

**ΣΧΟΛΗ ΕΠΙΣΤΗΜΩΝ ΥΓΕΙΑΣ**

**ΙΑΤΡΙΚΗ ΣΧΟΛΗ**

**ΚΟΙΝΟ ΠΡΟΓΡΑΜΜΑ ΜΕΤΑΠΤΥΧΙΑΚΩΝ ΣΠΟΥΔΩΝ**

**«ΕΝΔΑΓΓΕΙΑΚΕΣ ΤΕΧΝΙΚΕΣ»**

**ΕΘΝΙΚΟ ΚΑΙ ΚΑΠΟΔΙΣΤΡΙΑΚΟ ΠΑΝΕΠΙΣΤΗΜΙΟ ΑΘΗΝΩΝ**

**ΙΑΤΡΙΚΗ ΣΧΟΛΗ ΣΕ ΣΥΝΕΡΓΑΣΙΑ ΜΕ ΤΟ ΠΑΝΕΠΙΣΤΗΜΙΟ ΤΟΥ ΜΙΛΑΝΟΥ- BICOCCA**

**ΔΙΠΛΩΜΑΤΙΚΗ ΕΡΓΑΣΙΑ**

**ΘΕΜΑ: LATE POST-EVAR ABDOMINAL AORTIC ANEURYSM RUPTURE. A REVIEW METANALYSIS STUDY**

**ΜΕΤΑΠΤΥΧΙΑΚΟΣ ΦΟΙΤΗΤΗΣ:**

**ΠΑΠΑΔΟΥΛΑΣ ΣΠΥΡΙΔΩΝ**

**ΑΘΗΝΑ**

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**ΚΟΙΝΟ ΠΡΟΓΡΑΜΜΑ ΜΕΤΑΠΤΥΧΙΑΚΩΝ ΣΠΟΥΔΩΝ**

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**ΤΗΣ ΣΥΝΕΔΡΙΑΣΗΣ ΤΗΣ ΤΡΙΜΕΛΟΥΣ ΕΞΕΤΑΣΤΙΚΗΣ ΕΠΙΤΡΟΠΗΣ ΓΙΑ ΤΗΝ ΑΞΙΟΛΟΓΗΣΗ ΤΗΣ ΔΙΠΛΩΜΑΤΙΚΗΣ ΕΡΓΑΣΙΑΣ**

**του Μεταπτυχιακού Φοιτητή ΠΑΠΑΔΟΥΛΑ ΣΠΥΡΙΔΩΝΑ**

# Εξεταστική Επιτροπή

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H Tριμελής Εξεταστική Επιτροπή για την αξιολόγηση και εξέταση του. υποψηφίου **κ. Παπαδούλα Σπυρίδωνα**, συνεδρίασε σήμερα -/-/2023.

H Eπιτροπή **διαπίστωσε** ότι η Διπλωματική Εργασία του ΠΑΠΑΔΟΥΛΑ ΣΠΥΡΙΔΩΝΑ με τίτλο **«LATE POST-EVAR ABDOMINAL AORTIC ANEURYSM RUPTURE. A METANALYSIS»** είναι πρωτότυπη, επιστημονικά και τεχνικά άρτια και η βιβλιογραφική πληροφορία ολοκληρωμένη και εμπεριστατωμένη.

Η εξεταστική επιτροπή αφού έλαβε υπόψιν το περιεχόμενο της εργασίας και τη συμβολή της στην επιστήμη, με ψήφους ................ προτείνει την απονομή στον παραπάνω Μεταπτυχιακό Φοιτητή του Μεταπτυχιακού Διπλώματος Ειδίκευσης (Μaster's).

Στην ψηφοφορία για την βαθμολογία ο υποψήφιος έλαβε για τον βαθμό «ΑΡΙΣΤΑ» ψήφους ....................., για τον βαθμό «ΛΙΑΝ ΚΑΛΩΣ» ψήφους .................... και για τον βαθμό «ΚΑΛΩΣ» ψήφους ................. Κατά συνέπεια, απονέμεται ο βαθμός «......................».

Tα Μέλη της Εξεταστικής Επιτροπής:

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**GENERAL SECTION**

1. **Abdominal aortic aneurysm Repair**

An abdominal aortic aneurysm (AAA) is defined as an aortic dilatation with a diameter of more than 3 cm. The aim of repair is to prevent rupture and death from hemorrhage and is recommended for male patients with a maximum diameter of at least 5.5 cm and in female patients with the maximum diameter of at least 5.0 cm. Presence of symptoms or an increase in aneurysm size above 5 mm in a 6-month interval are additional indications for repair1.

Endovascular abdominal aortic aneurysm repair (EVAR) is a minimally invasive procedure introduced as an alternative to open repair (OR) for the treatment of these patients2. Open surgical repair requires a midline trans-abdominal or retroperitoneal incision to expose the aneurysm. After aortic and iliac clamping, the sac is opened and a tubular or bifurcated prosthetic graft is interposed3. During EVAR, the aneurysm is left intact and transient aortic clamping is not needed. After percutaneous or femoral cut down, blood flow is rerouted through catheter-based deployment of a stent-graft, which excludes the sac from the circulation. Commonly, a bifurcated, modular stent-graft is anchored below the renal arteries in a normal aortic neck and extended into normal common or external iliac arterial segments bilaterally. Other types of grafts use bare stent proximally for suprarenal fixation. Anatomical suitability for EVAR requires adequate sealing zones, defined as non-aneurysmal areas of parallel-walled artery above the AAA and below to the common or external iliac arteries, where a stent graft can be sealed. Additional requirements include adequate diameter of the femoral and iliac vessels to accommodate the introduction of the sheaths and delivery of devices. EVAR is unfeasible in case of excessive vessel angulations or severe atheromatous debris. Ideally, proximal neck length should be ≥ 15 mm, diameter < 32 mm, angulation < 600 with wall calcification extending to less than half of its circumference without significant thrombus apposition. Iliac arteries must not have prohibitive angulations or diffuse calcifications and external iliac artery diameter should be > 7 mm and < 14 mm. Computed Tomography Angiography (CTA) with thin slices (1 to 2 mm) of the abdomen and pelvis is indicated to decide whether the anatomy is suitable for EVAR2.

Compared to OR, EVAR has a lower operative morbidity, mortality and a shorter hospital stay4. The perioperative mortality of elective AAA repair is 1.1% for EVAR and 4.4% for OR internationally5. Conversely, OR is known to be more durable and the repair is likely to last for the rest of the patient’s lifetime6. The choice of repair strategy should include consideration of the patient’s anatomical suitability, operative risk, life expectancy and compliance to the lifelong annual follow-up imaging1,3,7. Patients with cardiac, pulmonary or renal comorbidity, obese, diabetic and octogenarians are considered at high risk for surgery and may be eligible for EVAR3,7,8. If patient’s surgical risk is low or intermediate, either EVAR or open repair would be reasonable9,10. European Society for Vascular and Endovascular Surgery (ESVES) guidelines recommend EVAR over OR in most patients with suitable anatomy and reasonable life expectancy (e.g. >2 years)7. Since the introduction of EVAR in 1991, the number of AAA repairs has increased dramatically and more than 80% of them are performed endovascularly in elective setting and nearly 30-50% urgently due to rupture5. Since EVAR has an early survival benefit but an inferior prolonged survival benefit compared to OR, it needs long-term post-repair surveillance and possible re-interventions to correct graft-related complications11,12. Although EVAR is associated with a higher risk of reintervention, most such interventions involve minor endovascular procedures. Over a patient’s lifetime, open repair is associated with a higher reintervention rate related to the abdominal incision4,6. Computed Tomography Angiography plays a critical role for both preprocedural planning and postprocedural surveillance of AAA patients13. Magnetic Resonance Angiography (MRA) may have a supplementary role in case of sac growth where CTA is negative or inconclusive7.

1. **Complications and causes of Failure after EVAR**

Complications after EVAR are divided into immediate (on the 1st postoperative day), early (during the 1st month) and late (after the 1st month) based on the time of presentation3,7,14. Regarding the degree of severity, a complication is characterized as “minor,” “moderate” or “severe”7. Furthermore, they are categorized as graft-related and systemic complications3,7. Graft-related complications include the endoleaks (ELs), migration, kinking, graft thrombosis, infection and access site complications7. Systemic complications include limb ischemia, bowel ischemia and spinal cord ischemia 2,7. Graft-related complications occur in 16–30% of patients after EVAR; the most common types include endoleak (EL), occurring in 15–30%, followed by graft migration (in 1–10%), graft limb thrombosis (in 0.5–11%), and structural stent-graft fatigue (in 5.5%)2,15. Consequently, re-interventions rates after EVAR vary between 20-40% in long-term follow-up and are more frequent after ruptured aneurysms (rAAAs) vs intact AAAs5.

Endoleaks are classified into primary which are present at the time of repair or secondary which occur after a prior normal imaging7. They may be also categorized as early or late/delayed (before or after 12 months) and as transient or persistent (resolved or not resolved 6 months)7. Regarding the cause of perigraft flow, there are five types of endoleaks3. Type I is caused by an incompetent seal at the proximal attachment site (type Ia), at the distal (type Ib) or at the iliac occluder (type Ic). Type Ic EL refers to the failure of occlusion of the contralateral common iliac artery in patients with aorto-uniliac stent-graft combined with a femoral-femoral bypass. Type II is caused by persistent flow into and out of the aneurysm sac via patent aortic side branch vessels such as the inferior mesenteric artery, lumbar arteries or accessory renal arteries. It is sub-divided into IIa (one side branch) and IIb (two or more side-branches). Type III EL is caused by structural failure of the endograft itself due to separation or dehiscence of modular graft components (type IIIa) or tears in the endograft fabric (type IIIb). They may occur due to maldeployment of stent grafts with inadequate overlap, proximal or distal stent graft migration, or material fatigue (e.g., stent or hook fractures). Type IV EL is caused by graft porosity, while type V EL or endotension is characterized by continued aneurysm sac expansion despite the lack of any detectable EL on imaging2,3,7. Anticoagulant therapy may increase the risk of EL development post EVAR2. Approximately half of the ELs (mainly Type II) resolve spontaneously, without any re-intervention after collateral thrombosis7.

Management of ELs varies based on the cause. In type II EL intervention is indicated if it is persistent over 6 months causing more than 10 mm of sac expansion7. Some centers intervene at 5 mm expansion, as this is the lower limit for detection of sac expansion between two imaging events using the same modality7. It includes embolization of the aneurysm sac and feeding vessels through transarterial, transcaval, translumbar, transabdominal or transsealing (between iliac graft and iliac arterial wall) approaches. It is successful in 60-80% of the cases2,16. Fortunately, type II ELs although the commonest, have a low risk of rupture (<1%). Type I and III ELs are considered high-risk due to intra-sac high-pressure and always warrant urgent management as they expose the aneurysm to the risk of rupture. Treatment of type I EL is achieved with embolization or with placement of aortic cuffs or iliac extenders 12,17. Treatment of type III ELs includes placement of a covered stent across the space between the original stent-graft components or across the fabric dehiscence18. Sometimes, it may warrant total endovascular relining7. Type IV EL is spontaneously resolves within 30 days and is uncommon with the new generation devices7. Endotension may be due to ultrafltration of blood through the stent-graft fabric, transmission of the blood pressure to the aortic wall through the thrombus around the device, infection and seroma or may be due to an occult endoleak19. Thus, the patient must be investigated using other methods like MRA or Contrast Enhanced Ultrasound20. Endotension is treated if sac expansion exceeds 10mm with graft relining, sac plication or graft explantation4,19,20,21.

Device migration is a movement of more than 10 mm on the centerline or movement of more than 15 mm on either the anterior or posterior aortic wall2. Remodeling of the aneurysm or aneurysmal sac expansion, hemodynamic forces and inadequate overlap between the graft and the aneurysm’s neck can lead to device migration3,22. Additionally, aneurysmal disease progression with neck dilatation (in relation to initial neck diameter) may be a cause of late migration7,22. Stent-graft migration can be the underlying cause of type I EL, type III EL and device kinking. Device migration may concern both the proximal and distal fixation zones of the stent-graft. Risk factors for proximal migration include short proximal fixation, angulated neck, large aneurysm size, stent graft type and possibly oversizing >30%. Migration of the iliac limb can lead to type Ib EL and type III EL23. The risk factors potentially influencing limb migration include a large aneurysm (>6 cm), dilated or aneurysmal common iliac artery (>18 mm), short fixation zone (<70%) or inadequate iliac limb oversizing (<10-20%)2,22,23,24. An iliac fixation length of >20 mm or preferably down to the IIA has been suggested to reduce the risk of proximal stent graft migration7. Adequate seal (10 mm proximally and distally) on the first post-operative CT scan predicts a better late EVAR outcome7. We must emphasize that most studies include previous generation stent grafts when migration was a relatively common issue7.

Device kinking may occur in 2–4% of patients, due to aneurysm shrinking over time, severe proximal aortic neck angulation and a narrow distal aortic neck. Device kinking can be localized at stent-graft limb and is defined as a sharp localized angulation >90° on imaging. Kinking can lead to device migration, type I and type III EL, endograft thrombosis and occlusion. Limb kinking treatments include angioplasty with or without stent placement or additional endograft limbs within the original graft2,7,25.

Graft thrombosis may affect 4% of patients and is often related to stent-graft kinking, migration, and dislocation. Extreme oversizing can also result in folding of the graft fabric, with distortion of the limbs and subsequent limb thrombosis. Treatment options include thrombectomy and stent placement. Sometimes, an open femoro-femoral bypass may be required2,23,26.

Access site complications include pseudoaneurysm, arterial thrombosis or dissection and other local wound complications (i.e., groin hematoma, cellulitis, and lymphocele) occurring in a rate of 3-5%. Graft infection (occurring <1%) may erode the surrounding tissues and compromise the integrity of the aneurysm wall2. Lower Limb ischemia is often the result of endograft limb occlusion7. Renal ischemia could be secondary to renal artery embolization or thrombosis, dissection, and inadvertent coverage of the origin of the renal arteries by the initial endograft or after endograft migration3,7. This risk is increased in case of a short aortic neck. In addition to ischemia, kidney may be exposed to contrast nephropathy2,3,27.

Bowel ischemia after EVAR most commonly involves the left colon and rarely the small bowel or the right colon. It occurs in case of insufficient mesenteric collateral circulation after coverage of the inferior mesenteric artery origin which is the rule in all cases of EVAR2. Pelvic ischemia after EVAR is more frequent in case of internal iliac artery (IIA) planned embolization7. Clinical signs may include buttock claudication, erectile dysfunction, rectal ischemia, and skin necrosis7. Spinal cord ischemia is rare, and it may cause paraplegia due to interruption of the collateral circulation from the iliolumbar and internal iliac arteries2,3,28.

Most of EVAR complications are treated by endovascular techniques but surgical conversion must always be considered if endovascular approach is not indicated or is unsuccessful29. Surgical treatment options include laparoscopic or open ligation of side-branch vessels feeding the EL, suturing of the ostia of the leaking branch after opening the aneurysm sac or stent graft explantation with conversion to OR29. This is obviously more invasive and reserved for cases where endovascular intervention has failed, with an estimated incidence of 0.8% to 5.9% after EVAR7,30. It is noteworthy that some have become disheartened with the longevity of endovascular secondary interventions and prefer an earlier open conversion (OC) as a durable solution30. The overall incidence of all delayed OCs after EVAR has been increasing31. Open conversion in an elective setting had a perioperative mortality of 6.2% in one report and 9.9% in another and is generally a durable solution30,31. In another study using the National Surgical Quality Improvement Program database, elective open conversion had higher perioperative mortality compared with primary open repair (10.0% vs 4.2%; P < .001)30.

**SPECIFIC SECTION**

1. **Late rupture after EVAR (post-EVAR LAR)**

**1.1 Introduction**

Late EVAR failure may lead to sac pressurization, expansion, and eventual aneurysm rupture3. Late rupture is defined as rupture occurring more than 30 days after the EVAR procedure14. It is a rare complication with an increasing incidence worldwide due mainly to the widespread application of EVAR7. However, it remains a devastating event, like a de novo AAA rupture, as it carries a mortality rate ranging from 20% to 60% in recent studies5,8,14,32-43. Thus, the fundamental aim of EVAR which is protection from rupture is not fulfilled, as a 0.5% to 6% of EVAR patients experienced rupture, so far44.

**1.2 Review of the literature**

Several risk factors for post-EVAR rupture have been identified and classified as anatomic, patient-related, and stent graft-related. Anatomic risk factors refer to aneurysm morphology during the index EVAR procedure indicative of a probable sub-optimal long-term patient course44. Stent-grafts are composite constructs comprised of fabric and a metal skeleton, which are bonded together with sutures and sometimes tapes45. All these components interact dynamically under the constant aortic pulsations. A wide (nearly 32mm), a short (about 1cm) and/or an angulated neck (above 600) are prognostic factors for long-term adverse effects. This becomes worse in case of a concomitant large aneurysmal sac (de Guerre JVS 2021)20. Graft sealing in wide, short, or angled common iliac arteries in the borderline area of the manufacturer’s graft instructions for use (IFU) may lead in the long-term to type Ib EL or limb disconnection from the native artery7,23,38,45. At the time of a post-EVAR aneurysm rupture the main intraoperative finding is type I or III EL44,46,47.

EVAR outside the manufacturer’s IFU, is a further negative predictor for late adverse sequela, presumably because of lack of adequate seal30. During the last years, accumulative experience leads surgeons to perform EVAR procedures in patient with unfavorable anatomy8. This is mainly driven by the preference to avoid open surgery from both the surgeon and the patient due to severe co-morbid conditions8. This may lead to inadequate modular overlap and compromised junctional integrity, when off-label combinations are used (e.g., one manufacturer’s limbs combined with another manufacturer’s main body)44. Instructions For Use adherence during initial EVAR was much lower in cases needed OC versus uncomplicated cases (43.8% vs 79.0%, p < .01)45. The need for elective OC for complications other than rupture is reported to vary between 0 to 9% with risk increasing over time45. There is much more concern in a relatively young and healthy patient with long life expectancy who has the time needed to express these adverse consequences7,27,28. Patients needing OC would have tolerated a primary OR more favorably many years earlier, when they were younger and possibly had fewer medical comorbidities30.

First generation grafts have been more prone to failure instead of later generation grafts which have improved design and materials26. Some kinds of grafts have already been abandoned48. Patient with these grafts should be monitored more frequently to reveal possible complications. Incomplete patient follow-up after the index procedure is a major pitfall as it leaves the patient without the protective effects of a secondary, usually percutaneous curative procedure, turning away any concerns for an imminent rupture13,49. Follow-up is essential not only because of the possible stent-graft fatigue but EVAR failure may be due to aneurysmal sac changes after the index procedure7,13. Shrinkage of the sac due to remodeling is a desired transformation, but it may lead to graft kinking or ELs50. On the contrary, aneurysm sac enlargement may lead to loss of the proximal and distal fixation and sealing zones leading to severe ELs and migration51. Patients with persistent ELs or with treated EVAR complications endovascularly are at increased risk for elective OC or LAR23,52,53. The presence of a type II EL at early follow up is an important indicator of possible late complications or need for re-intervention and follow-up with duplex scans for assessment of sac size is suggested7. Conversely, sac shrinkage which usually follows an adequate seal without EL in a favorable aneurysm anatomy is a predictor of low risk of failure during the first five post-operative years7,50. Unfortunately, even with meticulous follow-up adherence and without presence of ELs a small risk for post-EVAR LAR always exists47,53,54,55.

As EVAR repairs steadily increase the overall incidence of all post-EVAR LARs are also increasing43. In contemporary series EVAR may be affected with delayed rupture in 0.9-3.1% of cases within 5 years and may achieve a freedom from AAA rupture in 96% at ten years44. On the contrary, late ruptures after OR have been reported to be <0.8% in 5.5 years4. Perioperative mortality with OCs for rupture was about 40% in one report30. Late conversion urgently has a 10 times higher 30-day mortality rate compared with the elective setting6. As the latter is nearly equal with the mortality rate of primary elective AAA repair, efforts to prevent post-EVAR urgent operations for symptomatic aneurysms or ruptures are mandatory25,54.

As already mentioned, perioperative mortality is generally 1.1% for EVAR and 4.4% for OR52. If we could decrease the rate of post-EVAR ruptures after a deep knowledge of its causes, we could eventually alter the lost early survival benefit achieved with EVAR compared with OR24.53. Finally, the urgent repair of the ruptured AAA in LAR may be challenging and integrate special difficulties either with EVAR or OR15,43,56. Modern vascular surgeons should be familiar with these complications and the special intra-operative handling they need29,57.

1. **AIM OF THE STUDY**

The aim of this study is to present updated information in post-EVAR LAR, which increases steadily worldwide as the data in the literature are limited. It comprises a current literature review and metanalysis based on the recent evidence investigating the incidence, causes, treatment outcomes and prognosis of post-EVAR LAR.

1. **METHODS**

A review metanalysis was conducted according to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines58. Rupture of the AAA >30 days after the initial EVAR is defined as ‘late rupture’ and this was confirmed on imaging studies that revealed blood outside the aneurysm sac or on open conversion14.

**3.1 Information Sources and Search Strategy**

Studies were identified by searching electronic databases and scanning bibliographic references of articles. The National Library of Medicine’s Medline database was searched using the PubMed interface from 1991 to the present date. The last search was run on April 1, 2023. The databases were searched with an unrestricted search strategy, applying exploded Medical Subject Headings (MeSH) and keywords combined with the Boolean operators AND, OR and NOT to retrieve relevant reports. A second-level search included a manual screen of the reference lists of the articles identified through the electronic search. Eligibility assessment was performed independently in an unblinded standardized manner by 2 reviewers (S.P. and K.M.); disagreements between reviewers were resolved by consensus. The search identified 966 records. The literature search strategy is outlined in a study flow diagram **(Figure 1, table 1)**. Fifteen articles reporting a total of **398** patients with late AAA rupture after EVAR fulfilled the inclusion criteria (**Table 2**). The selected studies were published between 2000 and 2023, reflecting study periods extending from 1992 to 20225,14,32-43.

**3.2 Eligibility, Exclusion and Inclusion Criteria**

Cohort studies reporting late rupture after EVAR and case series including at least 6 patients were included in the study as this disease is relatively rare and this cutoff point was considered numerically significant but also relatively clinically relevant. Articles in languages other than English, case reports and small case series with less than 6 patients were excluded. Sporadic post-EVAR LARs included in observational studies primarily reporting clinical effectiveness of EVAR, elective open conversions or treatment of ruptured AAAs were considered ineligible due to inadequate relevant information.Patients with post-EVAR rupture of any age and sex and any type of stent-graft were included. Patients with symptomatic aneurysms without rupture were excluded. Patients with complex EVAR like chimney (chEVAR), fenestrated (fEVAR) or branched (bEVAR) were not included, as our study was focused in the standard infrarenal cases.

**3.3 Collection of data**

Year of publication of each study, study period**,** demographic data, and clinical characteristics such as haemodynamic stability at presentation, type of stent-graft initially implanted, causes of rupture, time to rupture after initial EVAR, previous secondary interventions and compliance with post-EVAR surveillance were retrieved and analyzed. In addition, the type of treatment, mortality and morbidity rate according to the type of reconstruction and overall mortality were assessed.

**3.4 Analysis of Data and statistical Analysis**

Standard descriptive statistics (reported as means ± std.dev) were used to summarize the demographic data of the recruited patients from all eligible studies. Proportions were used for estimation and expression of clinical variables. The primary endpoints of the meta-analysis consisted of in-hospital mortality and the comparison of mortalities between open repair and endovascular. The meta-analysis was conducted, in accordance with the recommendations of the Meta-analysis of Observational Studies in Epidemiology (MOOSE) group, of the two cohorts. The pooled proportion was calculated as the back-transformation of the weighted mean of the transformed proportions by using the random effects model proposed by DerSimonian-Laird. Heterogeneity among studies was estimated by using the chi-square test and the Cochran Q score (reported as I**2** and representing the percent value of the heterogeneity). Funnel plots were constructed, and the identified extreme studies were excluded to increase the robustness of our analyses. Frequency study-specific estimates were pooled and are reported as proportions with 95% confidence intervals (CI). The meta-analysis and the calculation assessment were carried out using the Comprehensive Meta-analysis Version 4 (Biostat, Englewood, NJ) statistical software.

1. **RESULTS**

**4.1 Clinical characteristics and treatment details**

The study characteristics at the time of presentation of AAA rupture are outlined in **Table 2**. The vast majority was men (**86.4**%), the mean age of all patients was **76.9** ± 2.43. The number of cases in the included studies ranged from **6 to 86** patients. All reports contained a total of **398** ruptures. Twelve case series studies reported a total number of **27364** EVARs performed over the study period giving an incidence of **1.11%** (95%, CI 0.77 to 1.05). The total number of ruptured AAAs over the study period, including de novo ruptures, was reported in only **5** studies. The proportion of late ruptures after EVAR to the total number of ruptured AAA was **12.4%** (78/628 pts). The mean time to rupture ranged from **16 to 72.3** months (mean **43.22** ±16.25) and the mean maximum aneurysm diameter at admission ranged from **6.4 to 9.5** cm (mean: **7.54** ± 1.13cm). The types of aortic stent-grafts used in the initial procedure are presented in **Table 3**.

The reported reasons for rupture, as identified intraoperatively or on preoperative computed tomography, are outlined in **Figure 2**. Type **Ia** EL was the cause for rupture in **93** pts **(32.7%)**, while type **Ib** EL was the cause in **64** pts **(22.6%)**. Type **III** EL was the cause of rupture after EVAR in **42** pts **(14.8%)**, whereas type **II** EL was specified as the cause of rupture in **20** patients **(7%****)**. Combined ELs were documented in **39** pts **(13.8%)**. Migration was encountered in **31** pts **(9%)**. The reason for aneurysm rupture was documented as “could not be determined” on **17** instances **(6%)**.

In **7** series reporting previous secondary endovascular interventions, nearly half of patients (**56.7%**) presenting with aneurysm rupture, had at least one such intervention following the initial EVAR procedure. Furthermore, in **13** series reporting patient compliance nearly one quarter of patients were reported to have missed at least one EVAR surveillance appointment before rupture occurred (**26.4%**). Haemodynamic instability at admission was not mentioned in all series. Τhe **34.8%** (69/198) of the patients with ruptured AAAs (in the series reporting instability) were hemodynamically unstable at presentation **(Table 4)**.

Of the 398 patients, **342** (85.9%, 95% CI 78 to 89) underwent interventional treatment: **190** (**55.5%**) open conversion, **149** (**43.6%**) endovascular repair and **3** **(0.9%)** hybrid treatment (aorto-uni-iliac graft with femoro-femoral bypass). The remaining **56** patients were managed with palliative care or died before reaching the operating table. One of the last patients remained alive during the first 30-days **(Table 5)**. Interventions for post-EVAR rupture were the following: A) Endovascular treatment including (1) chimney or fenestrated repair to extend the proximal sealing zone, (2) relining with a new stent-graft, (3) implantation of aortouni-iliac grafts plus femoro-femoral bypass, (4) implantation of Palmaz stents, aortic cuffs or iliac extensions and (5) side branch or landing zone embolization. B) Open surgical conversion involving (1) total stent-graft explantation and interposition of a standard tube or bifurcated graft along with sac plication, (2) partial proximal or distal stent-graft explantation and bridging with a standard graft along with sac plication, (3) oversewing of lumbar or IMA or a fabric tear from within the sac along with sac plication (4) aneurysmal neck banding or ligation of lumbar or Inferior Mesenteric Artery (IMA) or IIA without aneurysmal sac opening5,14,32-43.

**4.2 Mortality Rates and Outcome**

Treatment modalities and outcomes in the individual studies are presented in **Table 5***.* Meta-analysis of the case series studies revealed that the pooled estimate for in-hospital mortality was **35.6%** **(**95% CI 0.274 to 0.446, **Figure 3, 4a**). Moderate heterogeneity was identified among the studies (The Q-value was 34.4 p=0,002, I**2**=59%). Open surgical management was associated with a significantly higher perioperative mortality compared to endovascular intervention (pooled odds ratio 0.415, 95% CI 0.207 to 0.831, Z-value is -2.483 with p = 0.013), **(Figure 4b)**. No significant heterogeneity was identified among the studies (The Q-value was 7.21, I**2**=0%).

1. **TABLES AND FIGURES**

**Table 1:** Search Strategy

|  |  |  |
| --- | --- | --- |
|  | Search Strategy | Results |
| 1 | "late"[All Fields] OR ("postoperative"[All Fields] AND "period"[All Fields]) OR "postoperative period"[All Fields] OR ("post"[All Fields] AND "operative"[All Fields]) OR "post operative"[All Fields] OR "postoperative period"[MeSH Terms] | 746, 837 |
| 2 | ("aortic"[All Fields] AND "rupture\*"[All Fields]) OR "aortic rupture\*"[All Fields] OR ("aortic"[All Fields] AND "aneurysm\*"[All Fields] AND "rupture\*"[All Fields]) OR "aortic aneurysm rupture\*"[All Fields] OR "aortic rupture"[MeSH Terms] | 23,321 |
| 3 | ("endovascular"[All Fields] AND "aneurysm\*"[All Fields] AND "repair"[All Fields]) OR "endovascular aneurysm repair"[All Fields] OR "EVAR"[All Fields] OR "endovascular aneurysm repair"[MeSH Terms] | 17,555 |
| 4 | "fenestrated"[Title/Abstract] OR "chimney"[Title/Abstract] OR "branched"[Title/Abstract] OR "fEVAR"[Title/Abstract] OR "bEVAR"[Title/Abstract] OR "chEVAR"[Title/Abstract] OR "kilt"[Title/Abstract] OR "advanced"[Title/Abstract] OR "advanced techniques"[Title/Abstract] |  |
| 5 | #1 AND #2 AND #3 | 1,117 |
| 6 | NOT #4 |  |
| 7 | #5 AND #6 | 966 |

**Table2:** Included studies according to study period, demographics, number of patients, and incidence of rupture after EVAR and time to rupture.

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Senior Author** | **Publication Year** | **Study Period** | **Mean Age (y) / Men (%)** | **Number of REVARs** | **Rate of Rupture after EVAR (%)** | **Maximum AAA diameter (cm)** | **Time From EVAR to Rupture (Months)** |
| **Zarins** | 2000 | 1996-99 | 74/86 | 7 | 0.67 | ND | 16 |
| **Bernhard** | 2002 | 1993-2000 | 76/71 | 7 | 0.18 | ND | 38 |
| **Fransen** | 2003 | 1996-2002 | ND/ 91 | 34 | 0.79 | 6.6 | 18 |
| **May** | 2004 | 1992-2003 | 74 /100 | 18 | 2.96 | 6.9 | 29 |
| **Coppi** | 2009 | 1999-2007 | 83/ 86 | 14 | 1.7 | 8.2 | 50 |
| **Wyss** | 2010 | 1999-2004 | 77/ 86 | 22 | 2.59 | 6.7 | 36 |
| **Cho** | 2010 | 2001-2008 | 78 /83 | 18 | ND | 6.8 | 48 |
| **Mehta** | 2011 | 2002-2009 | ND/ 81 | 27 | 1.53 | 6.4 | 29 |
| **Candell** | 2014 | 2000-2010 | 79/ 73 | 15 | 0.86 | 6.4 | 37 |
| **Greiner** | 2014 | 2011-2013 | 75 /100 | 6 | ND | 8.3 | 48 |
| **Antonopoulos** | 2014 | 2006-2012 | ND/ 95 | 22 | 0.81 | ND | 49 |
| **Rajendran** | 2016 | 1992-2014 | 76/95 | 22 | 3.1 | 9.2 | 59 |
| **Andersson** | 2021 | 2001-2015 | 75/78 | 86 | 1.3 | ND | 47 |
| **Sen** | 2023 | 2000-2020 | 78/85 | 30 | 1.23 | 8.0 | 72 |
| **Moulakakis** | 2023 | 2008-2022 | 77.9/98.6 | 70 | ND | 9.5 | 72.3 |

**Table 3:** Types of stent-grafts used in the studies included in our metanalysis.

|  |  |
| --- | --- |
| **Type of graft Used** | **Number of pts** |
| AneuRx -Talent - Endurant - Unspecified **(Medtronic)** | 44/37/16/7 |
| Zenith - Renu **(Cook Medical)**  | 44/1 |
| Excluder **(Gore)** | 34 |
| Vanguard **(Boston Scientific Vascular)** | 24 |
| Stentor **(MinTec)** | 18 |
| Ancure - EVT **(Guidant)** | 13/9 |
| Powerlink - AFX **(Endologix)**  | 10/3 |
| White-Yu graft attachment device **-** Lifepath **(Edwards Lifesciences)** | 6/1 |
| Anaconda **(Terumo)** | 5 |
| Ovation - Nelix **(Endologix)** | 2/1 |
| Corvita **(Corvita Corporation)** | 2 |
| Multilayer **(Cardiatis)** | 2 |
| Endofit **(Le Maitre Vascular)** | 2 |
| Treovance **(Bolton Medical)** | 1 |
| Not reported | 36 |

**Table 4:** Characteristics and previous interventions and compliance to follow up of patients included in our study.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Author** | **Number of EVARs** | **Total AAA ruptures in the study period** | **Haemo-dynamic Instability at presentation****N / (%)** | **PreviousSecondaryInterventions****N / (%)** | **Lost to FU or Incomplete FU****N / (%)** |
| **Zarins** | 1046 | ND | 3 (42.8) | ND | 0 |
| **Bernhard** | 3946 | ND | ND | 1 (14.3) | 0 |
| **Fransen** | 4291 | ND | ND | ND | 21 (61.8) |
| **May** | 609 | 109 | 4 (22.2) | 3 (16.7) | 3 (16.7) |
| **Coppi** | 820 | 169 | 5 (35.7) | ND | 5 (35.7) |
| **Wyss** | 848 | ND | ND | 11 (50) | 3 (13.7) |
| **Cho** | ND | 251 | 10 (55.5) | 4 (22.2) | 3 (16.7) |
| **Mehta** | 1768 | ND | 5 (18.5) | ND | 20 (74.1) |
| **Candell** | 1736 | ND | ND | 3 (20) | 2 (13.3) |
| **Greiner** | ND | 30 | ND | ND | ND |
| **Antonopoulos** | 2730 | ND | 10 (45.5) | ND | 15 (68.2) |
| **Rajendran** | 679 | 69 | 9 (22.5) | 3 (7.5) | 10 (25) |
| **Andersson** | 6470 | ND | ND | ND | 0 |
| **Sen** | 2421 | ND | ND | 17 (56.7) | 3 (10) |
| **Moulakakis** | ND | ND | 23 (32.9) | ND | ND |

**Table 5:** Mortality and Morbidity rate in our analysis.

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Senior Author** | **Number of REVARs** | **EVAR (N)** | **OR (N)** | **Number of pts treated with no intervention (N)** | **Overall,** **In-hospital Mortality** **N / (%)** | **Mortality after Endo Repair****N / (%)** | **Mortality after OR****N / (%)** | **In-hospital Morbidity****N / (%)** |
| **Zarins** | 7 | 0 | 7 | 0 | 4 (57.1) | - | 3 (42.9) | ND |
| **Bernhard** | 7 | 0 | 6 | 1 | 4 (57.1) | - | 3 (50) | ND |
| **Fransen** | 34 | 7 | 19 | 8 | 12 (35.3) | 2 (28.6) | 10 (52.7) | 11 (32.4) |
| **May** | 18 | 4 | 14 | 0 | 3 (16.7) | 0 (0) | 3 (21.4) | ND |
| **Coppi** | 14 | 9 | 5 | 0 | 4 (28.6) | 2 (22.2) | 2 (40) | 7 (50) |
| **Wyss** | 22 | 5 | 3 | 14 | 15 (68.2) | 1 (20) | 0 (0) | ND |
| **Cho** | 18 | 11 | 7 | 0 | 7 (38.9) | 5 (45.5) | 2 (28.6) | 12 (66.7) |
| **Mehta** | 27 | 11 | 15 | 1 | 4 (14.9) | 1(9.1) | 2 (13.3) | ND |
| **Candell** | 15 | 5 | 4 | 6 | 9 (60) | 1 (20) | 3 (75) | 8 (53.3) |
| **Greiner** | 6 | 3 | 3 | 0 | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| **Antonopoulos** | 22 | 11 | 11 | 0 | 8 (36.4) | 1 (9.1) | 7 (63.6) | ND |
| **Rajendran** | 22 | 12 | 10 | 0 | 5 (22.7) | 2 (16.7) | 3 (30) | ND |
| **Andersson** | 86 | 41 | 16 | 26 | 36 (41.9) | ND | ND | ND |
| **Sen** | 30 | 17 | 13 | 0 | 3 (10) | ND | ND | 17 (56.7) |
| **Moulakakis** | 70 | 13 | 57 | 0 | 29 (41.4) | 3 (23) | 26 (45.6) | ND |

**Figure 1:** Flow-chart of search strategy and studies identification.

**Identification of studies via databases and registers**

**Identification**

Records identified from:

MEDLINE

 **(n =966)**

Records excluded as irrelevant **(n = 897)**

**Screening**

Records screened

**(n =966)**

Reports sought for retrieval

**(n = 83)**

Reports not retrieved **(n = 0)**

**Reports excluded:**

* Suprarenal AAAs **(n= 2)**
* Case reports / small case series **(n = 26)**
* Conversion / reintervention **(n = 25)**
* General follow-up / Early outcomes **(n = 15)**

Reports assessed for eligibility

**(n = 83)**

Studies included in review.

**(n = 15)**

**Included**

**Figure 2:** Causes of rupture

**Figure 3:** In hospital Mortality according to the type of Reconstruction. Blue: Overall Mortality, Red: Mortality after Endovascular Repair, Green: Mortality after Open repair



**Figure 4a:** Forest-plot for in-hospital mortality



**Figure 4b:** Forest-plot open versus endovascular repair.



1. **DISCUSSION**

 **6.1 Incidence of LAR**

In our days, there has been stated that 1 out of 10 AAA ruptures arriving in an emergency department have a history of an antecedent AAA repair25,52. This was also found in our study as the proportion of late ruptures after EVAR to the total number of ruptured AAAs was 12.4% (Tables 2, 4). Post-EVAR LARs are far more common than late ruptures after a prior open repair4,43. The incidence of post-EVAR LARs generally varies between 0.5% and 7% in many series44. There is a disparity in incidence mostly because a proportion of patients will die before reaching a hospital or will be presented to a different institution8,44. Conversely, the risk of LAR after OR is much lower varying between 0.3% to 0.8% of patients within 3.0 to 5.5 years5.

Generally, the risk of late aneurysm related death is < 3% in historic and modern studies, however, it is difficult to assess due to the uncertainty in cause of death registration and lack of adequate long-term cohorts7. EUROSTAR registry (European Collaborators on Stent/graft Techniques for aortic Aneurysm Repair) found a cumulative annual risk of rupture after EVAR of 2% at 6 years59. Our meta-analysis assessed a risk for LAR after EVAR of 1.11%. It varied between 0.18-3.1% in 12 case series, which reported the total number of EVARs performed over the study period. This rate agrees with other studies and with the results from two large databases. In Vascular Quality Initiative database, a 3% of 12.911 EVAR patients developed LAR at 5 years24. Moreover, in Medicare database a 5.4% of EVAR patients developed LAR at 8 years4.

 **6.2 Timing of post-EVAR LAR**

Our results indicate that post-EVAR LAR occurred between 16-72.3 months (mean 43.22), (Table 2). This agrees with other studies which state that the risk for LAR does not seem to decline over time, but it can occur at any time after the primary EVAR, with a peak at 3-5 years 6,44,52,54. In contrast, LAR after OR needs more than a decade to happen and is usually caused by ruptured para-anastomotic aneurysms43. Ranjedran et al found an increase to time interval between EVAR and rupture (from 2.4 to 4.9 years) during the later years of the study which extended from 1992 to 201442. He attributed this to improvements in graft design, surgeon’s experience, follow-up rates, and increased life expectancy after the procedure42. On the contrary, Moulakakis et al found a shortening of the time interval and attributed this partially to the fact that EVAR cases performed outside the manufacturer’s IFU or in patients with suboptimal anatomy, which have increased over time8. With the evolution of new-generation devices, larger studies are required to assess for potential reduction in post-EVAR ruptures42.

 **6.3 Risk factors**

 Known risk factors for post-EVAR LAR are increased age, a large initial aneurysm size (> 6cm), persisted sac expansion, a history of previous complications followed by endovascular secondary procedures and rupture as indication in the index operation5,53,60. In a case series the initial size was nearly 6 cm and size at rupture was nearly 8 cm while in another meta-analysis the size at rupture was 7cm42,44. Secondary interventions and incomplete follow-up are frequent prior to LAR, occurring in at least a third of patients, respectively5,44. These agree with our metanalysis which found that nearly one quarter of patients missed at least one EVAR surveillance appointment before rupture occurred (26.4%) and nearly half of them (56.7%) had previous secondary interventions (table 4). We noted that different kinds of stent grafts had been used in rAAAs, some of which have already been abandoned and others have been improved (table 3). In a recent report there was no significant difference in the post-EVAR rupture incidence rate between stent graft types and surprisingly, history of smoking was less frequent among post-EVAR rupture patients (60% vs. 82%; p <0.001)54.

 **6.4 Causes at rupture**

The mean maximum aneurysm diameter at the time of rupture ranged from 6.4 to 9.5 cm (mean: 7.54cm) in our study (Table 2). We found that the most common intraoperative findings at the time of rupture were ELs type I (Ia or Ib in 55.3%) and III (in 14.8%), (Figure 2). Late type I and III ELs pressurize the sac which might had shrinked in the past and became thin; thus, new-onset pressurization may lead to rupture8. Generally, if these ELs left untreated may lead to moderate sac expansion and subsequent rupture. Consequently, once diagnosed, they must be treated promptly with endovascular or open repair 7,44.

We found type II ELs in 7%. Type II ELs have a more benign course and are responsible for less than a tenth of late ruptures16. However, type II ELs may lead to sac expansion and graft distortion with subsequent graft related ELs28,44. We found endotension in 2.1% of post-EVAR LARs. Although endotension is a rare cause of LAR, rupture may affect up to 25% of endotension patients61,62. Graft migration was found in 9% of post-EVAR LAR patients in our study (Figure 2).

 **6.5 Mortality after post-EVAR rupture vs de novo rupture**

We found a pooled estimate for in-hospital mortality of 35.9% in our metanalysis (Table 5, Figure 3). It has been stated that patients with a post-EVAR rupture is more likely to present at the emergency department hemodynamically stable due to the protective effects of an existing intravascular stent-graft as massive exsanguination is hard to occur35,36,42. This would have a positive effect on patient outcome because stable patients show lower morbidity and mortality postoperatively. Unfortunately, this consideration does not agree with our study, where the mortality was substantial (35.9%). Other studies agree with these results30,38,63. Cho et al found similar rates of hemodynamic stability and mortality between post-EVAR LAR patients and de novo ruptures38. Coppi et al found a trend towards increased hemodynamic stability and mortality post-EVAR LAR patients but without statistical significance36. In contrast, in Ranjerdan’s et al reported series the proportion of unstable patients was significantly less after EVAR than after de novo ruptures (P < .01)42. Additionally, the difference in perioperative 30-day mortality rate (20% vs 49%) was also significant (P < 0.01). Rajendran et al claim that de novo ruptures occur at a smaller AAA size (6.9 vs 8.1cm) than post-EVAR ruptures, which indicates decreased sac pressurization owing to the presence of the intravascular devise42. Moreover, ruptures due to ELs may remain contained after thrombosis of the extravascular EL channel in contrast with de novo ruptures where the defect in the sac is unlikely to thrombose42. This belief is not confirmed in our meta-analysis which included a significant larger patient cohort and is consistent with recent literature data43,45. Our results agree with a recent publication, which found a 30-day mortality of 41.4% independently of the presence of an intravascular devise8. Additionally, in another recent publication with 60 ruptures after EVAR, which underwent interventional treatment (endovascular or OR), the overall mortality rate was 42% at 30 days5.A meta-analysis of 152 ruptures showed a pooled estimate for perioperative mortality of 32%, while some other studies have shown even higher mortality rates of up to 67%14,37,41,53. Mortality was 56% in a series with 100 graft explantations due to rupture31. Additionally, In the Vascular Quality Initiative registry mortality was 51.5% with open conversion for rupture compared with a 35.1% mortality for open primary ruptured AAA repair (P < .009)64. This mortality difference was attributed to a greater comorbidity burden in the open conversion patients and to the older age30. We must have in mind that the overall mortality rate across the three landmark randomized trials (IMPROVE, AJAX, ECAR) for ruptured AAAs was 32.6%65,66,67,68. Unfortunately, post-EVAR aneurysm-related mortality is increasing over time as has been reported in a recent meta-analysis of seven randomized trials27. Consequently, the assumption about the protective effects of the intravascular stent-graft needs further investigation.

 **6.6 Hemodynamic instability after post-EVAR rupture vs de novo rupture**

 We found that nearly one third of pts (34.8%) presented at the emergency department with hemodynamic instability (the rate varied between 22%-55.6% in 8 studies reporting unstable patients), (Table 4). In three of these studies, approximately one-third of patients are presented as unstable8,44,69. On the other hand, regarding the primary de novo ruptures, systematic reviews and metanalyses, have shown an occurrence of instability between 28% and 48%56,70. In a recent study hemodynamic status at presentation was the most importantpredictive factor of intraoperative and 30-day death, and hemodynamic instability was predictive of death either the patients treated endovascularly or by open repair8. Previous EVAR and hemodynamic stability are independent predictors for improved mortality rates after rupture42. A stable patient offers the advantage of time to obtain a CT scan, allowing appropriate planning and thereby reducing postoperative complications and mortality42.

 **6.7 Post-EVAR rupture treatment ‘endovascular vs open repair’**

Most LARs, regardless of the initial method of repair EVAR or OR, could be managed with endovascular techniques which are combined with lower morbidity and mortality43. We found lower mortality rates after EVAR than after OR in our study (19.8% vs 39.7%, p=0.013) (Table 5, Figure 3, 4). Other meta-analyses have reported similar results. Antoniou et al reported mortality rate after EVAR 21% vs 37% with OR44. In recent series, Moulakakis et al reported a mortality of 23.1% vs 45.6% and Rajendran et al a mortality of 16.7% vs 30%8,42. Rajendran et al and May et al reported their results from the same center in Australia in consecutive time periods; their combined mortality was 12.5% for EVAR and 25% after OR35,42. The profound causes are that the aortic clamping and the resulting physiological stress are obviated in EVAR instead of the majority of ORs. Additionally, OR is combined with greater blood loss43.

**6.8 Morbidity**

We encountered postoperative complications ranging between 32%-89% of post-EVAR LAR patients in the included studies (Table 5). Fransen et al reported complications in a 32% (11 of 34 pts)34. These were, in brief, sepsis in 2 pts, acute renal failure in 5 pts, and access site hematoma or false aneurysm in 4 pts. Coppi et al noted complications in 50% (7 of 14 pts): multi-organ failure in 3 pts, abdominal compartment syndrome in 1 pt and cardio-respiratory in 3 pts36. Cho et al experienced complications in 66.7% (12 of 18 pts)38. Candell et al reported complications in 89% (8 of 9 pts), cardio-respiratory in 6 pts, renal in 2, infectious in 3, moderate hematoma in 2 and multi-organ dysfunction in 1 patient14. Lastly, Sen et al reported complications in 42% of his patients, renal in 3, cardio-respiratory in 6, bowel ischemia in 2 and return to the operating room in 3 patients43.

**6.9 Survival**

In one recent study Sen et al reported a survival of 76% at 1 year, 52% at 3 years and 41% at 5 years43. One year survival reported to be 47% from Andersson et al, 20% from Candell et al and 27.8% from Cho et al5,14,38. In these older studies, survival seems to be inferior compared with survival after de novo ruptures.

**6.10 Follow-up and Surveillance**

In our study we found that a quarter of patients (26.4%, ranging from 0%-68.2% in the included studies) have not performed at least one recent follow-up appointment (Table 4). It is generally accepted that a significant proportion of post-EVAR LAR patients are noncompliant with surveillance protocols. In a recent publication one in four patients with post-EVAR LAR lacked a recent scheduled surveillance43. Multiple failed reinterventions have been preceded and type I and III endoleaks predominate at the time of LAR. Many of these adverse events would have been treated if had been timely diagnosed on a regular surveillance appointment13,25,43,44,59. Consequently, improvement in surveillance compliance must be a main task of vascular facilities worldwide. It is noteworthy that aneurysm sac expansion or visible EL is not always present before post-EVAR rupture and ELs may not be detectable, even in cases with complete loss of seal. Consequently, their absence cannot exclude the risk of post-EVAR rupture54. Anatomic signs on follow-up CTA considered precursors of the subsequent post-EVAR rupture had been noted in 31% of cases before rupture and in 84% of cases, if reviewed retrospectively, using a structured protocol54.

Patients with a ruptured AAA initially, need more intense follow-up protocol as they present with LAR more often and earlier. Possibly, this is due to decreased IFU adherence caused by limitations in case planning and device availability5. It is recommended to perform a predischarge CTA in case of a rAAA and select a high-risk group for more intense follow-up54.

Τhe radiation exposure should be taken into consideration, mostly for young patients71,72. Additionally, surgeons must inform patients for the value of surveillance adherence and unwilling patients should be advised for alternative open surgery. After OR, a re-examination with a CTA of the entire aorta is recommended after 5 years according to 2019 ESVES guidelines7.

**6.11 EVAR vs OR at the index procedure**

One interesting issue raised by our study is the durability of EVAR. Randomized controlled trials, metanalysis and real-world registry data have shown higher long-term all-cause mortality, higher reintervention rates, and secondary rupture rates after EVAR compared with open surgery4,6,11,53,73.Guidelines by the European Society for Vascular Surgery disclose that an open surgical first strategy should be recommended in younger fit patients with a long-life expectancy of more than 10 to 15 years (Class IIa, Level B)7.The National Institute for Health and Care Excellence (NICE) guidelines recommend not offering EVAR to people with an unruptured infrarenal AAA if open surgical repair is suitable9. This last recommendation has generated controversy and contention. In our opinion, EVAR should be offered with caution in young patients and in cases with aneurysm morphology incompatible with the manufacturer’s IFU.

**6.12 Technical considerations**

The approach for each post-EVAR LAR patient should be individualized, with the decision to choose between OC and EVAR depending on the patient’s fitness, haemodynamic stability and aortic anatomy44. Many of these complications can be treated by endovascular means urgently in a ruptured aneurysm or electively in an intact expanding aneurysm. Type I EL should be treated promptly to exclude the aneurysm from pressurized circulation. Endovascular options include graft balloon dilation, insertion of a bare metal stent or apposition of the stent graft fabric with endovascular staples (endoanchors) against the aortic wall, if the graft is adequately sized, has not migrated, and there is an appropriate landing zone to achieve a seal7. More commonly, extension of the landing zone is required with proximal tubular or fenestrated cuff insertion, or a branched repair to ensure a durable proximal seal, especially in those with aortic neck degeneration52. These innovations have reduced the need for open conversion for type Ia endoleak30. Distal seal can be achieved with iliac extenders7. Type II EL is treated with embolization and type III with relining7. EVAR is not an option when concern for infection is present43. Finally, if an endovascular solution is not available in reasonable time and the patient is fit, OC can be performed with acceptable results7.

The technical approach to LAR with OC and an existing stent-graft device inside depends on the device design and the cause of rupture. We prefer a transabdominal approach. The initial endograft and any subsequent device placed later to treat endoleaks or migration may pose additional technical complexity. Proximal cuffs and fixation anchors may necessitate a more proximal clamping or a longer clamp time to complete the proximal anastomosis30. Usually, infrarenal clamping is possible only in cases of type Ia EL secondary to graft migration, such that a clamp zone was available between the renal arteries and the aneurysm30. Alternatively, aortic clamping along with the intraluminal graft can be performed. Regardless to the level of the clamping, suprarenal stents, hooks, or barbs can be left in place to avoid injury to the friable aortic wall and the renal arteries30. Sometimes, type Ia EL may be treated by external banding of the aneurysm neck. This requires infrarenal circumferential dissection and placement of a synthetic tight cuff around the neck of the aneurysm to restore the proximal seal. Sutures are placed through the external cuff, aortic wall, and endograft to reinforce the repair30. Treatment of a type II EL is feasible by sacotomy and surgical ligation of the lumbar or inferior mesenteric artery30. Although, endograft preservation may be preferred to high-risk patients, mortality remains significant45. Others believe that graft preservation is a lower risk procedure, alternative to graft explantation, with improved postoperative outcomes and good midterm durability, and should be considered in the management algorithm30.

In addition, vascular surgeons must be familiar with the mechanisms of device failure and adequately trained to have advanced technical expertise and skills to perform a conversion to open repair, when necessary, especially in the emergent setting29,56,74. This may require dedicated open repair aortic workshops and training programs organized by medical societies or tertiary institutions8.

**6.13 Limitations**

The study has limitations that should be considered when interpreting its results. Although multi-centered, the study reflects an elaboration of the retrospective and prospective data collected. As such, there may be differences in the quality of data collected. We do not have data on whether patients with denovo AAAs succumb more than patients with rupture after EVAR before reaching a hospital. A selection bias in choosing the operative approach, based on the suitable anatomy of the aneurysm or the hemodynamic status, might also exist. In general, for unstable patients, vascular surgeons often prefer open repair without delay for a CT scan. In recent years, occlusion balloons have been implemented in clinical practice. Compliance with follow-up protocol and secondary procedures was available in a limited number of patients before rupture. As was mentioned, most patients did not present their AAA rupture in the same institution where they were initially treated with EVAR. Overall, as the study contains real-world data, it can provide valuable information representing this surgical entity's current status and treatment.

1. **CONCLUSION**

Our analysis provided evidence that the most common causes of rupture after EVAR were type Ia and Ib ELs. Post-rupture mortality after EVAR was high (35.6%) and comparable to the morbidity of de novo ruptures. Endovascular repair appears to have better results compared to conversion to open repair. A significant number of patients had prior endovascular reoperations and inadequate follow-up. Patient compliance with the surveillance protocol is mandatory.

1. **ABSTRACT**

 **8.1 English version**

**Introduction:** Late aneurysm rupture (LAR) after Endovascular Abdominal Aortic Aneurysm Repair (EVAR) is a known complication increasing worldwide. It has been characterized as the Achilles’s heel of EVAR, as it carries a considerable mortalityandcompromises the fundamental role of endovascular treatment, which is prevention of aneurysm rupture.

**Background:**  No specific guidelines exist regarding the ideal management of this life-threatening complication as many factors contribute to the decision making. Causes of EVAR failure, patient’s comorbidity, haemodynamic status, aortic anatomy and surgeon’s skills along with hospital’s facilities and resources are crucial factors for the treatment algorithm.

**Purpose:** The aim of this study is to present updated information in post-EVAR LAR as the data in the literature are limited. It comprises a current literature review metanalysis based on the recent evidence regarding the incidence, causes, treatment outcomes and prognosis of post-EVAR.

**Methods:** A review metanalysis was conducted according to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines. Studies were identified by searching electronic databases and scanning bibliographic references from 1991 to April 1st, 2023. Several factors were investigated but the primary endpoints of the meta-analysis consisted of in-hospital mortality and the comparison of mortalities between open repair and EVAR.

**Results:** We identified 15 articles encompassing 398 patients with post-EVAR LAR (86.4% men, mean age 76.9 ± 2.43). The incidence was 1.11% (95%, CI 0.77 to 1.05). Post-EVAR LAR represented the 12.4% of total aneurysm ruptures during the study period. The mean time to rupture ranged from 16 to 72.3 months (mean 43.22 ±16.25) and the mean maximum aneurysm diameter at admission ranged from 6.4 to 9.5 cm (mean: 7.54 ± 1.13 cm). Nearly half of patients (**56.7%**) had at least one previous secondary endovascular intervention. Nearly one quarter of patients (**26.4%**) had missed at least one surveillance appointment before rupture. Nearly one third (**34.8%)** of patients were hemodynamically unstable at presentation.

Of the 398 patients, **190** (**55.5%**) underwent open conversion, **149** (**43.6%**) endovascular repair and **3** **(0.9%)** hybrid treatment. The remaining **56** patients were managed with palliative care.

 Type Ia and Ib endoleaks (ELs) were the leading causes for rupture (55.3% in total). Type III ELs were apparent in 14.8%, whereas type II ELs in 7% of cases. Combined ELs were documented in a 13.8% and migration was encountered in 9%. In 6% the cause could not be clarified.

The pooled estimate for in-hospital mortality was 35.6% (95% CI 0.274 to 0.446). Open surgical management was associated with a significantly higher perioperative mortality compared to endovascular intervention (pooled odds ratio 0.415, 95% CI 0.207 to 0.831, Z-value is -2.483 with p = 0.013). No significant heterogeneity was identified among the studies (The Q-value was 7.21, I**2**=0%).

**Conclusion:** Our analysis provided evidence that the most common causes of rupture after EVAR were type Ia and Ib ELs. Post-rupture mortality after EVAR was high (35.6%) and comparable to the morbidity of de novo ruptures. Endovascular repair appears to have better results compared to conversion to open repair. A significant number of patients had prior endovascular reoperations and inadequate follow-up. Patient compliance with the surveillance protocol is mandatory.

**Keywords:** Abdominal aortic aneurysm, Endovascular abdominal aortic aneurysm repair, EVAR, open repair, open conversion, rupture, late rupture, post-EVAR rupture, post-EVAR complications, EVAR complications, endoleak, migration.

**8.2 Greek version**

**Εισαγωγή:** Η απώτερη ρήξη του ανευρύσματος της κοιλιακής αορτής μετά από Ενδαγγειακή Αποκατάσταση είναι μια γνωστή επιπλοκή με αυξανόμενη επίπτωση παγκοσμίως. Έχει χαρακτηριστεί ως η αχίλλειος πτέρνα της Ενδαγγειακής Αποκατάστασης, καθώς φέρει σημαντική θνησιμότητα και υποβαθμίζει τον βασικό ρόλο της ενδαγγειακής θεραπείας, που είναι η πρόληψη της ρήξης του ανευρύσματος.

**Υπόβαθρο:** Δεν υπάρχουν συγκεκριμένες κατευθυντήριες οδηγίες σχετικά με την ιδανική αντιμετώπιση αυτής της επικίνδυνης για τη ζωή του ασθενούς επιπλοκής, καθώς οι παράγοντες που συμβάλλουν στη θεραπευτική επιλογή είναι πολλαπλοί. Η αιτία της αποτυχίας της Ενδαγγειακής Αποκατάστασης, η συ-νοσηρότητα του ασθενούς, η αιμοδυναμική κατάσταση, η ανατομία της αορτής και οι δεξιότητες του χειρουργού μαζί με τον ιατρικό εξοπλισμό και τα διαθέσιμα υλικά του νοσοκομείου είναι κρίσιμοι παράγοντες για τον αλγόριθμο θεραπείας.

**Σκοπός:** Σκοπός αυτής της μελέτης είναι η παρουσίαση τρέχουσας γνώσης όσον αφορά την απώτερη ρήξη του ανευρύσματος της κοιλιακής αορτής μετά από Ενδαγγειακή Αποκατάσταση, καθώς τα δεδομένα στη βιβλιογραφία είναι περιορισμένα. Πρόκειται για μια μεταανάλυση η οποία έγινε μετά από μια τρέχουσα ανασκόπηση της βιβλιογραφίας σχετικά με τη συχνότητα εμφάνισης, τα αίτια, τα θεραπευτικά αποτελέσματα και την πρόγνωση της απώτερης ρήξης του ανευρύσματος της κοιλιακής αορτής μετά από Ενδαγγειακή Αποκατάσταση.

**Μέθοδοι:** Πραγματοποιήθηκε μεταανάλυση ανασκόπησης σύμφωνα με τις οδηγίες του PRISMA (Προτιμώμενα αναφερόμενα στοιχεία για συστηματικές ανασκοπήσεις και μεταναλύσεις). Οι μελέτες ανασύρθηκαν με αναζήτηση σε ηλεκτρονικές βάσεις δεδομένων και έλεγχο βιβλιογραφικών παραπομπών από το 1991 έως την 1η Απριλίου 2023. Διερευνήθηκαν αρκετοί παράγοντες, αλλά τα κύρια καταληκτικά σημεία της μετα-ανάλυσης ήταν η ενδονοσοκομειακή θνησιμότητα και η σύγκριση των θνησιμότητας μεταξύ Ανοικτής και Ενδαγγειακής αποκατάστασης.

**Αποτελέσματα:** Εντοπίσαμε 15 άρθρα που περιλάμβαναν 398 ασθενείς με απώτερη ρήξη του ανευρύσματος της κοιλιακής αορτής μετά από Ενδαγγειακή Αποκατάσταση (86,4% άνδρες, μέση ηλικία 76,9 ± 2,43). Η επίπτωση ήταν 1,11% (95%, CI 0,77 έως 1,05). Η απώτερη ρήξη μετά από Ενδαγγειακή Αποκατάσταση αντιπροσώπευε το 12,4% των συνολικών ρήξεων ανευρύσματος κατά την περίοδο της μελέτης. Ο μέσος χρόνος μέχρι τη ρήξη κυμαινόταν από 16 έως 72,3 μήνες (μέση τιμή 43,22 ±16,25) και η μέση μέγιστη διάμετρος ανευρύσματος κατά την εισαγωγή κυμαινόταν από 6,4 έως 9,5 cm (μέση τιμή: 7,54 ± 1,13 cm). Σχεδόν οι μισοί ασθενείς (56,7%) είχαν τουλάχιστον μία προηγούμενη δευτερογενή ενδαγγειακή παρέμβαση. Σχεδόν το ένα τέταρτο των ασθενών (26,4%) είχαν χάσει τουλάχιστον ένα ραντεβού παρακολούθησης πριν από τη ρήξη. Σχεδόν το ένα τρίτο (34,8%) των ασθενών ήταν αιμοδυναμικά ασταθείς κατά την εισαγωγή.

Από τους 398 ασθενείς, 190 (55,5%) υποβλήθηκαν σε ανοιχτή μετατροπή, 149 (43,6%) σε ενδαγγειακή αποκατάσταση και 3 (0,9%) σε υβριδική θεραπεία. Οι υπόλοιποι 56 ασθενείς αντιμετωπίστηκαν με παρηγορητική φροντίδα.

 Οι ενδοδιαφυγές τύπου Ια και Ιβ ήταν οι κύριες αιτίες ρήξης (55,3% συνολικά). Οι ενδοδιαφυγές τύπου ΙΙΙ βρέθηκαν σε 14,8%, ενώ οι ενδοδιαφυγές τύπου II στο 7% των περιπτώσεων. Συνδυασμός ενδοδιαφυγών διαπιστώθηκε σε ποσοστό 13,8% και η μετανάστευση του μοσχεύματος παρατηρήθηκε στο 9%. Στο 6% η αιτία δεν μπορούσε να διευκρινιστεί.

Η συνολική ενδονοσοκομειακή θνησιμότητα ήταν 35,6% (95% CI 0,274 έως 0,446). Η ανοικτή χειρουργική αντιμετώπιση συσχετίστηκε με σημαντικά υψηλότερη περιεγχειρητική θνησιμότητα σε σύγκριση με την ενδαγγειακή παρέμβαση (pooled odds ratio 0,415, 95% CI 0,207 έως 0,831, η τιμή Z είναι -2,483 με p = 0,013). Δεν εντοπίστηκε σημαντική ετερογένεια μεταξύ των μελετών (Η τιμή Q ήταν 7,21, I2=0%).

**Συμπέρασμα:** Η μελέτη μας έδειξε ότι η συχνότερη αιτία απώτερης ρήξης του ανευρύσματος της κοιλιακής αορτής μετά ενδαγγειακή αποκατάσταση είναι οι ενδοδιαφυγές τύπου Ι και ΙΙ. H μετεγχειρητική θνητότητα της απώτερης ρήξης είναι υψηλή (35.6%) και συγκρίσιμη με την αντίστοιχη της de novo ρήξης. Η ενδαγγειακή αποκατάσταση φαίνεται να έχει καλυτέρα αποτελέσματα σε σχέση με την μετατροπή σε ανοικτή επέμβαση. Ένα σημαντικό ποσοστό των ασθενών είχαν προηγηθείσες επανεπεμβάσεις και ανεπαρκή παρακολούθηση (follow-up). Η συμμόρφωση του ασθενούς με το πρωτόκολλο του τακτικού επανελέγχου είναι πολύ σημαντική.

**Λέξεις-Κλειδιά:** Ανεύρυσμα κοιλιακής αορτής, ενδαγγειακή αποκατατάσταση ανευρύσματος κοιλιακής αορτής, ενδαγγειακή αποκατατάσταση, ανοικτή αποκατάσταση, ανοικτή μετατροπή, ρήξη, απώτερη ρήξη, ρήξη μετά από ενδαγγειακή αποκατατάσταση, επιπλοκές μετά ενδαγγειακή αποκατατάσταση, ενδαγγειακές επιπλοκές, ενδοδιαφυγή, μετανάστευση.

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