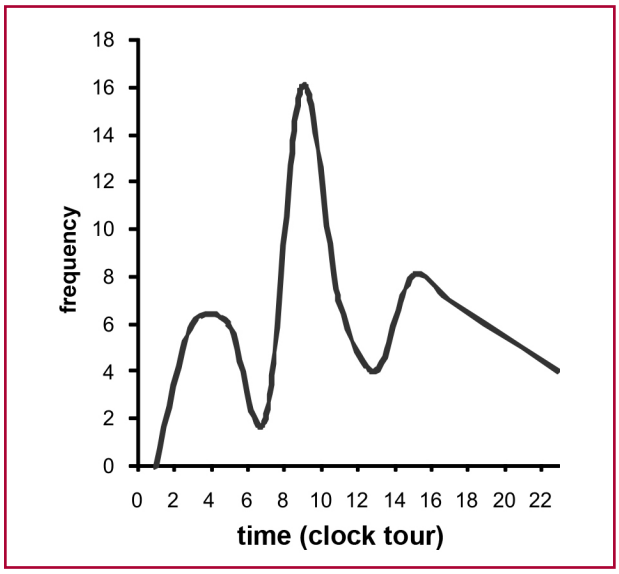

Fig. 1. Circadian variation in the onset of aortic dissection symptoms.

ciated aortic regurgitation included resuspension of the aortic leaflets (19.7%, 13 cases) and aortic valve replacement (48.5%, 32 cases). Coronary artery bypass graft surgery was performed in 13% of patients (9 cases) and reimplantation of the coronary arteries in 37.9% (25 cases). Surgical or combined strategies for type A dissections were replacement of aorta and aortic valve (composite graft) (50%, 31 cases) and implantation of a composite graft with reimplantation of the coronary arteries (37%, 25 cases).

Pharmacological treatment included beta blockers (67.4%, 64 cases), sodium nitroprusside (47.4%, 45 cases), acetyl salicylic acid (15.8%, 15 cases), anticoagulant agents (3.2%, 3 cases) and thrombolytic therapy (3.2%, 3 cases). That is to say, one fifth of the population (19%) received some kind of antithrombotic or thrombolytic therapy.

In 35% (7 cases) of patients with type B dissections a stent was implanted; surgical therapy was performed in 15% (3 cases): descending aorta replacement (15%, 3 cases) or surgical fenestration (10%, 2 cases).

Hospital outcomes

Global mortality was 32.6% (31 cases). Mortality rate of type A dissection was 37.8% (28 cases): 31% (21 cases) in patients undergoing surgery versus 87.5% (7 cases) in absence of surgical treatment; p = 0.01. Patients with type A dissections presenting with hypotension/shock or cardiac tamponade had greater mortality than those without these complications, versus 28% (p = 0.004). On the contrary, there were no significant differences either between patients referred from other centers *and* those admitted directly in the treating center, 33% versus 36% (p = ns), or between those admitted within 12 h from symptoms onset versus those admitted later: 36% versus 34% (p = ns). Mortality in type B dissections was 14% (3 cases): 1/5 patients undergoing surgery (20%) and 2/16 in those not operated on (12%) (p = ns). Table 3 shows the main complications during hospitalization according to the type of dissection.

Predictors of in-hospital mortality

Univariate analysis identified the variables at admission associated with in-hospital mortality: age > 70 years, hypotension/shock, acute kidney failure, pulse deficit, peripheral ischemia, small bowel ischemia, stroke, hypertension, moderate to severe aortic regurgitation, intramural hematoma and penetrating ulcer. The independent variables associated with mortality after logistic regression analysis with adjustment were hypotension/shock at admission (OR 10.1, 95% CI 1.4-73, p = 0.02) and age > 70 years (OR 7.7, 95% IC 2.2-27; p = 0.001).

DISCUSSION

In 1760, Dr Frank Nicholls, physician to King George II, first described on necropsy an acute aortic dissection in England. Dr Nicholls (15) described the presence of hemopericardium and distention of the ascending aorta, a tear in the aorta intima and blood passage through the tear separating the intima from the media. A year later, Morgagni (16) described and aortic dissection ruptured into the pericardial sac and made some interesting considerations. This was the case of King George II of England. Morgagni cited his case indirectly, mentioning that the reader "will identify him easily". The first surgery, a fenestration in the iliac artery, was performed by Gurin (17) in 1935. In 1953

Table 3. Complications during hospitalization according to the type of dissection

	Type A dissections n = 74	Type B dissections n = 21
Stroke, n (%)	5 (6.8)	0 (0)
Spinal cord ischemia, n (%)	3 (4.1)	3 (14.3)
Myocardial ischemia/ infarction, n (%)	3 (4.1)	0 (0)
Coma/disorders of consciousness - no (%)	7 (9.5)	1 (4.8)
Mesenteric ischemia, n (%)	2 (2.7)	1 (4.8)
Limb ischemia, n (%)	2 (2.7)	2 (9.5)
Dialysis, n (%)	6 (8.1)	1 (4.8)
Distress, n (%)	6 (80.1)	0 (0)
Sepsis, n (%)	9 (12.2)	1 (4.8)

Johns made a direct suture of the intima. DeBakey and Cooley (18) performed an open repair of a type B dissection in 1953 and Morris (19) operated the ascending aorta in 1963. In 1999 Dake (20) treated an acute dissection of the aorta with endovascular stent-graft placement.

Knowledge regarding the incidence of AAS in the general population is limited. Studies suggest an incidence of 2.6 to 3.5 cases per 100 000 person-years. (21)

Since dissection is a dynamic process that may occur anywhere within the aorta, the clinical spectrum of complications is broad, and symptoms may mimic more common disorders, such as acute myocardial infarction or stroke, and physical findings may be absent or suggest other diseases.

Despite the advent of novel diagnostic techniques, mortality is still high and the diagnosis remains difficult and requires high clinical index of suspicion.

The RADAR is the first multicenter continuous registry of AAS in referral hospitals in our environment.

The delay in the diagnosis may be > 24 hours in 39% of cases; (22) in 70% of patients included in *the Registro Español de Síndromes Aórticos* (RESA) the diagnosis was confirmed within the first 24 hours. This variable has implications in the outcomes, as the earlier the diagnosis, the worse the prognosis of the study population.

When the results of our study are compared with those of the International Registry of Acute Aortic Dissection (IRAD) (3) and of the RESA, (23), we observe that our population was younger, 58 versus 60.9 years in the IRAD and 63.1 years in the RESA; the proportion of men in our study is intermediate between that of the other studies (68% versus 77.5% and 65.3%, respectively). Chest X-ray was normal in more than 30% of patients as in other series and registries. (3, 23, 24) It is extremely important to make the differential diagnosis between AAS and acute coronary syndrome as the therapeutic strategy is completely different. The presence of chest pain with normal ECG suggests AAS; however, approximately 10% of patients had ECG changes at admission suggestive of ischemia/necrosis and 19% received an antithrombotic/thrombolytic strategy. (5, 6, 25)

Although the sensitivity and specificity of magnetic resonance imaging is high, (26) this study was rarely used probably due to lack of availability, impossibility of adequate monitoring or presence of metallic implants in a patient. Something similar happened with aortography which was considered the gold standard and was replaced by other techniques such as echocardiography and computed tomography.In our series two diagnostic studies were required in 52% of cases, similar to the findings of the RESA (53.2%).

Global mortality was 32.9%; 27.4% in the IRAD (3) and 35.4% in the RESA. (23) Mortality is greater within the first hours from symptoms onset, emphasizing the importance of rapid diagnosis for early management.

Other interesting issue is the fact that medical treatment was instituted in 28% of type A AAS in the IRAD, with a mortality of 58%, in 20% in the RESA, with mortality of 71.2% and in 11% in our series, with a mortality of 87%. Although the percentage of medical treatment for type A AAS was greater in the IRAD than in the Spanish Registry (23) and in our series, suggesting a better selection of surgical candidates, the low mortality (58%) draws the attention.

There is evidence indicating that several cardiovascular events demonstrate circadian patterns in their times of occurrence.

In our registry we found a greater frequency of occurrence between 9:00 AM and 11:00 AM and other two peaks between 3:00 AM and 00 AM, and between 03:00 PM and 05:00 PM.

Gallerani et al. (27) reported a significant variation of the circadian rhythm in AAS, with an initial peak between 8:00 AM and 10:00 AM and another in the evening, approximately at 8:00 PM.

In Japan, Sumiyoshi et al. (28) demonstrated that the highest peak of dissection occurred between the morning hours with a second peak between 5:00 PM and 7:00 PM. Yet, the statistical significance of these findings was low.

The IRAD also found a morning peak between 8:00 AM and 9:00 AM.

This chronobiological pattern is similar to that of other cardiovascular conditions, suggesting that similar physiopathological mechanisms may be responsible for the occurrence of these events early in the morning. Elevations in blood pressure, heart rate, sympathetic activity, basal vascular tone and prothrombotic activity show a circadian rhythm that correlates with that of cardiovascular events. These mechanisms might trigger the aortic tear in the early hours of the morning. (29, 30)

Our results are consistent with the IRAD model of predictors of in-hospital mortality: age > 70 years and hypotension/shock at presentation. Probably we might have identified other variables if we had included more patients as in the IRAD: migrating pain, prior cardiac surgery, ECG with signs of ischemia or infarction, cardiac tamponade or pulse deficit.

Study Limitations

The SAC Multicenter Registry of Acute Aortic Dissection is the first and largest experience of this kind ever performed in our country, yet some limitations should be mentioned.

The study was conducted at medium to high-volume aortic surgery referral centers located only in the city of Buenos Aires.

Only patients admitted alive to hospital were included and some data were obtained from the medical records.

The diagnosis of the condition was not confirmed by pathology in patients managed only with medical treatment; yet the evaluation was performed at referral centers with image tests with appropriate sensitivity and specificity.

CONCLUSIONS

Despite the advent and availability of modern imaging techniques, the detection of this lethal disease still depends on the degree of clinical suspicion from the first contact with health care providers, taking into account the low prevalence of the condition compared to other causes of chest pain, as coronary artery disease or pulmonary embolism. We should focus on this issue and try to improve it. It is worth pointing out that aortic dissection is still a very severe condition with similar mortality rate among the different series (1 out of 3 cases). Despite the limitations above mentioned, this type of continuous registries will allow us to learn more about the current status of the disease in terms of clinical presentation, diagnostic strategies used, surgical and percutaneous procedures, predictors of mortality useful at the moment of decision-making in high-risk patients and chronobiological patterns among other future aspects related with new strategies, with the single intention to getting closer to the problems related with the disease in our environment.

BIBLIOGRAPHY

1. Anagnostopoulos CE, Prashakar MJ, Kittle CF. Aortic dissections and dissecting aneurysms. Am J Cardiol 1972;30:263-73.

2. Miller DC, Mitchell RS, Oyer PE, Stinson EB, Jamieson SW, Shumway NE. Independent determinants of operative mortality for patients with aortic dissections. Circulation 1984;70:I153-64.

3. Hagan PG, Nienaber CA, Isselbacher EM, Bruckman D, Karavite DJ, Russman PL, et al. **The International Registry of Acute** Aortic Dissection (IRAD): new insights into an old disease. JAMA 2000;283:897-903.

4. Vilacosta I, Román JA. Acute aortic syndrome. Heart 2001;85:365-8.

5. Tsai TT, Nienaber Ch, Eagle KA. Acute aortic syndromes. Circulation 2005;112:3802-13.

6. Khan IA, Nair CK. Clinical, diagnostic, and management perspectives of aortic dissection. Chest 2002;122:311-28.

7. Mehta RH, Suzuki T, Hagan P, Bossone E, Gilon D, Llovet A, et al; International Registry of Acute Aortic Dissection (IRAD) Investigators. **Predicting death in patients with acute type A aortic dissection.** Behalf of the International Registry of Acute Aortic Dissection (IRAD) investigators. **Circulation 2002;105:200-6.**

8. Trimarchi S, Nienaber CA, Rampoldi V, Myrmel T, Suzuki T, Bossone E, et al. **Role and results of surgery in acute type B aortic** dissection: insights from the International Registry of Acute Aortic Dissection (IRAD). Circulation 2006;114:I357-64.

9. Umaña JP, Lai DT, Mitchell RS, Moore KA, Rodriguez F, Robbins RC, et al. Is medical therapy still the optimal treatment strategy for patients with acute type B aortic dissection? J Thorac Cardiovasc Surg 2002;124:896-910.

10. Bavaria JE, Brinster DR, Gorman RC, Woo YJ, Gleason T, Pochettino A. Advances in the treatment of acute type A dissection: an integrated approach. Ann Thorac Surg 2002;74:S1848-52.

11. Ehrlich MP, Ergin MA, McCullough JN, Lansman SL, Galla JD, Bodian CA, et al. Results of immediate surgical treatment of all acute type A dissections. Circulation 2000;102:III248-52.

12. Kallenbach K, Oelze T, Salcher R, Hagl C, Karck M, Leyh R, et al. Evolving strategies for treatment of acute aortic dissection type A. Circulation 2004;110:II243-9.

13. Evangelista A, Mukherjee D, Mehta R, O'Gara P, Fattori R, Cooper JM, et al; **International Registry of Aortic Dissection (IRAD)** Investigators. **Acute intramural hematoma of the aorta a mystery in** evolution. Circulation 2005;111:1063-70.

14. Suzuki T, Metha R, Ince H, Nagai R, Sakomura Y, Weber F, et al; International Registry of Aortic Dissection. Clinical profiles and outcomes of acute type B aortic dissection in the current era: lessons from the International Registry of Aortic Dissection (IRAD). Circulation 2003;108:II312-7.

15. Nicholls F. Observations concerning the body of his late majesty, October 26, 1760. **Philos Trans R Soc Lond A 1761;52:265-74.**

16. Morgagni GB. De sedibus et causis morborum per anatomen indagatis. **Venecia; 1761.**

17. Gurin D, Bulmer JW, Derby R. Dissecting aneurysms of the aorta: diagnosis and operative relief of acute arterial obstruction due to this cause. NY State J Med 1935;35:1200-2.

18. De Bakey ME, Cooley DA. Successful resection of aneurysm of thoracic aorta and replacement by graft. J Am Med Assoc 1953;152:673-6.

19. Morris Jr GC, Henly WS, De Bakey ME. Correction of acute dissecting aneurysm of aorta with valvular insufficiency. **JAMA** 1963;184:63-4.

20. Dake MD, Kato N, Mitchell RS, Semba CP, Razavi MK, Shimono T, et al. Endovascular stent-graft placement for the treatment of acute aortic dissection. N Engl J Med 1999;340:1546-52.

21. Bickerstaff LK, Pairolero PC, Hollier LH, Melton LJ, Van Peenen HJ, Cherry KJ, et al. Thoracic aortic aneurysms: a population-based study. Surgery 1982;92:1103-8.

22. Klompas M. Does this patient have an acute thoracic aortic dissection? JAMA 2002;287:2262-72.

23. Evangelista A, Padilla F, López-Ayerbe J, Calvo F, López-Pérez JM, Sánchez V, et al. Spanish Acute Aortic Syndrome Study (RESA). Better diagnosis is not reflected in reduced mortality. Rev Esp Cardiol 2009;62:255-62.

24. von Kodolitsch Y, Nienaber CA, Dieckmann C, Schwartz AG, Hofmann T, Brelenfeld C, et al. **Chest radiography for the diagnosis** of acute aortic syndrome. Am J Med 2004;116:73-7.

25. Hansen MS, Nogareda GJ, Hutchison SJ. **Frequency of and inap**propriate treatment of misdiagnosis of acute aortic dissection. Am J Cardiol 2007;99:852-6.

26. Shiga T, Wajima Z, Apfel C, Inoue T, Ohe Y. Diagnostic accuracy of transesophageal echocardiography, helical computed tomography, and magnetic resonance imaging for suspected thoracic aortic dissection: systematic review and meta-analysis. Arch Intern Med 2006;166:1350-6.

27. Gallerani M, Portaluppi F, Grandi E, Manfredini R. Circadian rhythmicity in the occurrence of spontaneous acute dissection and rupture of thoracic aorta. J Thorac Cardiovasc Surg 1997;113:603-4.

28. Sumiyoshi M, Kojima S, Arima M, Suwa S, Nakazato Y, Sakurai H, et al. Circadian, weekly, and seasonal variation at the onset of acute aortic dissection. Am J Cardiol 2002;89:619-23.

29. Mehta RH, Manfredini R, Hassan F, Sechtem U, Bossone E, Oh JK, et al; International Registry of Acute Aortic Dissection (IRAD) Investigators. Chronobiological patterns of acute aortic dissection. Circulation 2002;106:1110-5.

30. Portaluppi F, Manfredini R, Fersini C. From a static to a dynamic concept of risk: the circadian epidemiology of cardiovascular events. Chronobiol Int 1999;16:33-49.

Acknowledgments

As usual, to Liliana Capdevila for her capacitiy, cooperation and emotional nature.

PRINCIPAL INVESTIGATORS OF THE RADAR STUDY (by alphabetical order of the participant center)

- *Alemán, Hospital:* Pablo Comignani, Blas Mancini, Claudio Higa.
- *Argerich, Hospital:* Gustavo Bastianelli, Alberto Bartolomé, Sandro Belforte, Walter Esteban, Jorge Estrada, Victorio Picone.
- *Bazterrica, Clínica:* Miguel Rubio, Raúl A. Borracci, Víctor Mauro, Carlos Barrero.
- *CEMIC:* Javier Guetta, Diego Arakaki, Juan José Fuselli.
- *del Sol, Clínica:* Juan Gagliardi.
- *FLENI: Hernán* Cohen Arazi, Silvina Waldman, Carlos Nojek.
- *Fundación Favaloro:* María Pía Marturano, Raúl Merbilhaa, Roberto Favaloro.
- *Güemes, Sanatorio:* Ricardo Villaroel, Ariel Sosa.
- *Instituto Cardiovascular de Buenos Aires:* Mariano Benzadón, Fernando Botto, Daniel Navia.
- *Italiano, Hospital:* Ricardo Marenchino, Daniel Bracco.
- *de los Arcos, Sanatorio:* Félix Ramírez, Sergio Muryan, Alfredo Larraburu.
- *Santa Isabel, Clínica:* Yanina Castillo Costa.