

Editor's Choice — ECAR (Endovasculaire ou Chirurgie dans les Anévrysmes aorto-iliaques Rompus): A French Randomized Controlled Trial of Endovascular Versus Open Surgical Repair of Ruptured Aorto-iliac Aneurysms

P. Desgranges^{a,*}, H. Kobeiter^b, S. Katsahian^c, M. Bouffi^d, P. Gouny^e, J.-P. Favre^f, J.M. Alsac^g, J. Sobocinski^h, P. Julia^g, Y. Alimi^d, E. Steinmetzⁱ, S. Haulon^h, P. Alric^j, L. Canaud^j, Y. Castier^k, E. Jean-Baptiste^l, R. Hassen-Khodja^l, P. Lermusiaux^m, P. Feugier^m, L. Destrieux-Garnierⁿ, A. Charles-Nelson^c, J. Marzelle^a, M. Majewski^a, A. Bourmaud^o, J.-P. Becquemin^a, the ECAR Investigators

^aVascular Surgery Unit, CHU Henri Mondor, 51 avenue du Maréchal de Lattre de Tassigny, 94010 Creteil, France

^bRadiology Unit, CHU Henri Mondor, 51 avenue du Maréchal de Lattre de Tassigny, 94010 Creteil, France

^cPôle Recherche Clinique, CHU Henri Mondor, Creteil, France

^dVascular Surgery Unit, CHU Nord, Marseille, France

^eVascular Surgery Unit, CHRU Brest, Brest, France

^fVascular Surgery Unit, CHU Saint-Etienne, Saint-Etienne, France

^gVascular Surgery Unit, CHU HEGP, Paris, France

^hVascular Surgery Unit, CHRU Lille, Lille, France

ⁱVascular Surgery Unit, CHU Le Bocage, Dijon, France

^jVascular Surgery Unit, CHU Montpellier, Montpellier, France

^kVascular Surgery Unit, CHU Bichat, Paris, France

^lVascular Surgery Unit, CHU Nice, Nice, France

^mVascular Surgery Unit, CHU Lyon, Lyon, France

ⁿCHR Annecy, Annecy, France

^oICL Hygee, Saint Priest en Jarez, France

WHAT THIS PAPER ADDS

This study contributes to the debate surrounding the treatment of ruptured aorto-iliac aneurysms by endovascular or open surgical repair.

Objectives/Background: ECAR (Endovasculaire ou Chirurgie dans les Anévrysmes aorto-iliaques Rompus) is a prospective multicentre randomized controlled trial including consecutive patients with ruptured aorto-iliac aneurysms (rAIA) eligible for treatment by either endovascular (EVAR) or open surgical repair (OSR). Inclusion criteria were hemodynamic stability and computed tomography scan demonstrating aorto-iliac rupture.

Methods: Randomization was done by week, synchronously in all centers. The primary end point was 30 day mortality. Secondary end points were post-operative morbidity, length of stay in the intensive care unit (ICU), amount of blood transfused (units) and 6 month mortality.

Results: From January 2008 to January 2013, 107 patients (97 men, 10 women; median age 74.4 years) were enrolled in 14 centers: 56 (52.3%) in the EVAR group and 51 (47.7%) in the OSR group. The groups were similar in terms of age, sex, consciousness, systolic blood pressure, Hardman index, IGSII score, type of rupture, use of endoclamping balloon, and levels of troponin, creatinine, and hemoglobin. Delay to treatment was higher in the EVAR group (2.9 vs. 1.3 hours; $p < .005$). Mortality at 30 days and 1 year were not different between the groups (18% in the EVAR group vs. 24% in the OSR group at 30 days, and 30% vs. 35%, respectively, at 1 year). Total respiratory support time was lower in the EVAR group than in the OSR group (59.3 hours vs. 180.3 hours; $p = .007$), as were pulmonary complications (15.4% vs. 41.5%, respectively; $p = .050$), total blood transfusion (6.8 vs. 10.9, respectively; $p = .020$), and duration of ICU stay (7 days vs. 11.9 days, respectively; $p = .010$).

Conclusion: In this study, EVAR was found to be equal to OSR in terms of 30 day and 1 year mortality. However, EVAR was associated with less severe complications and less consumption of hospital resources than OSR.

© 2015 European Society for Vascular Surgery. Published by Elsevier Ltd. All rights reserved.

Article history: Received 18 September 2014, Accepted 12 March 2015, Available online 20 May 2015

Keywords: AAA rupture, EVAR, Open surgical repair

DOI of original article: <http://dx.doi.org/10.1016/j.ejvs.2015.03.040>

* Corresponding author.

E-mail address: pascal.desgranges@hmn.aphp.fr (P. Desgranges).

1078-5884/© 2015 European Society for Vascular Surgery. Published by Elsevier Ltd. All rights reserved.

<http://dx.doi.org/10.1016/j.ejvs.2015.03.028>

INTRODUCTION

The post-operative mortality after open surgical repair (OSR) of ruptured aorto-iliac aneurysms (rAIA) and the feasibility of endovascular repair (EVAR) of asymptomatic abdominal aortic aneurysms (AAAs) have led to the consideration of EVAR for rAIA as an alternative to OSR, and as the first line therapy in most centers.^{1–5} In a recent meta-analysis of observational studies and registries, EVAR was associated with a 50% risk reduction in mortality.⁶ These encouraging results are considered sufficient by “endo-enthusiasts”, but patients suitable for EVAR are usually selected because of hemodynamic stability and aneurysm morphology. The “endo-skeptics” thus argue that patient selection, as most of the patients at risk of post-operative complications are treated by OSR, plays an overly important role and await the results of randomized multicenter studies.⁷

To compare EVAR with OSR for rAIAs in homogeneous groups of patients, a multicenter randomized trial, ECAR (Endovasculaire ou Chirurgie dans les Anévrismes aorto-iliaques Rompus), was conducted.⁸ Two major requirements had to be fulfilled: (i) the patients had to be hemodynamically stable; and (ii) pre-operative computed tomography angiography (CTA) had to prove aortic rupture and document favorable anatomy.

METHODS

The study was registered at [clinicaltrials.gov](https://www.clinicaltrials.gov/ct2/show/NCT00577616) (<https://www.clinicaltrials.gov/ct2/show/NCT00577616>).

Study design

ECAR is a prospective, multicenter (14 centers), randomized (per week) controlled trial (RCT) in which all patients presenting with a rAIA amenable to both methods (OSR and EVAR) were included. The study was approved by the Counsel for the Protection of Persons Volunteering for Biomedical Research, Ile de France, in July 2007.

Because of the emergency context, informed consent was only obtained from survivors. The unit of randomization was the week (synchronous for all centers): patients were treated by OSR during the first week and subsequent odd numbered weeks, and by EVAR during the second week and subsequent even numbered weeks. A reminder of the treatment for the week was sent to all centers by automatic email and fax each Monday at 8.30 a.m. All patients with rAIA not enrolled in the study were listed in a non-inclusion registry for each center.

Study end points

The primary end point was to compare the mortality rate of the two groups at 30 days after treatment.

The secondary end points were 30 day post-operative morbidity (cardiac, pulmonary, digestive, renal, and neurological), duration of stay in the intensive care unit (ICU), amount of blood transfused (units), in hospital mortality, and 6 month and 1 year mortality and morbidity rates.

Complications were reported according to the guidelines of the Society for Vascular Surgery/International Society of Cardiovascular Surgery.⁹ Clinical, biological tests and radiological follow up were performed at 48 hours, 30 days, 6 months, and 1 year after intervention. At regular intervals, a committee for the validation of critical events evaluated all serious and undesirable events. In the event of an imbalance in serious undesirable events between the two arms, an independent monitoring committee could recommend interruption of the trial. All data were collected in a case report form and were available at the time of the usual assumption of responsibility of these patients. A registry of all treated rAIAs documented the number of patients not enrolled in the study during the same period.

A cost analysis was also carried out, which reported costs (€, 2010) according to the French National Health system. The cost of the hospital stay of an individual patient corresponds to a homogenous group of patients (HGP), similar to Medicare Diagnosis Related Groups. Patients treated by OSR are in a different HGP than patients treated by EVAR, for whom the mean cost of the stent-graft (€3,981) was added to the HGP. According to patients' comorbidities, a weight risk adjustment was done according to the OSR group case mix.

Patient selection, and inclusion, and exclusion criteria

Inclusion criteria. Inclusion criteria included a rAIA (i.e., ruptured aortic, aorto-iliac, or iliac aneurysm) documented by pre-operative CTA. Aneurysm rupture was defined by the existence of blood outside of the aorto-iliac aneurysm arterial wall: (i) retroperitoneal hematoma with peri-aortic blood in the peri-renal space and/or the para-renal space; or (ii) intraperitoneal hematoma. Arteriovenous fistulae to the inferior vena cava (IVC)/iliac vein and aortoenteric fistula were eligible criteria for the study, whereas contained or impending ruptures such as hemorrhage into a mural thrombus were not considered eligible. Patients had to be clinically and anatomically suitable to both OSR and EVAR. They also had to be hemodynamically stable, which was defined as a systolic blood pressure (SBP) on arrival >80 mmHg, in the absence of the need for continuous intravenous infusion and catecholamine administration in high dosage. The final inclusion criterion was the availability of a qualified surgeon (with minimum prerequisite of having carried out 15 EVAR procedures for asymptomatic/symptomatic AAA) and of devices and facilities for performing EVAR.

Intervention

Hemodynamically stable patients with a suspected diagnosis of rAIA were transferred to the CT suite. Other patients were referred with an initial CTA. Once rupture was confirmed, and if the inclusion criteria were met, the patient was operated on according to the treatment allocated for that week.

In the event of unstable hemodynamic status (SBP < 80 mmHg), a direct to theatre procedure for OSR was carried out and the patient was not included in the

Table 1. Pre-operative assessment of both groups of patients included in the ECAR trial.

	OSR (n = 51)	EVAR (n = 56)	p
Mean age (years)	73.8 (54.0–93.0)	75.0 (56.0–96.0)	.548
Sex (male), n (%)	46 (90.0)	51 (91.0)	.877
Height (cm)	175 (164–187)	172 (150–190)	.052
Weight (kg)	78.5 (55.0–117.0)	77.1 (50.0–125.0)	.630
SBP (mean mmHg)	110.9	105.9	.393
Endoclamping balloon, n (%)	11 (21.6)	7 (12.5)	.210
Loss of consciousness, n (%)	6 (11.8)	6 (10.8)	.863
Retroperitoneal rupture, n (%)	49 (96)	51 (91.0)	.335
Hardman index	1.1 (0–5)	1.0 (0–3.0)	.880
IGSII score	40.1 (18.0–82.0)	35.9 (0–83.0)	.128
Creatinine level (μmol/L)	123.7 (57.0–309.0)	137.5 (56.0–584.0)	.355
Hemoglobin level (g/dl)	10.6 (5.0–140.0)	13.5 (6.0–85.0)	.450
Troponin level	0.7 (0–15.0)	0.3 (0–4.8)	.386
Abnormal ECG, n (%)	9 (18)	10 (11)	1.000
Delay to treatment (h)	1.3 (0–5.5)	2.9 (0.2–17.0)	.005

Note. Values are given as mean (range) unless otherwise indicated. ECAR = Endovasculaire ou Chirurgie dans les Anévrismes aorto-iliaques Rompus; OSR = open surgical repair; EVAR = endovascular aneurysm repair; SBP = systolic blood pressure; ECG = electrocardiogram.

study. However, aortic endoclamping could be attempted.¹⁰ Once a stable hemodynamic status has been obtained for 10 minutes, inclusion in the study was considered. In all cases, SBP was maintained between 80 and 100 mmHg.

OSR. In order to avoid sudden hypotension due to the relaxation of the abdominal wall, no general anesthesia was administered until the patient was prepped and draped. The level of aortic cross-clamping was left to the operator's preferences (infra or suprarenal via a median laparotomy or thoracic via a left anterolateral thoracotomy), and aortic replacement was performed with a standard tube or bifurcated graft in the usual way. A retroperitoneal approach could be carried out in the event of previous laparotomy or of rupture in the IVC.

EVAR. Insertion of the endoprosthesis was performed under the same conditions as for asymptomatic AAA. According to the operator's preference, two types of devices could be inserted: (1) an aorto-uni-iliac stent graft combined with occlusion of the contralateral iliac artery, followed by a femoro-femoral crossover bypass; or (ii) a bifurcated aorto-bi-iliac stent graft.

EVAR was always performed within the instructions for use. Endoprostheses were Zenith (Cook Medical, Bloomington, IN, USA) and Talent (Medtronic, Minneapolis, MN, USA) aorto-uniiliac devices, or Excluder (WL Gore, Newark, DE, USA), Zenith TriFab (Cook), and Talent (Medtronic) bifurcated devices. Other more recent endoprostheses were allowed for the study provided they had been authorized for at least 1 year for treating asymptomatic AAA.

Statistical analysis

The sample size calculation of this superiority study was based on the primary efficacy variable: mortality at 30 days. The principal hypothesis was that EVAR would decrease the mortality by 20%. The expected mortality of patients presenting with a ruptured aneurysm of the abdominal aorta treated by OSR within the framework of this study was 40%.

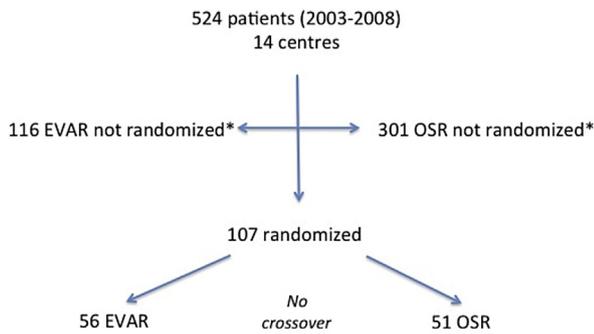
To achieve a power >80% with an alpha risk of 5%, 80 patients were required in each treatment group. The risk of losing patients to follow up at 30 days was minimal. It was initially the intention to include a total of 160 patients. In the end, only 107 patients were included because of the end of the trial after 5 year enrolment.

All variables were described at baseline and during follow up. Results were expressed as mean and SD for continuous variables and as a percentage for discontinuous variables. Description of the two groups on inclusion, comparison of 30 day mortality and survival without event (morbidity/mortality) rates were carried out in an intention to treat protocol according to a pre-specified analysis plan. Categorical parameters were compared between groups by chi-square test. Continuous parameters were compared after checking their distribution by a variance analysis or non-parametric test. Mixed model regression was used in multivariate analysis. Comparison of 30 day survival without event (morbidity/mortality) was performed using the Kaplan–Meier method with log rank test in univariate analysis and the Cox model for multivariate analysis. Exploratory subgroup analysis was performed according to previous results. A Cox score was drawn from variables identified by multivariate analysis of factors influencing 30 day mortality.

RESULTS

Enrolment

Between January 2008 and January 2013 107 patients with a rAIA, presenting at the 14 participating centers, were included. Fifty-six patients (52.3%) were included in the EVAR group and 51 (47.7%) in the OSR group. Groups were similar in terms of age, sex, consciousness, SBP, Hardman index, IGSII score, type of rupture, use of endoclamping balloon, and levels of troponin, creatinine, and hemoglobin (Table 1). Delay to treatment was longer in the EVAR group (2.9 vs. 1.3 hours; $p < .005$).



* Registry of non inclusion

Figure 1. CONSORT flow chart of the ECAR trial. *Note.* EVAR = endovascular aneurysm repair; OSR = open surgical repair; ECAR = Endovasculaire ou Chirurgie dans les Anévrismes aorto-iliaques Rompus.

Registry

As described by the CONSORT diagram in Fig. 1, during the 5 year study period, 417 patients operated on for rAIA but not enrolled in ECAR study (116 EVAR and 301 OSR) were recorded. The suitability rate (32.8%) for EVAR was calculated by dividing the overall number of patients treated by EVAR (56 randomized and 116 not randomized) by the overall number of patients treated in the 14 centers. Fig. 2 shows the variability of treatments amongst centers.

CTA

The CT findings showed that the rupture was aortic in 102 cases and iliac in five: mean diameters were 79.1 mm (range 43.0–140.0 mm) and 77.8 mm (range 55.0–90.0), respectively. Visceral artery occlusion was seen in six patients: one

renal artery occlusion and five patients at risk of colonic ischemia (two bilateral occlusions of internal iliac arteries [IIAs], two occlusions of one IIA and inferior mesenteric artery [IMA], one occlusion of both IIA). Thirty-seven additional patients had occlusion of the IMA alone. Mean proximal neck length and diameter were 29.0 ± 22.8 and 23.8 ± 4.5 mm, respectively. Mean angulation of the aortic neck was $33.5 \pm 25.6^\circ$. Peripheral occlusive arterial disease (i.e., significant iliac and/or femoropopliteal stenoses or occlusions) was present in 13.1% patients.

CT findings were retroperitoneal hematoma in 100 patients (93.5%), intraperitoneal hematoma in four (3.7%), and arteriovenous (IVC or iliac) or aortoenteric fistulas in three (2.8%). CT findings were comparable between groups ($p = .335$).

Hemodynamic stability

Eighty nine (83.2%) patients were hemodynamically stable on arrival, and in 18 patients (16.8%) initial hemodynamic instability was corrected by endovascular balloon occlusion.

Procedural data

Time from admission to treatment was longer in the EVAR group (2.9 vs. 1.3 hours; $p < .005$). Operative time (skin to skin) was similar between the OSR (3.4 hours; range 1.33–6.5 hours) and EVAR groups (3.2 hours; range 1.5–11 hours). In the OSR group, the level of clamping was thoracic in two cases (4%), suprarenal in eight (15.7%), and infrarenal in 41 (80.3%), with a mean time to clamping of 9 minutes. Bypasses were aorto-aortic ($n = 27$), bifurcated ($n = 22$), or axillo-bifemoral (after ligation of the infrarenal aorta; $n = 1$). One patient died before aortic replacement, and three additional patients died intra-operatively (two hemorrhagic shock, one multi-organ failure).

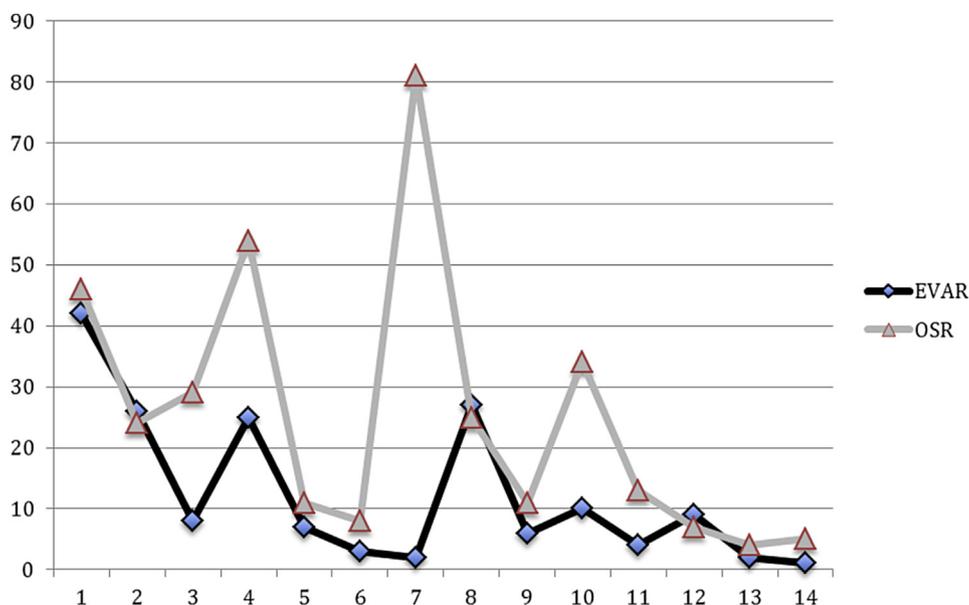


Figure 2. Type of intervention carried out in 14 centers participating in the ECAR trial (including non-enrolled patients) from January 2008 to January 2013. *Note.* EVAR = endovascular aneurysm repair; OSR = open surgical repair; ECAR = Endovasculaire ou Chirurgie dans les Anévrismes aorto-iliaques Rompus.

Table 2. Causes of death of patients included in the ECAR trial.

	EVAR (n = 56)	OSR (n = 51)	Overall (n = 107)
Intra-operative	1	4	5
MOF		1	
Hemorrhage	1	3	
Post-operative	12 (10)	14 (8)	26 (18)
In hospital			
Compartment syndrome	4 (4)	0	
MOF	1 (1)	5 (4)	
Sepsis	2 (1)	2 (1)	
ARDS	0	2	
Colonic ischemia	3 (2)	3 (2)	
Cardiac insufficiency	0	2 (1)	
Myocardial infarction	1 (1)	0	
Peritonitis	1 (1)	0	
Follow up	4	0	4
Respiratory failure	1		
Renal insufficiency	1	0	
Myocardial infarction	1	0	
Rupture	1	0	

Note. Values in parentheses are the 30 day values. ECAR = Endovasculaire ou Chirurgie dans les Anévrismes aorto-iliaques Rompus; EVAR = endovascular aneurysm repair; OSR = open surgical repair; MOF = multiorgan failure; ARDS = acute respiratory distress syndrome.

In the EVAR group, 48 patients were operated on under general anesthesia and eight under local anesthesia. Mean duration of intervention was 194.3 ± 153.7 minutes (range 60.0–1040.0 minutes). Forty-one patients (73.2%) were treated by aorto-uni-iliac stent graft, 12 (22.6%) had a bifurcated stent graft, and three (5.4%) had a stent graft limited to the iliac artery. Devices used were Zenith (Cook) ($n = 42$; 75.0%), Talent (Medtronic) ($n = 9$; 16.1%), Excluder (WL Gore) ($n = 3$; 5.3%), Anaconda (Vascutek, Inchinnan, UK) ($n = 1$; 1.8%), and Fluency (Bard, Tempe, AZ, USA) ($n = 1$, 1.8%). The IIA was embolized in eight patients, and bridged by the iliac limb in 18 (one bilateral). Mean duration of fluoroscopy was 31.2 ± 27.4 minutes and the mean volume of contrast used was 133.3 ± 60.6 mL.

In one patient a right renal artery was covered by the body of the stent graft, and in three patients polar renal arteries were covered. In two patients with aorto-uni-iliac stent graft, failure of the contralateral occluder stent graft was treated by IIA ligation via a retroperitoneal approach. In two patients endo-conversion by aorto-uni-iliac stent graft was performed owing to the inability to insert the contralateral limb. At the end of the procedure, endoleaks (one proximal type 1 endoleak successfully treated by complementary stenting; one type 2 endoleak left untreated) were observed in two patients (1.6%).

Post-operative outcomes

The primary end point (i.e., mortality rate at 30 days) was 18.0% ($n = 10$) in the EVAR group versus 25.0% ($n = 12$) in the OSR group (not significant [ns]). The in hospital mortality rate was 21.4% ($n = 12$) in the EVAR group versus 35.0% ($n = 18$) in the OSR group (ns). Causes of death ($n = 35$) are listed in Table 2. There was a trend towards

more intra-operative deaths in the OSR group (4/51; 7.8%) than in the EVAR group (1/56; 1.8%) (ns).

At 30 days, the incidence of major complications was similar between the EVAR ($n = 25$; 44.6%) and OSR ($n = 28$; 54.9%) groups. Post-operative complications are listed in Table 3.

Beyond 30 days, the requirements for hemodialysis were not significantly different (10.7% in the EVAR group versus 3.9% in the OSR group; $p = .345$). Compartment syndrome was observed in nine patients (8.4%; all treated by laparotomy): eight patients from the EVAR group (14.3%, four of whom died) and one patient (2%, who died) from the OSR group ($p = .052$). Colonoscopy within the first 48 hours, as recommended by the protocol, was performed in 34 patients (28.0%). Colonoscopies were not performed because of rapid death ($n = 5$), intra-operative colectomies ($n = 3$), and the absence of signs of colonic ischemia ($n = 65$). Colonoscopy was abnormal in five patients (8.9%) in the EVAR group versus 11 (21.6%) in the OSR group ($p = .049$). In the EVAR group, four colonic resections were performed and one patient survived; the last patient died prior to intervention. In the OSR group, seven colonic resections were performed, which led to three deaths; four

Table 3. Post-operative complications and features according to groups.

Covariate	EVAR (n = 56)	OSR (n = 51)	p
Post-operative death at 30 days	11 (19.6)	12 (24)	.239
In hospital post-operative death	13 (23.2)	18 (35)	.176
Death at 1 year	17 (30.3)	18 (35)	.296
Severe post-operative complications ^a	25 (44.6)	28 (54.9)	.291
Myocardial infarction	2 (3.6)	1 (2.0)	
Cardiac insufficiency	0	2 (4.0)	
Hemodialysis/renal insufficiency	6 (10.7)	2 (3.9)	.345
Colonic ischemia	5 (8.9)	11 (21.6)	.071
Mesenteric ischemia	0	1 (2.0)	
Peritonitis	1 (1.8)	0	
Compartment syndrome	8 (14.3)	1 (2.0)	.052
Major amputation	0	2 (4.0)	
Pulmonary complications	8 (15.3)	18 (41.4)	.012
Pulmonary embolism	1 (1.8)	0	
Post-operative hemorrhage	0	1 (2.0)	
Emboli/thrombosis	2 (3.6)	0	
MOF	3 (5.4)	5 (9.8)	.791
Sepsis	6 (10.7)	3 (5.9)	.638
Mean post-operative respiratory support, h (range)	59.3 (0–720.0)	180.3 (0–720.0)	.007
Re-intubation	45 (86.5)	29 (70.7)	.061
Mean units used in blood transfusion (range)	6.8 (0–25.0)	10.9 (0–53.0)	.024
Mean duration of stay in ICU, days (range)	7 (1–30)	11.9 (0–33.0)	.012
Mean duration of in hospital stay, days (mean)	14.3 (6.0–99.0)	17.1 (9.1–81.1)	.208

Note. Values are given as n (%) unless otherwise stated. EVAR = endovascular aneurysm repair; OSR = open surgical repair; MOF = multi-organ failure; ICU = intensive care unit.

^a Eighty-nine severe post-operative complications (42 after EVAR, 47 after OSR) in 53 patients.

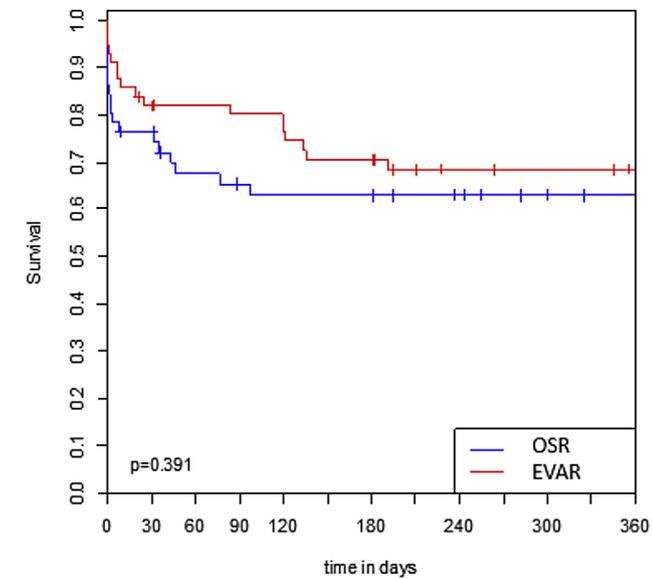


Figure 3. Kaplan–Meier estimates for survival between open surgical repair and endovascular aneurysm repair.

patients were not operated on (two died prior to intervention). The mortality associated with colonic ischemia was 8.4% of the overall population and 56.3% in patients with colonic ischemia.

There were nine septic events: six patients in the EVAR group (four cases of sepsis of femoro-femoral bypass, one case of sepsis of an endoprosthesis, and one case of septic hypogastric aneurysm) and three patients in the OSR group.

During the post-operative period, nine type 2 endoleaks were diagnosed by CT scan.

The composite rate of severe complications and death at 30 days, 6 months, and 1 year was 39.3%, 46.0%, and 48.0% in the EVAR group versus 41%, 47%, and 47% in the OSR group ($p = .239$, $p = .176$, and $p = .296$), respectively.

The amount of total blood transfusion in the EVAR group was significantly lower than in the OSR group (6.8 vs. 10.8 units; $p = .024$).

The duration of respiratory support was significantly lower in the EVAR group than in the OSR group (59.3 vs. 180.3 hours; $p = .007$). There was a trend towards more repeated intubation in the OSR group (29.3% vs. 13.5%; $p = .061$) and nearly 2.5 times more pulmonary complications in the OSR group (41.5% vs. 15.4%; $p = .005$).

The mean duration of ICU stay was lower in the EVAR group (7 vs. 11.9 days; $p = .012$).

The median total hospital stay was 17.1 days in the OSR group versus 14.3 days in the EVAR group ($p = .208$).

Long-term follow up

Mean duration of follow up was 231.8 days (range 31.0–365.0 days). No patient was lost to follow up.

Long-term survival curves of patients randomized to EVAR and OSR did not show any significant difference between the two groups at 30 days and 1 year (Fig. 3).

Most post-operative type 2 endoleaks resolved, but one was treated by embolization at 3 months. Three additional type 2 endoleaks were diagnosed on follow up CT scans: two resolved spontaneously and one persisted without significant increase in AAA diameter. One aneurysm rupture occurred 6 months after EVAR.

Morbidity indices

There was no significant difference in IGSII score between OSR and EVAR.

Univariate analysis identified factors influencing 30 day survival: age, use of endoclamping, SBP, creatinine clearance, bicarbonate, and Hardman index score. There was no center effect. There were only four variables identified from the multivariate analysis of factors influencing 30 day mortality: hemoglobin, SBP, creatinine clearance, and bicarbonate.

Hospitalization costs

The mean cost difference between EVAR (€7,087.5) and OSR (€9,329.4) was €2,241.9 per patient. When adjusting costs according to OSR case mix, there was still a difference of €525.6 between EVAR (€8,803.8) and OSTR (€9,329.4).

DISCUSSION

This study illustrates that at least 32.8% of rAIAs are suitable for EVAR, as it was assumed that all those who received OSR not randomized in ECAR trial were unsuitable for EVAR. The discrepancy between centers illustrates that some of the patients not enrolled in the trial and treated by OSR might have been suitable for EVAR (Fig. 2); however, extrapolating the results to an unselected cohort of rAIAs is not possible, as the reasons for non-inclusion could not be documented extensively.

To date, three RCTs of EVAR vs. OSR for rAIA have been reported. The first, a small pilot trial in which unstable patients were excluded, failed to demonstrate benefit of EVAR over OSR in terms of mortality.¹¹ The Dutch AJAX trial, which enrolled 116 hemodynamically stable patients with anatomy suitable for EVAR, also showed no difference in mortality rates between EVAR and OSR (21% vs. 25%).¹² In the UK IMPROVE trial, 30 day mortality results showed no difference between an endovascular strategy (patients underwent urgent CT followed by EVAR whenever this modality was possible) and an open repair strategy (CT scan optional) (35% vs. 37%).¹³

The ECAR trial was designed to avoid as many potential biases as possible.

As imposing one procedure on a surgeon used to practicing another procedure would introduce a bias, randomization by week was chosen, synchronously for all centers. This methodology has the advantage of facilitating planning of the emergency teams. Previous studies have been carried out according to this method, for example in comparing two methods of resuscitation after heart failure.¹⁴

It is difficult to randomize hemodynamically unstable patients because of the variation in the definition of

hemodynamic instability among different teams, which is related to the subjectivity of the definition itself. Some teams prefer a SBP as low as 50 mmHg without observing any increase of end-organ injury,¹³ however most teams believe that, to avoid widespread organ injury, SBP should be kept >80 mmHg unassisted by catecholamines, to be indicative of hemodynamic stability. In our experience, most patients treated with OSR were turned down for EVAR because of severe hemodynamic instability precluding CT scan.⁵

CT scanning prior to enrolment is mandatory to ensure the correct mortality and morbidity statistics of EVAR treated rAIAs in order to achieve the following three facts. The first is to establish the diagnosis of rupture. The mortality rate of acute non-ruptured AAAs, recently reported to be 15.8%,¹⁵ is lower than for rAIA, explaining an apparently low mortality in some series. The second is to exclude other abdominal pathologies.¹⁶ Hypotension and symptoms of pain may be confused with those of renal colic, diverticulitis, appendicitis, pancreatitis, bowel obstruction, bowel ischemia, gastrointestinal hemorrhage (typically from an ulcer), perforated duodenal or gastric ulcer, other aortic emergencies (dissection, intramural hematoma) lumbar compression fracture, and inferior wall myocardial infarction. The third is to allow pre-operative planning, that is, suitability for EVAR and graft size. Unsuitable access or inadequate graft landing zones may result in endoleak or conversion to OSR, which in most studies is associated with a higher mortality. Intra-operative calibration angiography has been proposed to avoid pre-operative delay due to CT scanning but fails to exclude other pathologies and is less accurate in predicting the correct size of graft in elective series. Thus, its reliability is questionable.

In this study, the selection criteria (i.e., both favorable anatomy and hemodynamic stability) explain the fact that the mortality rate after OSR (24.0%) is much lower than the expected 40.0% mortality rate on which the study design was based. Although the length of hospital stay of many patients exceeded 30 days, owing to complications, 30 day mortality, which is the reporting standard of most studies, was kept as the primary study end point, while in hospital mortality, and 6 month and 1 year mortality were secondary end points: in this trial, the mortality rates were not different between EVAR and OSR, both in intention-to-treat and per-protocol analyses, as there was no crossover. This finding is consistent with the results of previously published RCTs but may be due to an overly optimistic power calculation for the trial. Meta-analysis of all the trials should be the next step in producing high level evidence. However, total respiratory support time, pulmonary complications and abnormal colonoscopy rates, total blood transfusion, and duration of ICU stay were significantly lower in the EVAR group, confirming the suspicion that EVAR is less invasive than OSR. This study also found that EVAR reduces hospitalization costs: even if the cost of OSR compared with EVAR is lower when adjusted to patient status, EVAR is a cost-effective alternative to OSR. A prospective comparison of actual costs of EVAR with the current French

reimbursement system is necessary to allow extrapolation of the findings.

rAIA mortality is mostly related to patient status on arrival. This study carries a “national” bias as a group of “stable” patients would have arrived earlier—but less stable—in countries where the transport is performed by paramedics. In France, most patients are transported in dedicated ambulances where an anesthesiologist resuscitates the patient as well as possible and for as long as necessary to avoid hemodynamic variations during transport. This results in a loss of time to referral to a surgical ward and may jeopardize the results. The fact that three out of four parameters identified by multivariate analysis are biological seems to confirm this potential limitation of the findings.

This study, as with other RCTs, confirms that EVAR is feasible in an emergency setting, with the same reliability (i.e., only two endo-conversions to aorto-uni-iliac, and one complementary stenting for intra-operative type 1a endoleak), and secondary endoleaks compare favorably with EVAR performed in an elective setting.

Mortality remains a challenge of surgical treatment of rAIA. EVAR is only a step towards simplifying the strategy but does not significantly improve the survival rate. Other technical refinements such as endoclamping,¹⁴ are currently resulting in more stable patients receiving OSR or EVAR. The key point is that endovascular methods are now part of the strategy, and adopted by most teams. Although only 14.3% of patients in the EVAR group were operated on under local anesthesia, endoclamping, also performed under local anesthesia, allows a smoother induction in cases where general anesthesia is chosen.

Although the results do not allow EVAR to be advocated as a first line strategy for all suitable rAIAs, the authors are comfortable proposing an algorithm of treatment where endovascular techniques play a major role.

CONCLUSION

As in previous RCTs, the current study fails to demonstrate a mortality benefit of EVAR over OSR in suitable rAIAs. However, there is a trend towards lesser morbidity and lower costs when EVAR is used as the primary procedure in suitable patients. Pooling the data of the available RCTs may confirm this assertion. Endovascular management of ruptured aneurysms (endoclamping as well as EVAR) must now to be considered as major progress.

CONFLICT OF INTEREST

None.

FUNDING

A grant obtained from the French Ministry of Health (PHRC [Hospital Program of Clinical Research]) covered the cost of the study. The sponsor had no role in the study design.

APPENDIX A. SUPPLEMENTARY DATA

Supplementary data related to this article can be found at <http://dx.doi.org/10.1016/j.ejvs.2015.03.028>.

REFERENCES

- 1 Johansson G, Swedenborg J. Little impact of elective surgery on the incidence and mortality of ruptured aortic aneurysms. *Eur J Vasc Surg* 1994;**8**:489–93.
- 2 EVAR trial participants. Endovascular aneurysm repair versus open repair in patients with abdominal aortic aneurysm (EVAR trial 1): randomised controlled trial. *Lancet* 2005;**365**:2179–86.
- 3 Yusuf SW, Whitaker SC, Chuter TA, et al. Emergency endovascular repair of leaking aortic aneurysm. *Lancet* 1994;**344**:1645.
- 4 Marin ML, Veith FJ, Cynamon J, Sanchez LA, Lyon RT, Levine BA, et al. Initial experience with transluminally placed endovascular grafts for the treatment of complex vascular lesions. *Ann Surg* 1995;**222**:449–65.
- 5 Alsac JM, Desgranges P, Kobeiter H, Becquemin JP. Emergency endovascular repair for ruptured abdominal aortic aneurysms: feasibility and comparison of early results with conventional open repair. *Eur J Vasc Endovasc Surg* 2005;**30**:632–9.
- 6 Van Beek SC, Conijn AP, Koelemay MJ, Balm R. Editor's Choice—Endovascular aneurysm repair versus open repair for patients with a ruptured abdominal aneurysm; a systematic review and metaanalysis of short-term survival. *Eur J Endovasc Surg* 2014;**47**:593–602.
- 7 Vogel TR, Dombrovskiy V, Haser P, Graham AM. Has the implementation of EVAR for ruptured AAA improved outcomes? *Vasc Endovascular Surg* 2009;**43**:252–7.
- 8 Desgranges P, Kobeiter H, Castier Y, Senechal M, Majewski M, Krrimi A. The ECAR PROTOCOL update: (Endosvasculaire vs. Chirurgie dans les Anévrismes Rompus). *J Vasc Surg* 2010;**51**:267–70.
- 9 Chaikof EL, Blankensteijn JD, Harris PL, White GH, Zarins CK, Bernhard VM, et al. Reporting standards for endovascular aortic aneurysm repair. *J Vasc Surg* 2002;**35**:1048–60.
- 10 Raux M, Marzelle J, Kobeiter H, Dhonneur G, Allaire E, Cochenec F, et al. Endovascular balloon occlusion is associated with reduced intra-operative mortality of unstable patients with ruptured abdominal aortic aneurysm but fails to improve other outcomes. *J Vasc Surg* 2015;**61**:304–8.
- 11 Hinchliffe RJ, Bruijstens L, MacSweeney ST, Braithwaite BD. A randomised trial of endovascular and open surgery for ruptured abdominal aortic aneurysm—results of a pilot study and lessons learned for future studies. *Eur J Vasc Endovasc Surg* 2006;**32**:506–13.
- 12 Reimerink JJ, Hoornweg LL, Vahl AC, Wisselink W, van den Broek TAA, et al. Amsterdam Acute Aneurysm Trial Collaborators. Endovascular repair versus open repair of ruptured abdominal aortic aneurysms: a multicenter randomized controlled trial. *Ann Surg* 2013;**258**:248–56.
- 13 IMPROVE Trial Investigators, Powell JT, Sweeting MJ, Thompson MM, Ashleigh R, Bell R, et al. Endovascular or open repair strategy for ruptured abdominal aortic aneurysm: 30 day outcomes from IMPROVE randomised trial. *BMJ* 2014;**348**:f7661.
- 14 Plaisance P, Lurie KG, Vicaut E, Adnet F, Petit JL, Epain D, et al. A comparison of standard cardiopulmonary resuscitation and active compression-decompression resuscitation for out of-hospital cardiac arrest. French Active Compression-Decompression Cardiopulmonary Resuscitation Study Group. *N Engl J Med* 1999;**341**:569–75.
- 15 Haug ES, Romundstad P, Aadahl P, Myhre HO. Emergency non-ruptured abdominal aortic aneurysm. *Eur J Vasc Endovasc Surg* 2004;**28**:612–8.
- 16 Rakita D, Newatia A, Hines JJ, Siegel DN, Friedman B. Spectrum of CT findings in rupture and impending rupture of abdominal aortic aneurysms. *Radiographics* 2007;**27**:497–550.