ORIGINAL ARTICLE

Short- and Long-term Risk of Coronary Artery Bypass Graft Surgery in Acute Coronary Syndrome

Riesgo inmediato y alejado de la cirugía de revascularización miocárdica en el síndrome coronario agudo

MARIANO CAMPORROTONDO[1,I], JUAN C. ESPINOZA[1,I], JUAN P. COSTABEL[2], MARIANO VRANCIC[MTSAC,1], FERNANDO PICCININI[MTSAC,1], JUAN CAMOU[1], SOLANGE BONAZZI[3], BERNARDO LUPIAÑEZ [3], MARIANO BENZADÓN[MTSAC,2], DANIEL NAVIA[MTSAC,1Ş 1,2]

ABSTRACT

Introduction: Percutaneous coronary intervention is the revascularization procedure most widely used in patients with non-ST-segment elevation acute coronary syndrome (NSTEACS). However, coronary artery bypass graft surgery is a therapeutic alternative which allows treating these patients with a favorable outcome.
Objectives: The aim of this study was to compare in-hospital and long-term outcome of patients undergoing coronary artery bypass graft surgery according to their clinical presentation.
Methods: Between January 1998 and July 2013, 3604 consecutive patients underwent isolated coronary artery bypass graft surgery. The population was divided in patients with NSTEACS (ACS Group, n = 2079) or with chronic stable angina (CSA Group, n = 1525). Postoperative and at follow-up morbidity and mortality were analyzed.
Results: The CSA Group had greater use of double mammary artery (58.2% vs. 50.3%; p = 0.001) and longer operative time (211 min vs. 203 min; p = 0.002). The ACS Group presented lower postoperative cardiac output (4.5% vs. 3.1%; p = 0.043) and higher in-hospital mortality (2.8% vs. 1.8%; p = 0.046). After adjusting for risk score, there were no statistically significant differences in in-hospital mortality (1.3% in CSA vs. 1.6% in ACS; p = 0.681) or in the rate of postoperative complications between the two groups. Overall long-term survival at 10 years was not different between groups (CSA 85% ± 1.3% vs. ACS 83% ± 1.1%; p = 0.363). The time-related freedom from reintervention was similar for both groups (CSA 89.5% ± 1.2% vs. ACS 89.1% ± 0.9%; p = 0.1680). These results did not change after adjusting for risk score.
Conclusions: Patients with NSTEACS submitted to coronary artery bypass graft surgery presented greater perioperative mortality, but a long-term outcome similar to patients undergoing elective surgery. No difference in perioperative mortality was found between both groups after adjusting for risk score.

Key words: Coronary Artery Bypass Graft Surgery – Coronary Disease – Acute Myocardial Infarction

RESUMEN

Introducción: En pacientes con síndrome coronario agudo sin elevación del segmento ST (SCASEST), la angioplastia transluminal coronaria es el método de revascularización más utilizado; sin embargo, la cirugía de revascularización miocárdica es una alternativa terapéutica que permite tratar a este tipo de pacientes con buenos resultados.
Objetivos: Comparar la evolución hospitalaria y alejada de los pacientes sometidos a cirugía de revascularización miocárdica según el cuadro clínico de presentación.
Material y métodos: Entre enero de 1998 y julio de 2013 se realizó cirugía de revascularización miocárdica aislada en 3.604 pacientes en forma consecutiva. La población se dividió en pacientes con SCASEST (Grupo SCA, n = 2.079) o con angina crónica estable (Grupo ACE, n = 1.525). Se efectuó un análisis de la morbimortalidad posoperatoria y al seguimiento.
Resultados: El Grupo ACE tuvo mayor uso de mamaria bilateral (58,2% vs. 50,3%; p=0,001) y mayor tiempo operatorio (211 min vs. 203 min; p=0,002). El Grupo SCA presentó más bajo gasto cardíaco posoperatorio (4,5% vs. 3,1%; p=0,043). La mortalidad hospitalaria fue mayor en los pacientes con SCA (2,8% vs. 1,8%; p=0,046). Luego de ajustar por puntaje de riesgo no hubo diferencia estadísticamente significativa en la mortalidad hospitalaria (1,3% en ACE vs. 1,6% en SCA; p = 0,681) ni en la tasa de complicaciones posoperatorias. La sobrevida global alejada en el seguimiento a 10 años no fue diferente entre grupos (ACE 85% ± 1,3% vs. SCA 83% ± 1,1%; p =0,363). El tiempo libre de reintervención a los 10 años fue similar entre ambos grupos (ACE 89,5% ± 1,2% vs. SCA 89,1% ± 0,9%; p = 0,1680). Estos resultados se mantuvieron luego de ajustar por puntaje de riesgo.
Conclusiones: Los pacientes sometidos a cirugía de revascularización miocárdica en el contexto de un SCASEST presentaron una mortalidad perioperatoria mayor, pero con una evolución a largo plazo similar a la de los pacientes intervenidos en forma electiva. No hubo diferencias en la mortalidad perioperatoria cuando se ajustó por puntaje de riesgo.

Palabras clave: Cirugía coronaria - Enfermedad coronaria - Infarto agudo de miocardio.

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Address for reprints: Dr. Mariano Camporrotondo - ICBA – Instituto Cardiovascular de Buenos Aires - Av. Libertador 6302 - Piso 10 - (1428) CABA, Argentina - e-mail: mcamporrotondo@icba.com.ar

Instituto Cardiovascular de Buenos Aires (ICBA)
[MTSAC] Full Member of the Argentine Society of Cardiology
[I] To apply as Full Member of the Argentine Society of Cardiology
[1] Department of Cardiac Surgery - ICBA
[2] Department of Cardiology - ICBA
[3] Department of Anesthesiology – ICBA

Abbreviations

CSA	Chronic stable angina
PCI	Percutaneous coronary intervention
CPB	Cardiopulmonary bypass
CABG	Coronary artery bypass graft surgery
CD	Coronary disease
AMI	Acute myocardial infarction
IQR	Interquartile range
ACS	Acute coronary syndrome
NSTEACS	Non-ST-segment elevation acute coronary syndrome

INTRODUCTION

Acute coronary syndrome (ACS) is one of the most frequent forms of coronary disease (CD) and one of the main causes of morbidity and mortality. (1) Percutaneous coronary intervention (PCI) is the most commonly used revascularization treatment in non-ST-segment elevation acute coronary syndrome (NSTEACS); however, between 6 and 10% of patients undergo coronary bypass graft surgery (CABG) (2-4). According to the latest clinical practice guidelines, the choice of revascularization technique depends on CD extension and patient characteristics (2, 3). Coronary artery bypass graft surgery is still the treatment of choice in patients with extensive CD, (5) especially in diabetic patients, (6-8) or with ventricular function impairment. (2, 3)

Historically ACS has been associated with worse postoperative outcome; however, surgical progress (surgery without cardiopulmonary bypass, arterial bridges) in the last decades has significantly reduced the risks of this procedure. (9-11)

The aims of the present study were to compare short-term (in-hospital) morbidity and mortality, long-term mortality, and the rate of reintervention during follow-up between patients operated on for ACS and for chronic stable angina (CSA).

METHODS

Study patients

All patients undergoing isolated coronary artery bypass graft surgery between January 1998 and July 2013 at the Instituto Cardiovascular de Buenos Aires were consecutively included in the study (n = 3604). A comparative analysis of postoperative risk and long-term follow-up in patients undergoing CABG for NSTEACS (ACS Group, n = 2079) or for chronic stable angina (CSA Group = 1525) was performed in all patients and in groups matched by propensity score-based risk adjustment. Patient demographic and surgical data as well as in-hospital outcome were obtained from the prospectively loaded computerized database of the Department of Cardiac Surgery. Long-term survival, as well as the incidence of reintervention for new revascularization procedures (PCI and/or CABG) was analyzed during follow-up. Long-term outcome was obtained through outpatient clinical visits, as well as standardized telephone calls performed by specially trained staff who contacted patients or relatives every six months recording their evolution.

Definitions

- NSTEACS (2, 3): non-ST-segment elevation acute myocardial infarction or unstable angina.
- Non-ST-segment elevation acute myocardial infarction (12): elevation of myocardial injury markers (preferably troponin) above the 99thpercentile reference value and at least one of the following factors:
  - Symptoms of myocardial ischemia.
  - New ST-segment or T wave abnormalities or new left bundle branch block.
  - Development of pathological Q-waves in the ECG.
  - New wall motion abnormalities documented by imaging methods.
  - Thrombotic image in the coronary angiography.
- Unstable angina: fast progressive signs or symptoms of myocardial ischemia or new signs and symptoms at rest, without elevation of cardiac enzymes.
- Chronic stable angina: Signs and symptoms of reversible myocardial ischemia normally induced by exercise, emotions or other stressful situations.
- Postoperative complications:
  - Low cardiac output: need for intraaortic balloon pump counterpulsation or use of inotropic drugs for more than 48 hours.
  - Post CABG acute myocardial infarction (postoperative AMI) (12): new Q wave or loss of R wave progres sion in precordial leads with increased cardiac enzymes 10 times above normal values.
  - Postoperative bleeding: blood loss requiring surgical re-exploration.
  - Stroke: persistent central neurological deficit for more than 24 hours with or without confirmation by imaging study.
  - Mediastinitis: deep sternal infection requiring surgical reexploration.
  - Prolonged mechanical respiratory assistance (MRA): need of mechanical respiratory assistance for > 48 hours.
- Operative mortality: All-cause death during postoperative hospitalization
- Reintervention: New PCI or new CABG at follow-up.
- Overall mortality: All-cause mortality at follow-up.

Type and moment of surgery

Coronary artery bypass graft surgery was performed with and without cardiopulmonary bypass (CPB). Surgical access was by median sternotomy in all patients. Sodium heparin 3 mg/kg was used for anticoagulation and protamine at a 1:1 ratio to reverse heparin effect. Coronary artery bypass graft surgery with CPB was performed in normothermic conditions, with single ascending aortic cross-clamping and cold blood cardioplegic cardiac arrest. From 2003 onwards, all patients were operated on with the purpose of performing CABG without CPB (intention-to-treat). The technique employed for the surgical procedure without CPB has been previously explained. (13, 14) The anterior descending coronary artery was revascularized using the left mammary artery, and the right mammary artery, the radial artery or the internal saphenous vein were used for the remaining vessels. The moment of surgery was defined for each patient by medical agreement between cardiologists and surgeons (Heart Team),

Statistical analysis

For the descriptive analysis, categorical variables were expressed as percentages and continuous variables as mean and standard deviation (SD) or median and 25-75 interquartile range (IQR). Student´s t test was used to compare continuous variables and the chi square test or Fischer´s exact test for categorical variables. Survival curves were built using the Kaplan-Meier method including in-hospital mortality and were compared using the log-rank test. Short-term morbidity and mortality, mortality at follow-up and long-term reintervention rate were analyzed in groups matched by propensity score-based risk adjustment. An ACS propensity score was calculated for each patient using a logistic regression model that included all preoperative variables shown in Table 1. Patients were matched using a 1:1 "greedy" nearest neighbor algorithm with caliper width of 0.0002. A p value < 0.05 was considered as statistically significant. Statistical analysis was performed using IBM® SPSS® Statistics (version 21) software package.

Ethical considerations

The Institutional Ethics Committee approved the study and an informed consent was obtained from each patient to perform the surgical procedure and postoperative assessments.

RESULTS

Preoperative and operative characteristics and short-term outcome

Table 1 shows baseline population characteristics. Among the total number patients undergoing CABG, 2079 were operated on for NSTEACS (ACS Group) and 1525 for CSA (CSA Group). Patients from the CSA Group presented greater incidence of left ven-

Table 1. Preoperative baseline characteristics

	Not adjusted by risk			Adjusted by risk		
	CSA	ACS	p	CSA	ACS	p
	n = 1525	n = 2079		n = 831	n = 831	
Age (years)	63.9 ± 9.5	64 ± 9.9	0.603	63.2 ± 8.9	63.1 ± 8.8	0.793
Female gender, n (%)	165 (10.8%)	278 (13.4%)	0.021	72 (8.7%)	75 (9.0%)	0.796
LV dysfunction (EF < 40%), n (%)	202 (13.2%)	210 (10.1%)	0.003	52 (6.3%)	50 (6.0%)	0.838
Prior AMI, n (%)	493 (32.3%)	519 (25.0%)	0.0001	182 (21.9%)	173 (20.8%)	0.590
Prior CABG, n (%)	15 (1.0%)	62 (3.0%)	0.0001	3 (0.4%)	3 (0.4%)	1.00
Peripheral vascular disease, n (%)	74 (4.9%)	69 (3.3%)	0.02	8 (1.0%)	10 (1.2%)	0.636
Carotid disease, n (%)	62 (4.1%)	88 (4.2%)	0.804	9 (1.1%)	10 (1.2%)	0.818
Carotid surgery, n (%)	18 (1.2%)	31 (1.5%)	0.426	4 (0.5%)	4 (0.5%)	1.00
Prior PCI, n (%)	264 (17.3%)	466 (22.4%)	0.0001	126 (15,2%)	115 (13.8%)	0.443
Chronic obstructive pulmonary disease, n (%)	63 (4.1%)	95 (4.6%)	0.525	13 (1.6%)	7 (0.8%)	0.177
Prior stroke, n (%)	62 (4.1%)	58 (2.8%)	0.035	10 (1.2%)	13 (1.6%)	0.529
Chronic renal failure			0.192			1.00
No, n (%)	1453 (95.3%)	2002 (96.3%)		823 (99.0%)	823 (99.0%)	
Yes, n (%)	67 (4.4%)	68 (3.3%)		7 (0.8%)	7 (0.8%)	
Dialysis, n (%)	5 (0.3%)	9 (0.4%)		1 (0.1%)	1 (0.1%)	
HT, n (%)	1078 (70.7%)	1535 (73.8%)	0.037	629 (75.7%)	630 (75.8%)	0.954
Dyslipidemia, n (%)a	1106(72.5%)	1522(73.2%)	0.648	648 (78.0%)	642 (77.3%)	0.724
Main left coronary artery disease, n (%)	249 (16.3%)	489 (23.5%)	0.0001	121 (14.6%)	127 (15.3%)	0.680
Smoking			0.002			0.858
No, n (%)	635 (41,6%)	836 (40.2%)		357 (43.0%)	346 (41.6%)	
Active, n (%)	411 (27.0%)	669 (32.2%)		242 (29.1%)	249 (30.0%)	
Ex	479 (31.4%)	574 (27.6%)		232 (27.9%)	236 (28.4%)	
Diabetes Mellitus, n (%)	391 (25.6%)	520 (25.0%)	0.669	164 (19.7%)	162 (19.5%)	0.902
Family history of CD, n (%)	299 (19.6%)	425 (20.4%)	0.536	133 (16.0%)	133 (16.0%)	1.00
Additive EuroSCORE			0.001			0.105
0-2	741 (48.6%)	877 (42.2%)		464 (55.8%)	426 (51.3%)	
3-5	554 (36.3%)	776 (37.3%)		285 (34.3%)	302 (36.3%)	
≥6	230 (15.1%)	426 (20.5%)		82 (9.9%)	103 (12.4%)	

CSA: Chronic stable angina. ACS: Acute coronary syndrome. LV: Left ventricular. EF: Ejection fraction. AMI: Acute myocardial infarction. PCI: Percutaneous coronary intervention. HT: Hypertension. CD: Coronary disease

tricular dysfunction, previous AMI, peripheral vascular disease and previous stroke. The ACS Group, in turn, had greater percentage of women, greater history of prior cardiac surgery, higher incidence of prior PCI, were more hypertensive and active smokers, had greater rate of left main coronary artery disease and higher additive EuroSCORE.

Operative results are shown in Table 2. Patients from the CSA Group had higher use of bilateral internal mammary artery (58.2% vs. 50.3%, p=0.001) and longer operative time (211 vs. 203 minutes, p=0.002), while the ACS Group presented greater incidence of postoperative low cardiac output syndrome (4.5% vs. 3.1%, p=0.043).

Preoperative and perioperative data of patients matched by propensity score are shown in Tables 1 and 2, respectively. Although in-hospital mortality was higher in ACS patients (2.8 vs. 1.8%, p = 0.046), after adjusting for risk score, no significant differences were found in in-hospital mortality (1.3% in CSA vs. 1.6% in ACS, p = 0.681), or in the postoperative complication rate.

Long-term outcome

Long-term follow-up ratio was 90%. Median follow-up was 7 years (IQR 4-10 years). Overall long-term mortality at follow-up was similar between both groups, with an overall survival rate of 85% ± 1.3 for the CSA Group and 83% ± 1.1for the ACS Group at 10 years (p = 0.363 (Figure 1 A). There were no significant differences after adjusting for risk score (Figure 1 B).

Freedom from reintervention at 10 years showed no statistically significant difference between both groups: 89.5% ± 1.2 for the CSA Group and 89.1% ± 0.9 for the ACS Group (p = 0.1680) (Figure 2 A). These results were preserved after adjusting for risk score (Figure 2 B).

DISCUSSION

The study showed that in-hospital mortality of patients operated on within the context of an ACS was higher than of those operated on for a stable condition. However, this difference in mortality was not confirmed in the long-term. Our results agree with those of Fukui et al. who compared short- and long-term outcome of patients with surgical revascularization and found that ACS was an independent predictor of in-hospital mortality but not of long-term mortality. (9) This difference in mortality concentrated in the first postoperative weeks is probably related with numerous physiopathological phenomena typical of the ACS which are different from those of stable patients. The patient with an unstable condition usually presents higher levels of systemic inflammation which can produce numerous complications with different degrees of severity, as respiratory distress and vasoplegic syndromes. (15) In addition, the patient who has just suffered a myocardial ischemic insult may have a certain degree of transient ventricular dysfunction which could explain the higher rate of low cardiac output observed in our study. (16) By definition, the group undergoing elective surgery has a much shorter prior hospitalization period. This lower

Table 2. Operative and postoperative characteristics

	Not adjusted by risk			Adjusted by risk		
	CSA	ACS	p	CSA	ACS	p
	n = 1525	n = 2079		n = 831	n = 831	
Number of anastomoses per patient	2.96 ± 0,8	2.92 ± 0,8	0.241	2.95 ± 0.8	2.972 ± 0.8	0.596
Bilateral IMA use, n (%)	887 (58.2%)	1045 (50,3%)	0.001	534 (55.2%)	533 (55.1%)	1.00
CABG without cardiopulmonary bypass, n (%)	1108 (72.7%)	1520 (73.1%)	0.761	570 (68.6%)	592 (71.2%)	0.239
Skin to skin operative time, min	211 ± 66	203 ± 79	0.002	209 ± 71	206 ± 79	0.367
Postoperative low cardiac output syndrome, n (%)	1525 (3.1%)	2079 (4.5%)	0.043	23 (2.8%)	28 (3.4%)	0.477
Dialysis, n (%)	13 (0.9%)	16 (0.8%)	0.783	5 (0.6%)	4 (0.5%)	0.738
Postoperative AMI, n (%)	21 (1.4%)	47 (2.3%)	0.054	15 (1.8%)	15 (1.8%)	1.00
Postoperative bleeding, n (%)	30 (2.0%)	49 (2.4%)	0.430	16 (1.9%)	9 (1.1%)	0.158
Stroke, n (%)	11 (0.7%)	10 (0.5%)	0.349	4 (0.5%)	2 (0.2%)	0.413
Mediastinitis, n (%)	17 (1.1%)	30 (1.4%)	0.391	7 (0.8%)	6 (0.7%)	0.781
Atrial fibrillation, n (%)	172 (11.3%)	243 (11.7%)	0.703	100 (12.0%)	84 (10.1%)	0.211
Prolonged MRA, n (%)	36 (2.4%)	46 (2.2%)	0.768	11 (1.3%)	11 (1.3%)	1.00
Operative mortality, n (%)	27 (1.8%)	58 (2.8%)	0.046	11 (1.3%)	13 (1.6%)	0.681
In-hospital stay (days)	7.6 ± 16	8.1 ± 10	0.271	7.8 ± 22	7.2 ± 13	0.497

CSA: Chronic stable angina. ACS: Acute coronary syndrome. IMA: Internal mammary artery. CABG: Coronary artery bypass graft surgery. AMI: Acute myocardial infarction. MRA: Mechanical respiratory assistance.

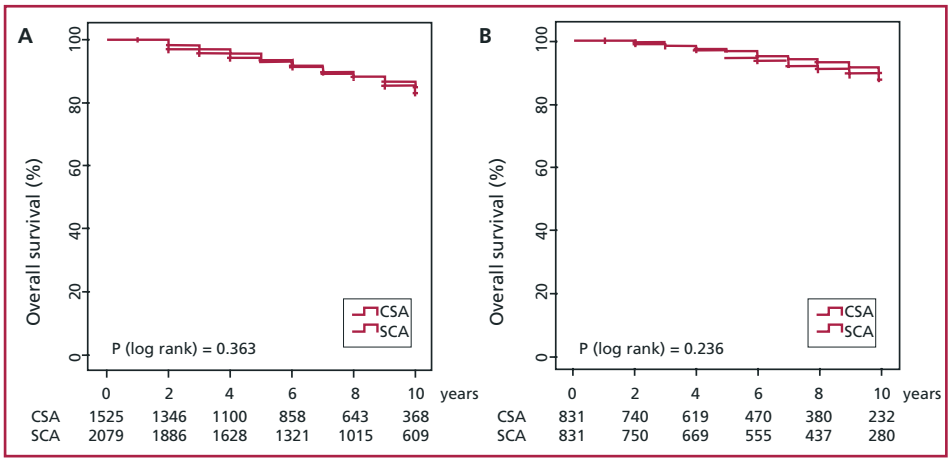

Fig. 1. Kaplan-Meier survival analysis free from events for overall mortality (see text for description)

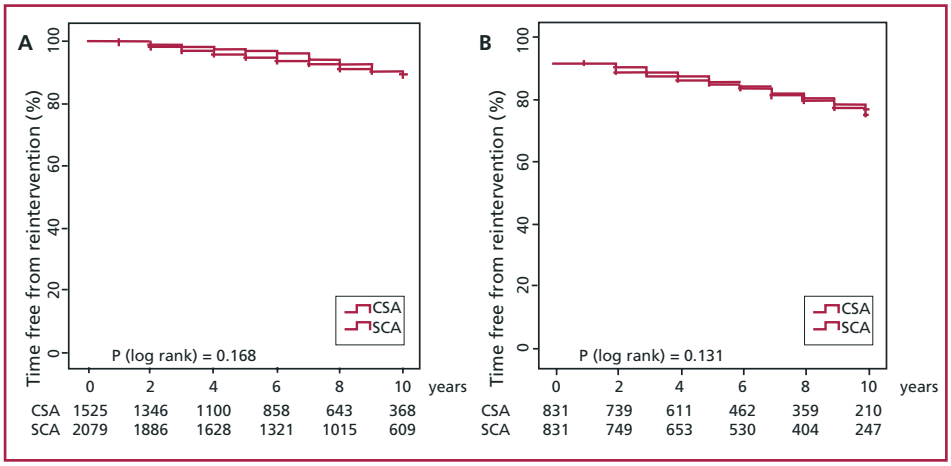

Fig. 2. Kaplan-Meier survival analysis free from reintervention (see text for description)

exposition to the harmful effects of prolonged hospitalization may also be associated with better outcome of patients operated on for CSA. (17) Mortality in ACS patients was higher than in stable patients; however, after adjusting by propensity score, in-hospital mortality was similar in both groups.

Patients with ACS presented higher additive EuroSCORE, suggestive of greater in-hospital mortality. Although the current EuroSCORE II (18) is a better predictor of mortality, (19) both EuroSCORE models have an inadequate performance in non-elective cardiac surgery. (20)

Another finding was that patients operated on for ACS had a similar rate of long-term reintervention: 89.5% ± 1.2 for the CSA Group and 89.1% ± 0.9 for the ACS Group (p = 0.1680). These results contradict those of Inci et al. who reported a significantly higher reintervention rate in a series of 485 patients operated on with ACS diagnosis. (21)

Study limitations

One of the main study limitations is its retrospective design. However, prospective database loading and standardized follow-up will probably decrease biases associated with this type of studies.

This is an observational study, and although propensity score matching adjusting by observed covariants results in comparable groups, the study is non-randomized, so that additional effects of occult variables (not measured) cannot be ruled out.

Another limitation is the long study period. During the first years, most patients were operated on with cardiopulmonary bypass and using one mammary artery, while the experience without cardiopulmonary bypass and using double mammary artery started after 2003, with a consequent shorter follow-up period. This might explain seemingly paradoxical findings, as a similar long-term outcome with lower use of double mammary artery in the ACS Group, which contradicts the literature. (22)

CONCLUSIONS

Coronary artery bypass graft surgery in ACS patients is associated with greater perioperative mortality, but after adjusting for risk score mortality was similar to that of patients operated on for CSA. No differences in survival or need for reintervention at follow-up were found between both groups operated on according to their clinical presentation.

Conflicts of interest

None declared.
(See authors' conflicts of interest forms in the web / Supplementary Material)

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