Eur J Vasc Endovasc Surg (2019) 58, 258–281

SYSTEMATIC REVIEW

Systematic Review and Meta-Analysis on the Management of Open Abdominal Aortic Graft Infections

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WHAT THIS PAPER ADDS

A systematic review of the literature was performed adhering to the PRISMA guidelines with strict selection criteria for study design, patient inclusion and exclusion criteria, and outcome reporting. This contributed to comparability of the individual study data. Since 2006 many new studies have been performed and these are included in the systematic review. Strict definitions and outcome criteria were used to improve comparability between the outcome data of the included studies.

Objective: Aortic graft infection (AGI) is a disastrous complication with an incidence of 0.2–6% in operated patients. With little or no high quality evidence, the best treatment option remains unclear. Therefore, the literature on the management of open abdominal AGI was systematically reviewed to determine optimal treatment.

Methods: In accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, a systematic review and meta-analysis was conducted for AGI. MEDLINE, Embase, and the Cochrane Database of Systematic Reviews were searched. Methodological quality was assessed using the Methodological Index for Non-randomised Studies (MINORS) score. Primary outcomes were 30 day mortality and one year survival. Secondary outcomes were survival, infection recurrence, limb salvage, and graft patency.

Results: Of 1574 studies identified, 32 papers were included in the study. The overall quality of the studies was moderate, with an average MINORS score of 11.9. Pooled overall 30 day mortality and one year survival were 13.5% (95% CI 10.5–16.4) and 73.6% (95% CI 68.8–78.4), respectively. The lowest 30 day mortality and highest one year survival were found for *in situ* repair compared with extra-anatomic repair and for prosthetic grafts compared with venous grafts or arterial allografts. The infection recurrence rate was highest for prosthetic grafts.

Conclusions: There is a lack of well designed, qualitative comparative studies making conclusive recommendations impossible. The current best available data suggests that partial graft removal should be avoided and the lowest 30 day mortality and best one year survival are achieved with *in situ* repair using prosthetic grafts. Initiatives such as the MAGIC database to collaboratively collect prospective data are an important step forward in obtaining more solid answers on this topic.

Keywords: Aorta, Graft, Infection, Open, Prosthesis, Treatment
Article history: Received 15 November 2018, Accepted 1 March 2019, Available online 7 June 2019

INTRODUCTION

Aortic graft infection (AGI) is a disastrous complication following open abdominal aortic surgery and is associated with considerable mortality and morbidity. Reported incidences are low and range from 0.2% to 6%.[1,2] The incidence varies and is higher in patients presenting with septic conditions, having distal anastomoses in the groin, requiring emergency and revision procedures, and is dependent on the indication for treatment.[2]

Because of the relative rarity of the condition, randomised trials are lacking and recommendations in guidelines are based mainly on retrospective series resulting in a low level of evidence. As many centres adhere to an endovascular first policy for the treatment of abdominal aortic

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https://doi.org/10.1016/j.ejvs.2019.03.013

aneurysms, the numbers at risk of AGI are further decreasing. Additionally, the lack of a gold standard for the non-invasive diagnosis of AGI and a wide range of reported treatment modalities complicate interpretation of the reported literature.

Historically, the gold standard for the treatment of AGI was complete graft removal with extra-anatomic repair (EAR). However, the high mortality and morbidity rates reported warranted a search for more effective or safer treatment modalities, and several alternatives emerged, including *in situ* repair, partial graft removal, use of cryopreserved allografts, or autologous venous repair. A previously reported systematic review and meta-analysis in 2006 raised the question of whether complete removal and EAR should remain the gold standard and suggested that *in situ* repair could be an appropriate alternative in selected patients.[1] However, more than a decade has passed since this publication and several studies have been published in that time.

Therefore, a systematic review and meta-analysis was performed of the currently available literature to assess and compare the outcomes of reported management options for open abdominal AGI.

METHODS

This report was written in accordance to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines for reporting systematic reviews and meta-analyses.[3] The review protocol was prospectively registered in the PROSPERO database (CRD42018098991).

Literature search

Two authors (ICP, CGV) independently searched the literature to identify studies describing management of AGI. MEDLINE, Embase, and the Cochrane Database of Systematic Reviews were searched for papers published between January 1966 and May 2018, using the following keywords: aortic, graft, prosthesis, bypass, infection. Free text words with Boolean operators besides Medical Subject Headings were used to avoid missing recent publications that had not yet been given Medical Subject Headings. The "related articles" function in PubMed and reference lists of retrieved articles were also used to identify articles not found in the original search. The search was not language restricted. Unpublished data or abstracts were not included. The full search string for MEDLINE, according to PRISMA guidelines, is given in Table S2.

Validity assessment

After duplicates were removed, ICP and CGV independently screened the titles and abstracts of the identified studies for relevance. Full texts were obtained of the remaining relevant studies, and ICP and CGV read the full text papers and a final selection was made of relevant studies. ICP and CGV independently assessed the methodological quality of the retrospective articles using the Methodological Index for Non-randomised Studies(MINORS) score, with a global ideal score of 24 for comparative studies and 16 for non-comparative studies.[4] For this review, a score of $\leq$8 was considered to be poor quality, 9—14 moderate quality, and 15—16 good quality for non-comparative studies. Cutoff points were $\leq$14, 15—22, and 23—24, respectively, for comparative studies. Discrepancies between the authors during the search, selection, and quality assessment were resolved by discussion. In case of disagreement an external peer was consulted.

Inclusion and exclusion criteria

Studies. Articles were eligible if they described one or more management strategies for open abdominal AGI, were published in English, included human subjects, and had a full text available. Published material without a published full text article, such as published abstracts from conferences, were excluded. There were no restrictions on aortic graft material or treatment modality reported. Finally, the same criteria were used to screen all cross references for potentially relevant studies not identified by the initial literature search. Retrospective studies with a MINORS score $\leq$8 were not included in the meta-analysis.

Participation. Studies reporting outcomes of the management of patients with infected prosthetic open abdominal aortic grafts (i.e., aortic tube graft, aorto(bi)iliac- or aorto(bi)femoral grafts) were included. Studies reporting on infected endografts, mycotic aneurysms or thoracic grafts were excluded. Enrolment of patients with an aorto-enteric fistula (AEF) was not a reason for exclusion. If studies included both infected abdominal aortic grafts and mycotic aneurysms or other infected segments (i.e., thoracic grafts, peripheral grafts), these studies were only included if at least the primary outcomes were reported separately for the included infected abdominal aortic grafts. Treatment modalities were grouped as antibiotic treatment, drainage and/or irrigation procedures, *in situ* prosthetic repair, extra-anatomic bypass grafting, in situ repair with venous or arterial autologous grafts or allografts, or combinations of these treatment modalities. If studies reported more than one treatment arm, only treatment arms including $\geq$10 patients were included in the analyses.

Outcome measures. The primary outcome measures were 30 day mortality and one year survival. Secondary outcomes were survival, recurrence of infection, limb salvage, and graft patency. Articles were eligible for inclusion only if they reported at least the primary outcome measures.

Data analysis

Two independent authors (ICP, CGV) performed data extraction. Data extracted included study design, sample size, study period, inclusion criteria, exclusion criteria, age, sex, type of graft, type of bacteria, methods used to diagnose infection, location of infection, antibiotics used, type of treatment modalities used (such as debridement techniques, reconstruction or bypass techniques, materials used for graft replacement, etc.), outcome measures as described above, and follow up duration. Discrepancies were solved by discussion. OpenMeta[Analyst] version 3.1 was used for

the meta-analysis. Rates were pooled using a random effects model. The presence of heterogeneity between the studies was determined using a forest plot and by performing a $\chi 2$ heterogeneity test. The I^2 index was also calculated. Data are reported as pooled proportions and 95% CI, mean (SD) or median (range) as appropriate.

RESULTS

Description of studies

The search identified 1574 studies (Fig. 1). After duplicates were removed and the titles and abstracts were screened for relevance, 128 full text papers were assessed for eligibility. After the inclusion and exclusion criteria were applied, 32 papers were included in this systematic review.[5–36] The characteristics of included studies are summarised in Table 1. Ninety-six articles were excluded after assessment of the full text.[37–132] Most studies (n = 61) were excluded because the primary outcome measures were not reported.[39,40,44–46,48–50,52–56,58,59,61,62,65,66,68,70,72,73,76,79–86,90,91,96–98,100,102–109,111,113–118,120,121,124,127–129,131,132] Sixteen more studies were excluded because they described irrelevant topics other than abdominal AGI.[37,57,60,63,69,74,75,78,87,89,92,112,119,122,123,126] Finally, studies were excluded because of study design (n = 5),[47,51,94,95,125] overlapping data (n = 3),[42,43,99] language (n = 9),[38,41,64,67,71,77,88,101,130] or a MINORS score < 9 (n = 2).[93,110] A flow chart of the selection procedure is shown in Fig. 1. An overview with rationale for excluded studies is available on request.

The included studies described a total of 1316 patients with a mean sample size of 41 patients (range 11–187) and were published between 1984 and 2018. Thirty of the 32 included studies were retrospective cohorts,[5–16,18–27,29–36] and seven of these were comparative studies.[12,23,26–29,31] Two prospective cohort studies were included.[17,28] The majority of the included studies also included patients with AEF and the median proportion of patients with AEF was 26% (range 0–50%). In three studies patients with AEF were excluded,[7,16,21] and in one study it was not reported whether patients with AEF were included or not.[22] The mean follow up duration was 33 months and ranged from 8 to 77 months. Four studies did not report the duration of follow up.[10,14,22,31]

One study included patients with AGI only if a culture proven infection by *Staphylococcus epidermidis* was present.[5] Another study excluded patients with an AGI entirely situated above the inguinal ligament,[7] while a third study

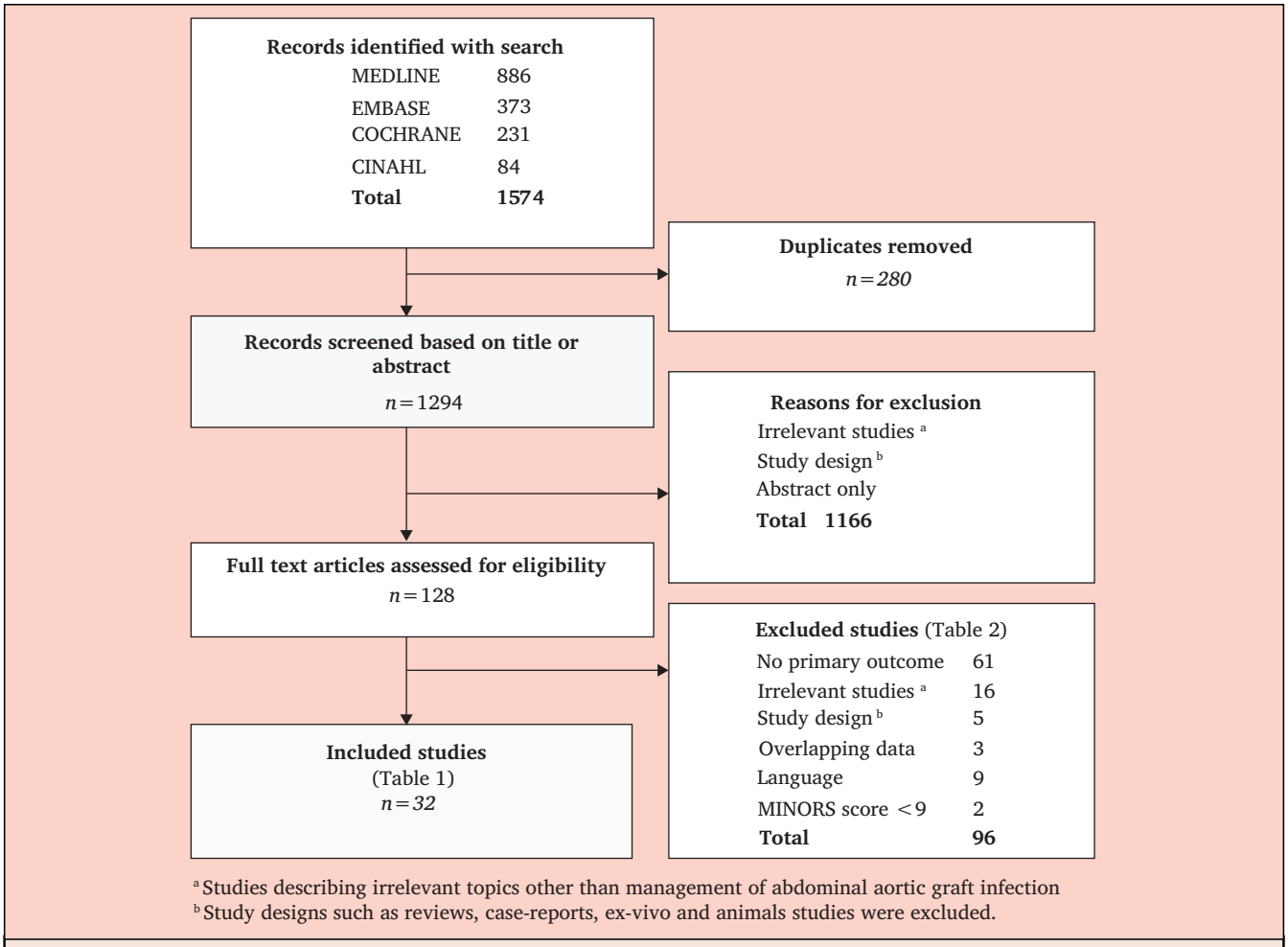

Figure 1. Flowchart of study selection. MINORS = methodological index for non-randomized studies.

Table 1. Characteristics of included studies

First author	Sample size	Study design	Study period	Inclusion criteria	Patients			Intervention	Antibiotic regime	Outcome	Follow up (months)	MINORS score (max)
					Age, mean (range)	Sex, male (%)	Microorganisms					
Bandyk 1984[5]	18	Retrospective cohort	1972–1982	Type of grafts Aortofemoral grafts (dacron) infected by *Staphylococcus epidermidis* AEF 2 (11%) Infection diagnosis - WBC count - Blood cultures - Gram's stain - Culture of perigraft exudate or wound drainage	61 (53–74)	18 (100%)	*Staphylococcus epidermidis*	Complete graft removal ($n = 18$) and: - EAR ($n = 15$) - ISR (Dacron) ($n = 2$) - graft removal only ($n = 1$)	IV cefazolin, cefamandole, or vancomycin	30 day mortality 1/18 (6%) Survival: 1 year: 12/18 (66%) Recurrent infection 2/18 (11%) Limb salvage 10/18 (56%)	18 (6–60)	10 (16)
O'Hara 1986[6]	84	Retrospective cohort	1961–1985	Type of grafts Aortic tube ($n = 4$) Aorto(bi)iliac ($n = 23$) Aorto(bi)femoral ($n = 57$) AEF 33 (39%) Infection diagnosis NR	61 (NR)	71 (85%)	No microorganisms: 16 (19%) Single microorganism: 35 (41%) Multiple microorganisms: 33 (39%)	Complete graft removal and EAR ($n = 54$) Complete graft removal - no repair ($n = 13$) Partial graft removal and EAR ($n = 8$) Miscellaneous procedures without graft removal ($n = 9$)	NR	30 day mortality Overall: 24/84 (28%) AEF: 17/33 (51%) No AEF: 7/51 (14%) Survival 1 year: 35/84 (42%) 5 years: 15/84 (18%) Limb salvage 61/84 (73%)	13 (1–99)	11 (16)
Schellack 1988[7]	13	Retrospective cohort	1980–1985	Type of grafts Aorto(bi)femoral grafts Exclusion: aortic graft infection entirely situated above inguinal ligament AEF None Infection diagnosis NR	62 (40–83)	10 (77%)	No microorganisms: one (8%) Single microorganism: 10 (77%) Multiple microorganisms: two (15%)	Partial graft removal and EAR ($n = 5$) Compete graft removal and EAR ($n = 5$) Complete graft removal and no repair ($n = 2$) Local repair of femoral pseudo-aneurysm and muscle flaps ($n = 1$)	NR	30 day mortality 2/13 (15%) Survival 1 year: 6/11 (2 lost to follow up) Limb salvage 8/13 (62%)	17 (0–60)	10 (16)
Jacobs 1991[8]	21	Retrospective cohort	1972–1989	Type of grafts Aortic tube ($n = 1$) Aortobiiliac ($n = 7$) Aortobifemoral ($n = 13$) AEF 9 (43%) Infection diagnosis NR	61 (36–81)	15 (71%)	No microorganisms: 12 (57%) Single microorganism: 9 (43%) Multiple microorganisms: 0 (0%)	Complete graft removal and ISR ($n = 18$) Complete graft removal and EAR ($n = 3$)	Broad spectrum antibiotics before, during, and after surgery based on cultures	30 day mortality 5/21 (24%) Survival 1 year: 16/21 (76%) Recurrent infection 2/21 (10%) Limb salvage 19/21 (90%)	77 (NR)	10 (16)
Quinones-Baldrich 1991[9]	45	Retrospective cohort	1970–1988	Type of grafts Aortobiiliac ($n = 6$) Aortobifemoral ($n = 32$) Not reported ($n = 7$) AEF 7 (16%) Infection diagnosis NR	63 (30–84)	34 (76%)	No microorganisms: 8 (21%) Single microorganism: 15 (39%) Multiple microorganisms: 15 (39%)	Complete graft removal without reconstruction ($n = 9$) Complete graft removal and EAR ($n = 35$) Complete graft removal and ISR (autogenous vein) ($n = 1$)	All patients received peri-operative antibiotics	30 day mortality 11/45 (24%) Survival 1 year: 26/41 (64%) 3 years: 23/41 (55%) 5 years: 20/41 (49%) Recurrent infection 1 year: 5/30 (17%) 5 year: 6/30 (20%) Limb salvage 1 year: 24/30 (79%) 3 years: 23/30 (75%) 5 years: 20/30 (67%) Primary patency 1 year: 18/30 (59%) 3 years: 13/30 (43%) 5 years: 9/30 (29%)	36 (2–144)	10 (16)

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Table 1-*continued*

First author	Sample size	Study design	Study period	Inclusion criteria	Patients			Intervention	Antibiotic regime	Outcome	Follow up (months)	MINORS score (max)
					Age, mean (range)	Sex, male (%)	Microorganisms					
Sharp 1994[10]	27	Retrospective cohort	1982–1992	Type of grafts Aortic tube ($n = 2$) Aorto(bi)iliac ($n = 5$) Aorto(bi)femoral ($n = 20$) AEF 9 (33%) Infection diagnosis NR	66 (51–77)	24 (89%)	No microorganisms: 7 (26%) Single microorganism: 16 (59%) Multiple microorganisms: four (15%)	Complete graft removal and: - EAR ($n = 20$) - ISR ($n = 4$) Partial graft removal and EAR ($n = 2$) No graft removal and EAR ($n = 1$)	NR	30 day mortality Overall: 1/27 (4%) Graft removal + EAR 1/20 (5%) Survival Overall: 1 year: 24/27 3 years: 23/27 Graft removal + EAR 3 years: 18/20 (90%) Limb salvage 26/27 (96%) Primary patency 1 year: 20/23 (86%) 3 years: 18/23 (80%)	NR	11 (16)
Speziale 1997[11]	18	Retrospective cohort	1989–1995	Type of grafts Aortic tube ($n = 5$) Aortobiiliac ($n = 1$) Aortofemoral ($n = 2$) Aortobifemoral ($n = 10$) AEF 9 (50%) Exclusion criteria Severe sepsis and lower limb emboli Infection diagnosis: Clinical signs, CT scan with peri-prosthetic gas or fluid and leucocyte accumulation on leucocyte scintigraphy scan	65 (31–77)	17 (94%)	No microorganisms: one (6%) Single microorganism: 12 (67%) Multiple microorganisms: five (28%)	Complete graft removal and ISR (PTFE)	Culture positive IV cephalosporins, ciprofloxacin, imipenem Culture negative IV cephalosporins and metronidazole or imipenem for six weeks post-operatively followed by two weeks oral antibiotics	30 day mortality 2/18 (11%) Survival 1 year: 16/18 (89%) 3 years: 16/18 (89%) 5 years: 15/18 (83%) Recurrent infection 0/18 (0%) Limb salvage 18/18 (100%) Primary patency 30 days: 18/18 (100%) 1 year: 16/18 (89%) 3 years: 16/18 (89%) 5 years: 16/18 (89%)	37 (8–59)	11 (16)
Belair 1998[12]	23	Retrospective comparative study	1985–1997	Type of grafts Aortic tube ($n = 2$) Aortobiiliac ($n = 5$) Aortobifemoral ($n = 16$) AEF 6 (26%) Exclusion criteria Isolated groin infection Infection diagnosis: Fluid surrounding graft above inguinal ligament on CT scan AND clinical signs of infection (fever, WBC $> 10\times10^9$/L) or pus discharge	67 (NR)	20 (87%)	No microorganisms: 0 (0%) Single microorganism: six (26%) Multiple microorganisms: 17 (74%)	Group A: Percutaneous drainage and IV antibiotics ($n = 11$) Group B: Surgery ($n = 12$): - complete graft removal (9) and EAR (8) or no revascularisation ($n = 1$) - surgical debridement only ($n = 3$)	All patients received IV antibiotics	30 day mortality Overall: 6/23 (26%) Group A: 0/11 (0%) Group B: 6/12 (50%) 1 year survival Overall: 15/23 (65%) Group A: 10/11 (91%) Group B: 5/12 (42%) Recurrent infection Overall: 8/23 (35%) Group A: 4/11 (36%) Group B: 4/12 (33%) Primary patency Overall: 17/23 (74%) Group A: 10/11 (91%) Group B: 7/12 (58%)	24 (6–84)	17 (24)

Table 1-*continued*

First author	Sample size	Study design	Study period	Inclusion criteria	Patients			Intervention	Antibiotic regime	Outcome	Follow up (months)	MINORS score (max)
					Age, mean (range)	Sex, male (%)	Microorganisms					
Locati 1998[13]	18	Retrospective cohort	1994–1997	Type of grafts Aortic tube ($n = 2$) Aortobifemoral ($n = 16$) AEF 8 (44%) Infection diagnosis CT angiography Leucocyte scan Angiography	65 (49–78)	16 (89%)	No microorganism: 5 (28%) Single organism: 9 (50%) Multiple organisms: 4 (22%)	Complete graft removal and ISR (arterial allograft)	IV antibiotics started before or during operation and continued for six weeks	30 day mortality 3/18 (17%) Survival 1 year: 15/18 (83%) Recurrent infection 4/18 (22%) Primary patency 1 year: 16/18 (89%)	22 (3–36)	10 (16)
Hayes 1999[14]	11	Retrospective cohort	1992–1997	Type of grafts Aortobifemoral ($n = 3$) Aortic graft not further specified ($n = 8$) AEF 4 (36%) Infection diagnosis (CT) Angiography Leucocyte scan	66 (49–78)	8 (73%)	No microorganism: one (9%) Single organism: 8 (73%) Multiple organisms: two (18%)	Complete graft removal and ISR (Dacron + rifampicin)	2 weeks IV cefuroxime and metronidazole from diagnosis of graft infection, revised based on culture results if necessary. After two weeks IV, six weeks oral antibiotics were prescribed	30 day mortality 2/11 (18%) Survival 1 year: 7/11 (64%) Recurrent infection 4/18 (22%)	NR	10 (16)
Seeger 1999[15]	53	Retrospective cohort	1983–1994	Type of grafts Aortic tube ($n = 3$) Aortobiiliac ($n = 11$) Aortobifemoral ($n = 39$) AEF 10 (19%) Infection diagnosis Clinical signs and imaging findings	64 (NR)	46 (87%)	No microorganism: 12 (23%) Single organism: 25 (47%) Multiple organisms: 16 (30%)	Local debridement and irrigation ($n = 3$) Partial graft removal and EAR ($n = 13$) Complete graft removal and ISR ($n = 5$) Complete graft removal and EAR (32)	NR	30 day mortality 12/53 (23%) Survival 1 year: 33/53 (62%) Recurrent infection 4/53 (8%) Limb salvage 30 day: 48/53 (91%) 1 year: 44/53 (83%)	30 (0–132)	11 (16)
Seeger 2000[16]	36	Retrospective cohort	1989–1999	Type of grafts Aortic tube ($n = 2$) Aortobiiliac ($n = 2$) Aortobifemoral ($n = 32$) Exclusion criteria: AEF, thoracic or suprarenal grafts or patients treated with graft removal alone Infection diagnosis Clinical signs and imaging findings	62 (NR)	27 (75%)	NR	Complete graft removal and EAR (staged procedure: EAR first, followed by complete graft removal)	IV antibiotics starting at EAR until two weeks after graft removal, followed by six weeks oral antibiotics based on cultures	30 day mortality 4/36 (11%) Survival 1 year: 32/36 (89%) 3 year: 26/36 (72%) 5 year: 20/36 (56%) Recurrent infection 1/36 (3%) Limb salvage 1 year: 36/36 (100%) 3 year: 33/36 (92%) 5 year: 29/36 (81%)	32 (NR)	11 (16)
Leseche 2001[17]	23	Prospective cohort	1992–2000	Type of grafts Aortic tube ($n = 2$) Aortofemoral ($n = 3$) Aortobifemoral ($n = 18$) Mycotic aneurysm ($n = 5$)[a] AEF 10 (36%) Infection diagnosis Clinical signs and imaging findings	64 (44–82)	27 (96%)	No microorganism: 0 (0%) Single organism: 23 (82%) Multiple organisms: 5 (18%)	Complete graft removal and ISR (arterial allograft; $n = 13$) Partial graft removal and ISR (arterial allograft; $n = 10$)	Broad spectrum IV antibiotics	30 day mortality 3/23 (13%) Survival 1 year: 19/23 (83%) Recurrent infection 0/23 (0%) Limb salvage 1 year: 23/23 (100%) 3 year: 23/23 (100%) 5 year: 23/23 (100%)	35 (6–101)	12 (16)

Continued

Table 1-*continued*

First author	Sample size	Study design	Study period	Inclusion criteria	Patients			Intervention	Antibiotic regime	Outcome	Follow up (months)	MINORS score (max)
					Age, mean (range)	Sex, male (%)	Microorganisms					
Cardozo 2002[18]	12	Retrospective cohort	1995–1999	Type of grafts Aortobiiliac ($n = 2$) Iliofemoral ($n = 2$) Aortobifemoral ($n = 9$) AEF 0 (0%) Infection diagnosis clinical and/or laboratory and/or CT-diagnosis of infection	61 (40–80)	11 (92%)	No microorganism: three (25%) Single organism: 7 (58%) Multiple organisms: 2 (17%)	Complete ($n = 3$) or partial ($n = 9$) graft removal and ISR (superficial femoral vein)	- IV antibiotics started pre-operatively, continued until discharge. For patients with partial graft removal antibiotics were continued for six weeks	30 day mortality: 2/12 (17%) Survival 1 year: 9/12 (75%) Recurrent infection 1/12 (8%) Limb salvage 9/12 (75%)	22 (6–65)	9 (16)
Chiesa 2002[19]	68	Retrospective cohort	1994–2000	Type of grafts Aortic-tube ($n = 12$) Aortobiiliac ($n = 7$) Aortofemoral ($n = 9$) Aortobifemoral ($n = 40$) AEF 22 (32%) Infection diagnosis NR	65 (40–78)	NR	Multiple microorganisms: 24 (35%)	Complete graft removal and ISR (fresh arterial allograft ($n = 11$) OR cryopreserved arterial allograft ($n = 57$))	- Broad spectrum antibiotics, replaced with selective antibiotics based on cultures.	30 day mortality 11/68 (16%) Survival 1 year: 46/68 (68%) 3 years: 39/68 (57%) Limb salvage 65/68 (96%) Primary patency 1 year: 43/68 (63%) 3 years: 28/68 (41%)	41 (1–68)	9 (16)
Ten Raa 2002[20]	38	Retrospective cohort	1991–2000	Type of grafts Aortic-tube ($n = 4$) Aortobiiliac ($n = 12$) Aortobifemoral ($n = 22$) AEF 17 (45%) Infection diagnosis Clinical signs, laboratory results and imaging findings	69 (56–87)	36 (95%)	No microorganism: 10 (40%) (out of 25 grafts cultured)	Complete graft removal and EAR ($n = 18$) Complete graft removal and ISR (Dacron + rifampicin; ($n = 8$) Partial graft removal and - ISR (Dacron; $n = 6$, Vein; $n = 1$) - EAR ($n = 2$) - no repair ($n = 2$) Local irrigation and antibiotics ($n = 1$)	Antibiotics for a mean of three weeks (range: 1 day –14 weeks)	30 day mortality 8/38 (21%) Survival 1 year: 23/38 (61%) 3 years: 22/38 (58%) 5 years: 8/38 (21%) Recurrent infection 6/38 (16%) Limb salvage 1 year: 37/38 (97%) 3 years: 36/38 (95%)	45 (0–60)	11 (16)
Daenens 2003[21]	49	Retrospective cohort	1990-NR	Type of grafts Aortic tube ($n = 3$) Aortobiiliac ($n = 3$) Aortobifemoral ($n = 43$) Exclusion criteria - Graft-enteric complications Infection diagnosis Clinical signs	65 (47–78)	45 (92%)	No microorganisms: 4 (8%) Single organism: 35 (71%) Multiple organisms: 10 (20%)	Complete graft removal and ISR (superficial femoral vein)	Pre-operative IV antibiotics If no pre-operative positive cultures: vancomycin per-operatively after bacterial samples were taken and changed according to culture results Post-operatively antibiotics continued for six weeks	30 day mortality 4/49 (8%) Survival 1 year: 42/49 (86%) 3 years: 40/49 (82%) 5 years: 29/49 (60%) Limb salvage 1 year: 48/49 (98%) 3 year: 48/49 (98%) 5 year: 48/49 (98%) Primary patency 1 year: 47/49 (96%) 3 years: 45/49 (91%) 5 years: 45/49 (91%)	41 (1–101)	10 (16)
Faulk 2005[22]	17	Retrospective cohort	1999–2004	Type of grafts Aortic graft infection requiring neo-aortic vein reconstruction AEF NR Infection diagnosis NR	63 (51–85)	11 (65%)	NR	Complete graft removal and ISR (superficial femoral vein)	NR	30 day mortality 2/17 (12%) Survival 1 year: 10/17 (59%) 3 year: 10/17 (59%) Primary patency 1 year: 10/17 (59%) 3 year: 10/17 (59%)	NR	11 (16)

Table 1-*continued*

First author	Sample size	Study design	Study period	Inclusion criteria	Patients			Intervention	Antibiotic regime	Outcome	Follow up (months)	MINORS score (max)
					Age, mean (range)	Sex, male (%)	Microorganisms					
Hart 2005[23]	30	Retrospective comparative study	1993–2003	Type of grafts Aortic tube ($n = 3$) Aortobiiliac ($n = 9$) Aortobifemoral ($n = 18$) AEF 11 (37%) Infection diagnosis NR	70 (43–87)	27 (90%)	No microorganisms: 6 (20%) Single organism: 17 (57%) Multiple organisms: 7 (23%)	Group A: Complete graft removal and EAR ($n = 15$) Group B: Partial graft removal ($n = 15$) + ISR ($n = 9$) + EAR ($n = 4$) + drainage + coverage ($n = 2$)	NR	30 day mortality Overall: 6/30 (20%) Group A: 5/15 (33%) Group B: 1/15 (7%) Survival 1 year: Overall: 17/30 (57%) Group A: 8/15 (53%) Group B: 9/15 (60%) 2 year: Overall: 16/30 (57%) Group A: 8/15 (53%) Group B: 8/15 (53%) Recurrent infection Overall: 6/30 (20%) Group A: 2/15 (13%) Group B: 4/15 (27%) Limb salvage 1 year Overall: 28/30 (93%) Group A:14/15 (93%) Group B:14/15 (93%)	15 (NR)	16 (24)
Oderich 2006[24]	52	Retrospective study	1981–2001	Type of grafts Aortic tube ($n = 13$) Aortobiiliac ($n = 14$) Aorto(bi)femoral ($n = 25$) AEF 30 (44%) Infection diagnosis NR	69 (40–87)	40 (77%)	No microorganisms: 5 (11%) Single organism: 19 (37%) Multiple organisms: 27 (52%)	Complete ($n = 35$) or partial ($n = 17$) graft removal and ISR (Dacron + rifampicin; $n = 50$ or PTFE; $n = 2$)	Peri-operative IV antibiotics and lifelong oral antibiotics	30 day mortality 3/52 (6%) Survival 1 year: 44/52 (84%) 3 year: 39/52 (75%) 5 year: 33/52 (63%) Recurrent infection 6/52 (12%) Limb salvage 1 year: 52/52 (100%) 3 year: 52/52 (100%) 5 year: 52/52 (100%) Primary patency 1 year: 49/52 (94%) 3 year: 49/52 (94%) 5 year: 46/52 (89%)	41 (2–115)	11 (16)
Ali 2009[25]	187	Retrospective cohort	1990–2006	Type of grafts Aorto(bi)iliac ($n = 21$) Aorto(bi)femoral ($n = 144$) Axillo(bi)femoral ($n = 22$) Exclusion criteria - Unstable patients - No femoropopliteal vein available AEF 26 (14%) Infection diagnosis: - Clinical signs and fluid around graft on imaging studies - During surgery: purulent fluid around a non-incorporated graft	63 (29–88)	119 (64%)	No microorganisms: 31 (17%) Single organism: 81 (45%) Multiple organisms: 67 (37%)	Complete graft removal and ISR (superficial femoral vein)	NR	30 day mortality 19/187 (10%) Survival: 1 year: 144/187 (77%) 3 year: 120/187 (64%) 5 year: 97/187 (52%) Recurrent infection 10/187 (5%) Limb salvage 1 year: 172/187 (92%) 3 year: 168/187 (90%) 5 year: 166/187 (89%) Primary patency 1 year: 172/187 (92%) 3 year: 161/187 (86%) 5 year: 153/187 (82%)	32 (12–168)	11 (16)

Continued

Table 1-*continued*

First author	Sample size	Study design	Study period	Inclusion criteria	Patients			Intervention	Antibiotic regime	Outcome	Follow up (months)	MINORS score (max)
					Age, mean (range)	Sex, male (%)	Microorganisms					
Biro 2011[26]	33	Retrospective comparative study	1994–2008	Type of grafts Aortic tube ($n = 3$) Aortoiliac patch ($n = 2$) Aortofemoral ($n = 2$) Iliacofemoral ($n = 5$) Aortobifemoral ($n = 21$) AEF 7 (21%) Infection diagnosis Clinical signs of infection and CT imaging findings or gastroscopy findings	63 (NR)	25 (76%)	No microorganisms: three (9%) Single microorganism: 15 (45%) Multiple microorganisms: 15 (45%)	Group A: Complete graft removal and ISR (superficial femoral vein; $n = 14$) Group B: Complete graft removal and ISR (cryopreserved arterial allograft; $n = 19$)	NR	30 day mortality Overall: 6/33 (18%) Group A: 2/14 (14%) Group B: 4/19 (21%) Survival Group A: 1 year: 11/14 (79%) 3 year: 11/14 (79%) 5 year 11/14 (79%) Group B: 1 year: 13/19 (68%) 3 year 13/19 (68%) 5 year:13/19 (68%) Recurrent infection Group A: 0/14 (0%) Group B: 3/19 (16%) Primary patency Group A: 1 year: 13/14 (93%) 5 year: 13/14 (93%) Group B: 1 year: 16/19 (87%) 5 year: 16/19 (87%)	34 (2–168)	17 (24)
Bisdas 2011[27]	22	Retrospective comparative study	2004–2009	Type of grafts Infected abdominal aortic grafts with positive intra-operative cultures Aortic graft ($n = 22$) Mycotic aneurysms ($n = 11$)[a] AEF 12 (36%) Infection diagnosis Positive intra-operative cultures	66 (NR)	32 (97%)	No microorganisms: 0 (0%) Single microorganism: 9 (41%) Multiple microorganisms: 13 (59%)	Group A: Complete graft removal and ISR (cryopreserved arterial allograft; $n = 19$) Group B: Complete graft removal and ISR (silver coated Dacron; $n = 3$)	Intra-operative IV cefuroxime, post-operatively switched to organism specific oral antibiotics for at least two weeks after discharge	30 day mortality Group A: 3/19 (16%) Group B: 1/3 (33%) Survival Group A: 1 year: 16/19 (84%) Group B: 1 year: 2/3 (66%)	26 (NR)	19 (24)
Pupka 2011[28]	77	Prospective cohort	2001–2008	Type of grafts Aortic tube ($n = 7$) Aorto(bi)iliac ($n = 2$) Aortobifemoral ($n = 53$) Aortofemoral ($n = 1$) Iliofemoral ($n = 14$) AEF 18 (23%) Infection diagnosis Clinical and radiological findings, such as purulent fistulas to skin and/or perigraft fluid	58 (42–71)	74 (96%)	No microorganisms: 0 (0%)	Group A: Complete graft removal and ISR (arterial allograft) with immunosuppressive therapy ($n = 24$) Group B: Complete graft removal and ISR (arterial allograft) without immunosuppressive therapy ($n = 26$) Group C: Complete graft removal and ISR (silver coated Dacron; $n = 27$)	Broad spectrum IV antibiotics (vancomycin, ciprofloxacin, and imipenem) before and for a period of up to 30 days post-operatively. Antibiotics were adjusted according to culture results	30 day mortality Group A: 1/24 (4%) Group B: 4/26 (15%) Group C: 2/27 (7%) Survival Group A: 1 year: 22/24 (92%) 2 year: 22/24 (92%) Group B: 1 year: 20/26 (77%) 2 year: 20/26 (77%) Group C: 1 year: 24/27 (89%) 2 year: 24/27 (89%) Recurrent infection Group A: 0/24 (0%) Group B: 1/26 (4%) Group C: 1/27 (4%)	23 (NR)	17 (24)

Table 1-*continued*

First author	Sample size	Study design	Study period	Inclusion criteria	Patients			Intervention	Antibiotic regime	Outcome	Follow up (months)	MINORS score (max)
					Age, mean (range)	Sex, male (%)	Microorganisms					
Batt 2012[29]	82	Retrospective comparative study	2000–2008	Type of grafts Aortofemoral grafts (55) Aortoiliac grafts (27) AEF 30 (37%) Infection diagnosis: - Clinical signs and fluid around graft on imaging studies - During surgery: purulent fluid around a non-incorporated graft	70 (45–87)	79 (96%)	Single organism: 29 (35%) Multiple organisms: 31 (38%) Unknown: 22 (27%)	Complete ($n = 58$) or partial ($n = 15$) graft removal Group A (ISR; $n = 63$): - Silver coated Dacron ($n = 26$) - Dacron + rifampicin ($n = 8$) - PTFE ($n = 2$) - Cryopreserved allograft ($n = 21$) - Superficial femoral vein ($n = 6$) Group B (EAR; $n = 11$) Group C Conservative treatment in high risk patients with patent grafts and localised infection ($n = 5$) Group D No reconstruction in occluded grafts without signs of ischaemia ($n = 3$)	Pre-operative vancomycin or according to sensitivity in cultures if available Post-operative Peri-procedural IV antibiotics, oral antibiotics continued for at least 8 weeks according to cultures	30 day mortality Overall: 27/82 (33%) Group A: 20/63 (32%) Group B: 5/11 (45%) Group C: 2/5 (40%) Survival: Overall: 1 year: 49/82 (60%) 3 year: 35/82 (43%) 5 year: 30/82 (36%) Group A: 1 year: 42/63 (66%) 3 year: 30/63 (47%) 5 year: 26/63 (41%) Group B: 1 year: 2/11 (18%) 3 year: 1/11 (9%) 5 year: 1/11 (9%) Recurrent infection Overall: 15/82 (18%) 1 year: 8/82 (9%) 3 year: 12/82 (15%) 4 year: 15/82 (18%) Recurrence rate significantly lower in Group A compared with Group B ($P = 0.04$). Limb salvage 1 year: 79/82 (96%) 3 year: 79/82 (96%) 5 year: 71/82 (86%) Primary patency 1 year: 73/82 (89%) 3 year: 71/82 (86%) 5 year: 64/82 (78%)	41 (2–89)	18 (24)
Maze 2013[30]	18	Retrospective cohort	1999–2010	Type of grafts Aortic tube ($n = 5$) Aortobiiliac ($n = 6$) Aortobifemoral ($n = 7$) AEF 1 (6%) Infection diagnosis Fever or inflammatory reaction and: - isolation of microorganism from graft material OR - perigraft fluid with or without gas on CT scan OR - isolation of microorganism from blood culture together with CT imaging features of graft infection	71 (48–85)	16 (89%)	No microorganisms: 0 (0%) Single microorganism: 12 (67%) Multiple microorganisms: six (33%)	Antibiotic treatment without graft removal ($n = 17$) - Antibiotics only ($n = 9$) - Percutaneous drainage ($n = 7$) - Bypass and aneurysm repair ($n = 1$) Complete graft removal and aortic patch angioplasty ($n = 1$), excluded from analysis	All patients received IV antibiotics 14 were treated for six weeks 1 for four weeks 2 for two weeks	30 day mortality 0/18 (0%) Survival 1 year: 15/17 (88%) 3 year: 13/17 (76%) 5 year: 8/17 (46%) Recurrent infection 6/17 (35%)	54 (NR)	11 (16)

Continued

Table 1-*continued*

First author	Sample size	Study design	Study period	Inclusion criteria	Patients			Intervention	Antibiotic regime	Outcome	Follow up (months)	MINORS score (max)
					Age, mean (range)	Sex, male (%)	Microorganisms					
Erb 2014[31]	27	Retrospective comparative study	2001–2012	Type of grafts Aortic tube ($n = 6$) Aorto(bi)iliac ($n = 21$) Thoracic grafts ($n = 24$)[a] Peripheral grafts ($n = 10$)[a] AEF 4 (15%) Infection diagnosis - microorganism isolated from the immediate area around the graft, OR - histopathological or radiological evidence of graft infection, OR - continuous bacteremia and a graft present with no other apparent focus of infection	70 (NR)	25 (93%)	No microorganisms: 0 (0%) Single microorganism: 9 (33%) Multiple microorganisms: 18 (67%)	Debridement and antibiotic treatment without graft removal ($n = 18$) Complete graft removal and - EAR ($n = 2$) - ISR (cryopreserved homograft; $n = 3$, Dacron; $n = 1$) Antibiotic treatment ($n = 3$)	Empirical IV antibiotic therapy, adjusted according to culture results: - rifampicin based regimen for *Staphylococcus* infection - ciprofloxacin based regime for gram negative infections Median duration: 92 days (range NR)	30 day mortality 9/27 (33.3%) Survival 1 year: 12/27 (44%)	NR	18 (24)
Crawford 2016[32]	15	Retrospective cohort	2001–2014	Type of grafts Isolated unilateral aortobifemoral graft limb infection AEF 1 (7%) Exclusion criteria - Complete aortobifemoral graft excision - aortic tube grafts - aortic endografts Infection diagnosis NR	68 (NR)	10 (67%)	No microorganism: two (13%)	Partial graft removal and: - EAR (femorofemoral bypass; $n = 10$, axillofemoral bypass; $n = 3$) - ISR ($n = 2$) Conduits used: Superficial femoral vein ($n = 7$) PTFE ($n = 6$) Cryopreserved allograft ($n = 1$) Saphenous vein ($n = 1$)	IV antibiotics post-operatively, median duration: 42 days (range NR)	30 day mortality 0/15 (0%) Survival 1 year: 14/15 (93%) 3 year: 11/15 (73%) 5 year: 8/15 (53%) Recurrent infection 8/15 (53%) Primary patency 13/15 (87%)	45 (NR)	9 (16)
Heinola 2016[33]	55	Retrospective cohort	2000–2013	Type of grafts Aortic graft infection treated with graft excision and *in situ* repair with an autologous venous neo-aortoiliac system. AEF 18 (33%) Infection diagnosis Clinical symptoms, blood samples, and positive findings in at least one imaging modality	67 (NR)	42 (76%)	No microorganisms: 16 (29%) Single microorganism: 21 (38%) Multiple microorganisms: 18 (33%)	Complete graft removal and ISR (superficial femoral vein) + strengthening of proximal anastomosis with tensor fascia lata	Pre-operative cefuroxime and vancomycin or targeted based on culture results if available In cases of AEF metronidazole was added Post-operatively IV antibiotics for at least six weeks	30 day mortality 5/55 (9%) Survival 1 year: 45/55 (82%) 3 year: 39/55 (71%) 5 year: 32/55 (58%) Recurrent infection 2/55 (4%) Limb salvage 1 year: 50/55 (91%)	32 (1–157)	11 (16)

Table 1-*continued*

First author	Sample size	Study design	Study period	Inclusion criteria	Patients			Intervention	Antibiotic regime	Outcome	Follow up (months)	MINORS score (max)
					Age, mean (range)	Sex, male (%)	Microorganisms					
Lejay 2017[34]	53	Retrospective cohort	2005–2014	Type of grafts Aortobiiliac ($n = 20$) Aortobifemoral ($n = 5$) Peripheral grafts ($n = 28$)[a] AEF 11 (44%) Infection diagnosis At least three of the following: - clinical presentation with pain and fever - positive blood cultures - CT with perigraft fluid with gas or abscess persisting ≥ 6 weeks after surgery - focus of intense radiotracer uptake	65 (NR)	20 (80%)	No microorganisms: 0 (0%) Single microorganism: 11 (44%) Multiple microorganisms: 14 (56%)	Complete graft removal and ISR (cryopreserved arterial allograft)	Targeted IV antibiotics pre-operatively if blood cultures were positive When blood cultures were negative, empiric antibiotics were started during surgery after cultures were obtained and adjusted based on culture results Median duration: 34 months	30 day mortality 2/25 (8%) Survival 1 year: 20/25 (80%) 3 year: 16/25 (64%) 5 year: 10/25 (40%) Limb salvage: 1 year: 25/25 (100%) 3 year: 25/25 (100%) 5 year: 25/25 (100%) Primary patency 1 year: 24/25 (96%) 3 year: 24/25 (96%) 5 year: 22/25 (88%)	47 (NR)	11 (16)
Ben Ahmed 2018[35]	71	Retrospective cohort	2000–2016	Type of grafts Aortic tube ($n = 4$) Aortobiiliac ($n = 8$) Aortofemoral ($n = 8$) Aortobifemoral ($n = 51$) AEF 16 (23%) Infection diagnosis Based on clinical signs, imaging findings (perigraft fluid, gas or inflammation and laboratory findings	65 (41–84)	65 (92%)	No microorganisms: 31 (44%) Single microorganism: 23 (32%) Multiple microorganisms: 17 (24%)	Complete graft removal and ISR (cryopreserved arterial allografts)	Broad spectrum IV antibiotics, secondarily adapted to culture results. Antimycotic agent was added for patients with aorto-enteric fistula Length of antibiotic treatment: six (3–20) weeks	30 day mortality 10/71 (14%) Overall mortality 35/71 (49%) Survival: 1 year: 53/71 (75%) 3 year: 46/71 (65%) 5 year: 38/71 (54%) Recurrent infection 3/71 (4%) Primary patency 1 year: 71/71 (100%) 3 year: 67/71 (94%) 5 year: 67/71 (94%)	45 (0–196)	11 (16)
Elens 2018[36]	20	Retrospective cohort	2000–2015	Type of grafts Aorto(bi)iliac ($n = 4$) Aorto(bi)femoral ($n = 16$) Peripheral grafts ($n = 42$)[a] AEF 5 (25%) Infection diagnosis Based on clinical signs and imaging findings.	76 (NR)	NR	No microorganisms: 19 (30%) Single microorganism: 20 (33%) Multiple microorganisms: 23 (37%)	Complete graft removal and - ISR (cryopreserved arterial allograft; $n = 13$, superficial femoral vein; $n = 3$) - EAR ($n = 4$)	Broad spectrum IV antibiotics, adapted to culture results	30 day mortality 0/20 (0%) Survival: 1 year: 13/20 (65%) 3 year: 9/20 (45%) 5 year: 9/20 (45%) Recurrent infection 2/20 (10%)	8 (NR)	11 (16)

Values are mean (range) or *n* (%) unless stated otherwise. AEF = aorto-enteric fistula; CNS = coagulase negative *Staphylococcus*; CT = computed tomography; DVT = deep vein thrombosis; EAR = extra-anatomic repair, in all cases an axillo (bi)femoral graft; ISR = *in situ* repair; IV = intravenous; MRSA = methicillin resistant *Staphylococcus aureus*; NR = not reported; PTFE = polytetrafluoroethylene; Spp. = species; WBC = white blood cell count; MINORS = methodological index for non-randomized studies.

[a] All non-abdominal aortic grafts, non-aortic grafts, and mycotic aneurysms are excluded from further analysis.

excluded patients with isolated groin infections.[12] One study excluded patients presenting with severe sepsis and lower limb emboli,[11] and another study excluded unstable patients or patients without an available superficial femoral vein that could be used for *in situ* repair (ISR).[25] Crawford et al. excluded patients requiring complete graft removal or patients with aortic tube grafts or aortic endografts, as they investigated patients with unilateral limb infections that could be treated by partial graft removal.[32] The diagnostic criteria used to establish the diagnosis of an infected aortic graft showed considerable variation, as summarised in Table 1, and typically included a combination of clinical signs of infection in combination with imaging findings of perigraft fluid or gas. In a minority of studies positive cultures were required for inclusion. In 10 studies the diagnostic criteria for the diagnosis of an infected aortic graft were not reported.[6–10,19,22–24,32]

Culture results were described in most of the included studies and the pathogens most frequently identified, in 13–54% of patients, were *Staphylococcus* species. These were generally *coagulase negative Staphylococcus* (CNS) or *Staphylococcus aureus*. Up to 20% of *S. aureus* were methicillin resistant resistant (MRSA). Other frequently identified species included *Enterococcus* species, *Pseudomonas aeruginosa*, *Klebsiella*, *Enterobacter*, *Escherichia coli*, and *Streptococcus* species.

Surgical management of AGI described in the included studies could consist of complete graft removal without any revascularisation ($n = 26$), complete graft removal and EAR ($n = 247$) or ISR ($n = 846$), partial graft removal and EAR ($n = 47$) or ISR ($n = 74$), local debridement procedures with or without irrigation without graft removal or conservative management with percutaneous drainage and antibiotic treatment ($n = 79$). EAR was in all cases an axillo(bi)femoral graft. For patients treated by ISR, the conduit material used in the studies was: dacron ($n = 136$), PTFE ($n = 27$), superficial femoral vein ($n = 348$), arterial and venous allografts ($n = 102$), and cryopreserved arterial allografts ($n = 257$). In one study complete graft removal, ISR using the superficial femoral vein and reinforcement of the proximal anastomosis with tensor fascia lata was performed.[33]

Antibiotic regimens varied considerably between studies and eight studies (25%) did not report any details on the antibiotic therapy applied.[6,7,10,15,22,23,25,26] When reported, most often treatment started with broad spectrum antibiotics which were replaced based on culture results. Duration of treatment varied and ranged from two weeks to lifelong oral antibiotic treatment.

According to the MINORS scoring scale, all 32 included studies were of moderate methodological quality (Fig. 2). The average total MINORS score was 10.5 for non-comparative studies (range 9–12) and 17.4 for comparative studies (range 16–19). None of the studies performed a sample size calculation or reported blinding of outcome assessment. Only two studies collected data prospectively[17,28] and in eight studies it was not reported whether prospective collection of data was performed.[5,8,9,13,14,18,19,21] In two studies the proportion lost to follow up was not reported[28,32] and one study had a loss to follow up of 15% for the primary outcome one year survival.[7] Follow up was, however, complete for 30 day mortality in this study.[7] In four of the seven comparative studies baseline characteristics were not equivalent[12,26,31] or not reported.[23] In four of the seven comparative studies no confidence intervals or relative risks or equivalents were reported.[12,23,28,29] There was complete agreement between authors regarding the inclusion and exclusion of studies and the assessment of methodological quality.

OUTCOMES

Thirty day mortality and survival

Thirty day mortality and one year survival were available for all studies as this was the primary outcome and an inclusion criterion for enrolment. The pooled overall 30 day mortality and one year survival were 13.5% (95% CI 10.5–16.4) and 73.6% (95% CI 68.8–78.4), respectively (Fig. 3). The overall three and

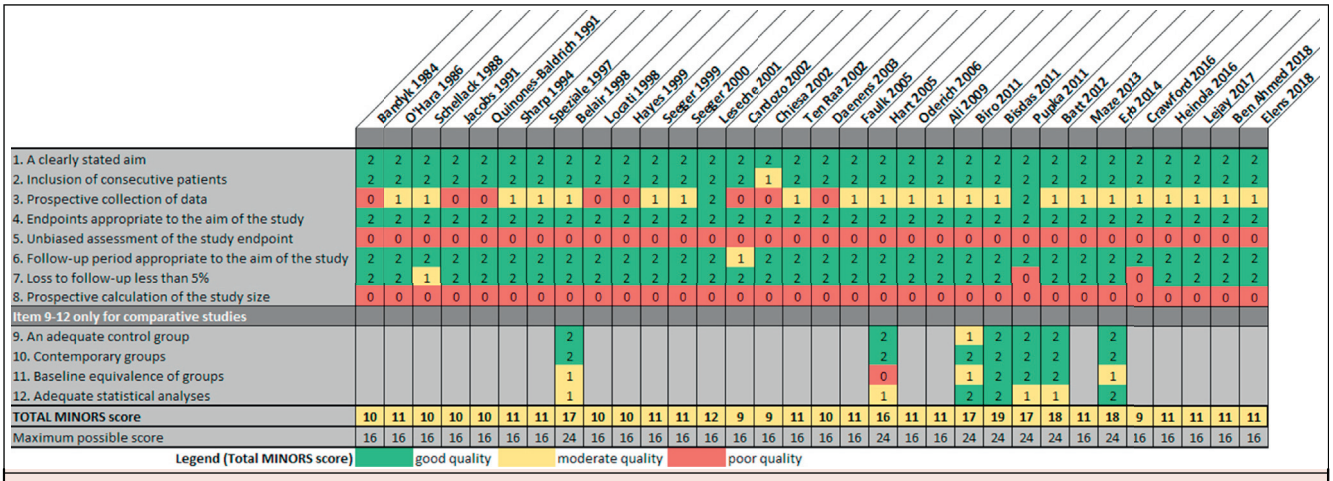

Figure 2. The Methodological Index for Non-randomised Studies (MINORS) was used to assess the methodological quality for each study. Items are scored as follows: 0, not reported; 1, reported but inadequate; 2, reported and adequate. The global ideal score is 16 for non-comparative studies and 24 for comparative studies.

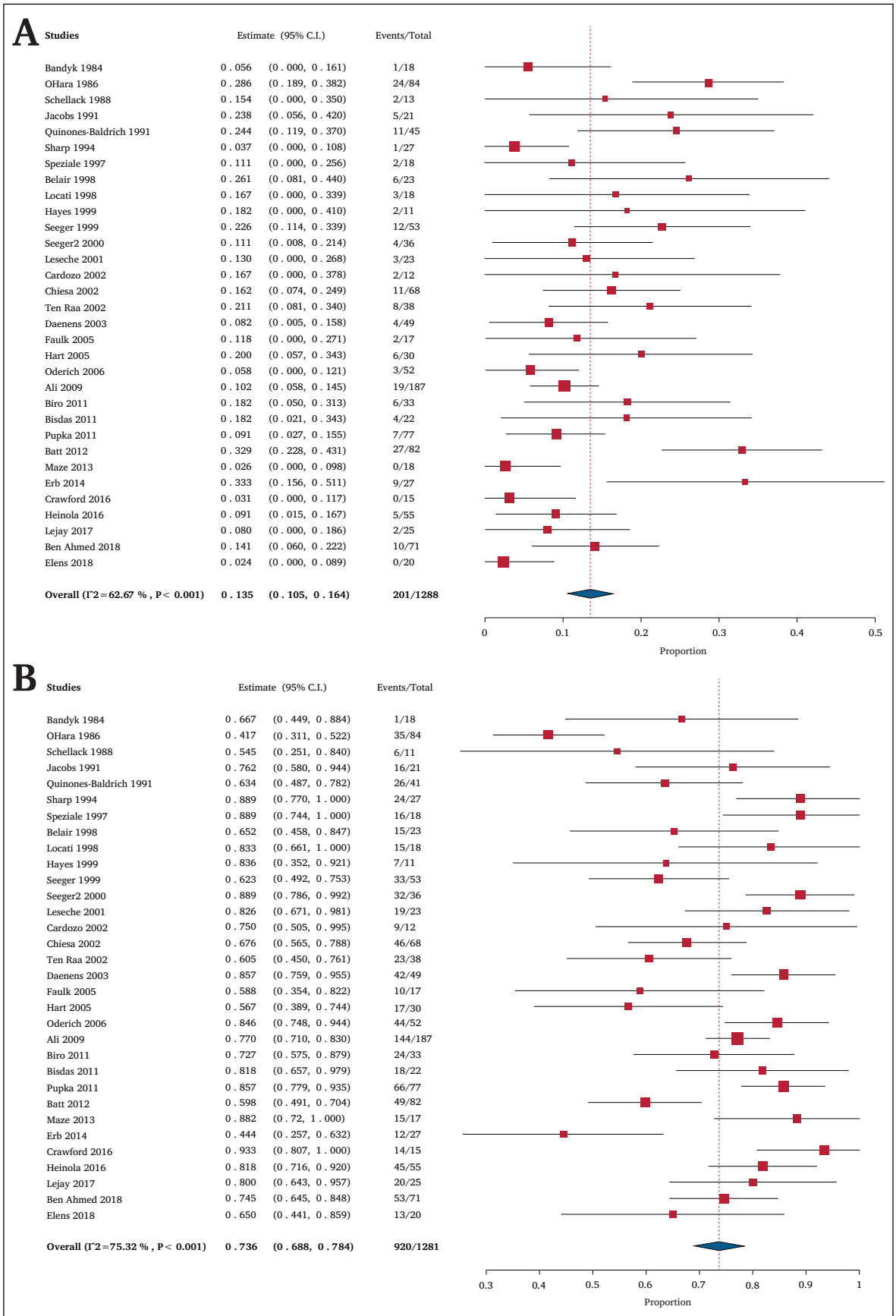

Figure 3. The forest plot shows the pooled analysis of overall 30 day mortality (A) and one year survival (B). The box size, which is proportional to study sample size, shows the point estimate; diamond, summary estimate; the horizontal lines indicate the 95% CI. CI = confidence interval; I^2 = percentage of variation.

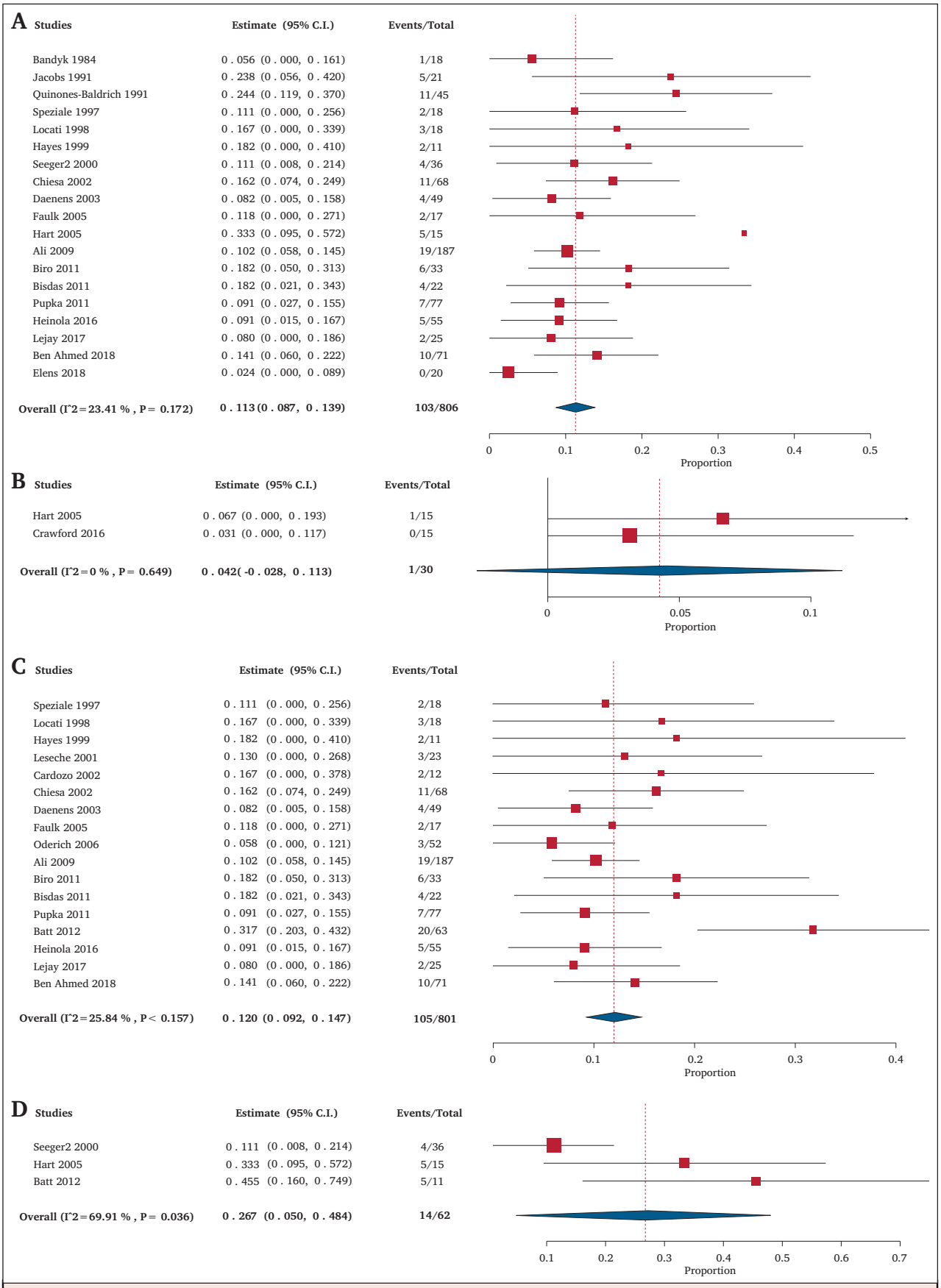

Figure 4. The forest plot shows the pooled analysis of 30 day mortality for the subgroups treated by complete graft removal (A), partial graft removal (B), *in situ* repair (C), and extra-anatomic repair (D). The box size, which is proportional to study sample size, shows the point estimate; diamond, summary estimate; the horizontal lines indicate the 95% CI. CI = confidence interval; I^2 = percentage of variation.

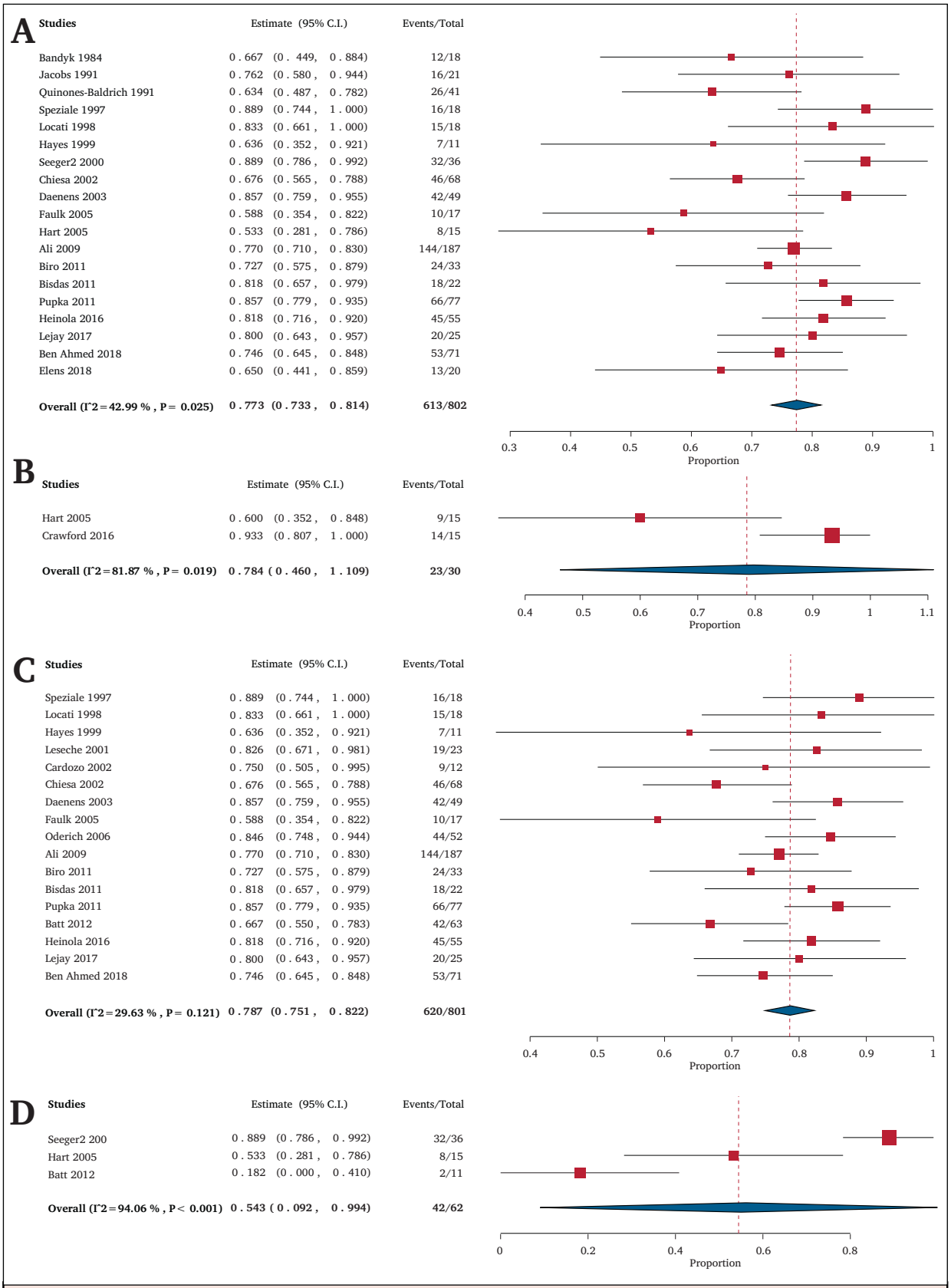

Figure 5. The forest plot shows the pooled analysis of one year survival for the subgroups treated by complete graft removal (A), partial graft removal (B), *in situ* repair (C), and extra-anatomic repair (D). The box size, which is proportional to study sample size, shows the point estimate; diamond, summary estimate; the horizontal lines indicate the 95% CI. CI = confidence interval; I^2 = percentage of variation.

five year survival rates were 67.3% (95% CI 61.3—73.3; $n = 18$)[9—11,16,19—22,24—26,29,30,32—36] and 50.1% (95% CI 40.9—59.3; $n = 16$), respectively.[6,9,11,16,20,21,24—26,29,30,32—36]

The pooled 30 day mortality and one year survival in studies that performed complete graft removal were 11.3% (95% CI 8.7—13.9; $n = 19$) and 77.3% (95% CI 73.3—81.4; $n = 19$), respectively.[5,8,9,11,13,14,16,19,21—23,25—28,33—36] Three and five year survival in this subgroup were 67.5% (95% CI 61.4—73.5; $n = 12$)[9,11,16,19,21,22,25,26,33—36] and 56.9% (95% CI 50.2—63.7; $n = 10$),[9,11,16,21,25,26,33—36] respectively. In the subgroup of studies where partial graft removal was performed, the pooled 30 day mortality and one year survival were 4.2% (95% CI 0.0—11.3) and 78.4% (95% CI 46.0—100), respectively.[23,32]

The pooled 30 day mortality rates for ISR and EAR were 12.0% (95% CI 9.2—14.7; $n = 17$)[11,13,14,17—19,21,22,24—29,33—35] and 26.7% (95% CI 5.0—48.4; $n = 3$),[16,23,29] respectively. For one year survival rate, pooled proportions were 78.7% (95% CI 75.1—82.2; $n = 17$) for ISR[11,13,14,17—19,21,22,24—29,33—35] and 54.3% (95% CI 9.2—99.4; $n = 3$) for EAR.[16,23,29] Three and five year survival rates for ISR were 68.0% (95% CI 61.3—74.7; $n = 11$)[11,19,21,22,24—26,29,33—35] and 57.7% (95% CI 50.0—65.3; $n = 9$),[11,21,24—26,29,33—35] respectively. Three and five year survival rates for EAR were available in two studies[16,29] and after pooling were 40.8% (95% CI 0.0—100) and 32.4% (0.0—77.9), respectively. The pooled analyses of 30 day mortality for all subgroups (complete graft removal, partial graft removal, ISR, and EAR) are summarised in Fig. 4. The results for one year survival for the same subgroup analyses are summarised in Fig. 5. The results of all pooled analyses are summarised in Table 2. Pooled subgroup analyses were also performed for the different graft materials used for ISR:

Table 2. Pooled analyses of 30 day mortality, and long term patient survival and limb salvage

Outcome	# of studies	Events/*N*	Proportion, %	95% CI	I^2 index, %	Quality of the evidence[a]
30 day mortality						
Overall	32	201/1288	13.5	10.5—16.4	63	10.8
Complete graft removal	19	103/806	11.3	8.7—13.9	23	10.7
Partial graft removal	2	1/30	4.2	0.0—11.3	0	9.8
In situ repair	17	105/801	12	9.2—14.7	26	10.9
Extra-anatomic repair	3	14/62	26.7	5.0—48.4	70	11.2
One year survival						
Overall	32	920/1281	73.6	68.8—78.4	75	10.8
Complete graft removal	19	613/802	77.3	73.3—81.4	43	10.7
Partial graft removal	2	23/30	78.4	46.0—100		9.8
In situ repair	17	620/801	78.7	75.1—82.2	30	10.8
Extra-anatomic repair	3	42/62	54.3	9.2—99.4	94	11.2
Three year survival						
Overall	18	551/851	67.3	61.3—73.3	71	10.7
Complete graft removal	12	408/620	67.5	61.4—73.5	59	10.7
Partial graft removal	-	-	-	-	-	-
In situ repair	11	419/638	68	61.3—74.7	69	10.8
Extra-anatomic repair	2	27/47	40.8	0.0—100	97	11.5
Five year survival						
Overall	16	396/823	50.1	40.9—59.3	87	10.8
Complete graft removal	10	294/535	56.9	50.2—63.7	56	10.8
Partial graft removal	-	-	-	-	-	-
In situ repair	9	304/553	57.7	50.0—65.3	69	11
Extra-anatomic repair	2	21/47	32.4	0.0—77.9	93	11.5
One year limb salvage						
Overall	12	618/660	95.7	93.5—98.0	57	11
Complete graft removal	7	369/397	95	92.8—100	58	10.7
Partial graft removal	-	-	-	-	-	-
In situ repair	6	370/391	96.4	93.6—99.2	57	11
Extra-anatomic repair	2	50/51	98.2	94.7—100	0	10.8
Recurrent infection						
Overall	23	101/947	9.7	6.7—12.7	66	10.7
Complete graft removal	14	43/617	5.4	3.2—7.5	23	10.7
Partial graft removal	2	12/30	39.3	13.2—65.4	58	9.8
In situ repair	11	40/564	5.7	3.5—8.0	19	10.8
Extra-anatomic repair	2	3/51	4.8	-3.3—12.8	24	10.8
One year primary patency						
Overall	13	588/673	87.8	82.6—92.9	85	10.7
Complete graft removal	10	446/516	86.4	79.9—92.9	88	10.5
Partial graft removal	-	-	-	-	-	-
In situ repair	10	477/538	89.6	84.2—95.0	85	10.6
Extra-anatomic repair	-	-	-	-	-	-

N = total sample size; CI = confidence interval; I^2 = percentage of variation; MINORS = Methodological Index for Non-randomised Studies.
[a] Average MINORS score of included studies reporting the outcome.

superficial femoral vein, prosthetic grafts, or arterial allografts. The results of these analyses are summarised in Table 3.

Limb salvage

Of the 20 studies that reported on limb salvage[5–11,15–21,23–25,29,33,34] eight reported an overall limb salvage without a specified time interval with a median limb salvage rate of 82.5% (range 56–100%).[5–8,10,11,18,19] The mean follow up duration in these studies was 32 months (median 22; range 13–77). Twelve studies reported one year limb salvage rates.[9,15–17,20,21,23–25,29,33,34] The pooled overall one year limb salvage rate was 95.7% (95% CI 93.5–98.0). The pooled one year limb salvage rates for subgroups of treatment options are summarised in Table 2. Pooled subgroup analyses were also performed for the different graft materials used for ISR, these results are summarised in Table 3.

Graft patency

Fifteen of the included studies reported the graft primary patency.[9–13,19,21,22,24–26,29,32,34,35] Two studies reported an overall primary patency, without specifying a time interval. The overall primary patency rates reported were 74% (17 of 24) with a mean follow up of 24 months (range 6–84)[13] and 87% (13 of 15) with a mean follow up of 45 months (range unreported),[32] respectively. The remaining 13 studies reported at least a one year primary patency.[9–11,13,19,21,22,24–26,29,34,35] The pooled one year primary patency was 87.8% (95% CI 82.6–92.9; 13 studies).[9–11,13,19,21,22,24–26,29,34,35] After three years, the primary patency was 81.6% (95% CI 73.6–89.6; $n = 11$).[9–11,19,20,22,24,25,29,34,35] The pooled five year primary patency, reported in nine studies, was 82.4% (95% CI 74.2–90.6).[9,11,20,24–26,29,34,35] Pooled patency rates for subgroups treated by complete or partial graft removal and ISR or EAR are summarised in Table 2, while the pooled patency rates for different graft types used for ISR are listed in Table 3. There were no included studies that performed partial graft removal or EAR that also reported primary patency rates for these subgroups.

Recurrence of infection

The proportion of patients with a recurrent infection was reported in 23 studies and ranged from 0 to 53%, with a pooled recurrence rate of 9.7% (95% CI 6.7–12.7).[5,8,9,11–18,20,23–26,28–30,32,33,35,36] No time interval for the recurrence of infection was reported. However, the average follow up period in the different studies varied from 8 to 77 months.

An attempt was made to compare the recurrence rate between complete and partial graft removal, ISR and EAR

Table 3. Pooled analyses of 30 day mortality, and long term patient survival, limb salvage, recurrent infection and primary patency, stratified by graft material used for *in situ* repair

Outcome	# of studies	Events/*N*	Proportion, %	95% CI	I^2 index, %	Quality of the evidence[a]
30 day mortality						
Superficial femoral vein	6	34/334	10	6.8–13.2	0	10.6
Prosthetic graft	5	10/111	7.6	2.7–12.4	0	11.2
Arterial allograft	8	41/293	13.3	9.4–17.1	0	11
One year survival						
Superficial femoral vein	6	261/334	79	74.2–83.9	9	10.6
Prosthetic graft	5	93/111	85.4	78.9–91.9	0	11.2
Arterial allograft	8	224/293	77.8	73.0–82.5	3	11
Three year survival						
Superficial femoral vein	5	220/322	71	62.6–79.5	54	10.9
Prosthetic graft	2	55/70	81.3	67.7–94.8	53	11
Arterial allograft	4	115/183	63	56.1–70.0	0	10.6
Five year survival						
Superficial femoral vein	4	169/305	58.5	49.7–67.4	49	10.8
Prosthetic graft	2	48/70	72.6	53.2–92.0	69	11
Arterial allograft	3	61/115	53.5	40.0–67.0	48	11.1
One year limb salvage						
Superficial femoral vein	3	270/291	94.1	89.5–98.7	63	10.7
Prosthetic graft	2	48/70	72.6	53.2–92.0	69	11
Arterial allograft	2	48/48	98	94.1-100	0	11.5
Recurrent infection						
Superficial femoral vein	4	13/268	4.8	2.3–7.4	0	10.6
Prosthetic graft	4	11/115	7.1	0.9–13.3	46	10.8
Arterial allograft	5	11/184	4.1	0.2–8.0	42	11.1
One year primary patency						
Superficial femoral vein	4	242/267	90.9	83.6–98.2	68	10.8
Prosthetic graft	2	65/70	93.4	87.6–99.2	0	11
Arterial allograft	5	170/201	87.1	74.9–99.2	90	-

N = total sample size; CI = confidence interval; I^2 = percentage of variation; MINORS = Methodological Index for Non-randomised Studies.
[a] Average MINORS score of included studies reporting the outcome.

and between graft materials used for ISR. Studies including different treatment types (i.e. complete and partial graft removal, ISR and EAR or different graft materials) without reporting outcomes per treatment type were excluded from this analysis. The results are summarised in Tables 2 and 3. Two studies that performed partial graft removal reported recurrence rates.[23,32] Interestingly, these studies had the highest pooled recurrence rate of 39.3% (95% CI 13.2—65.4),[23,32] while the average recurrence rate in 14 studies performing complete graft removal was 5.4% (95% CI 3.2—7.5).[5,8,9,11,13,14,16,23,25,26,28,33,35,36]

Analysis of the studies performing ISR demonstrated a pooled recurrent infection rate of 5.7% (95% CI 3.5—8.0)[11,13,14,17,18,24—26,28,33,35] vs. a 4.1% (95% CI 3.3—12.8) recurrence rate for studies performing EAR.[16,23] Further analysis of the graft material used in those studies performing ISR demonstrated a pooled infection recurrence rate of 4.8% (95% CI 2.3—7.4; four studies) when autologous veins were used.[18,25,26,33] Pooled recurrence rates were 7.1% (95% CI 0.9—13.3; $n = 4$) in the studies performing prosthetic ISR[11,14,24,28] and 4.1% (95% CI 0.2—8.0; $n = 5$) in the studies where allografts were used.[13,17,26,28,35]

Certainty of the evidence

The overall quality of the included studies reporting on the primary outcomes was moderate (10.5 for non-comparative studies and 17.4 for comparative studies; Fig. 2). Eleven studies reported on venous substitutes with an average score of 10.6.[9,18,21,22,25,26,29,32,33,35,36] Regarding the studies on arterial and prosthetic reconstructions, the average MINORS scores were 13.3 [13,17,19,26—29,32,34,35] and 13.1.[5—12,14—16,20,23,24,27—32] None of the studies met the criteria for good quality. In all studies, data collection, assessment of study endpoints, and calculation of study sizes was a major issue. With respect to comparative studies the non-equivalence of baseline groups and poor statistical analysis were the main concerns. The quality of the evidence for each outcome is also reported in Tables 2 and 3.

DISCUSSION

Our systematic review and meta-analysis of the currently available literature shows that overall 30 day mortality and one year survival for treatment of aortic graft infection is 13.5% and 73.6%, respectively, underlining the severe implications of this complication of open aortic surgery. Extra-anatomic repair, once the gold standard, had the highest 30 day mortality (26.7%) and lowest one year survival (54.3%) rates. Limb salvage rates were high ($\geq$95%) for all subgroups and recurrent infection rates were low ($\sim$5%) except for those studies in which partial graft removal was performed (39.3%). Subgroup analyses of graft material used for ISR demonstrated better survival and mortality rates for prosthetic grafts, although these grafts performed worse compared with superficial femoral veins and arterial allografts in terms of limb salvage and infection recurrence rates. Patency at one year was comparable between all subgroups studied.

The present findings show similarities to the findings of a previous meta-analysis from 2006, although the design of this study was different.[1] The main purpose of the previous meta-analysis was to analyse and compare outcomes between the subgroups: EAR, rifampicin bonded prosthetic repair, cryopreserved allografts and autogenous vein. They also reported the highest early and late mortality rates following EAR. In contrast to the present study, the authors also included studies including mycotic aneurysms and the outcomes of the included studies were reported globally, and not separately per pathology (mycotic aneurysms vs. graft infection). This is relevant as patients with mycotic aneurysms might have more virulent bacteria and more advanced infection influencing outcomes and those patients might be more likely to be treated by graft removal and EAR. This could be an important source of bias. Moreover, the inclusion and exclusion criteria were less extensively described (e.g., “Clinical studies with poor reporting of patient characteristics and relevant outcomes data”). Furthermore, one of the major drawbacks of their study was that they analysed event rates for outcomes such as late mortality, re-infection without taking the interval measured into account. They roughly compensated for this by performing a sensitivity analysis comparing outcomes between studies with a follow up of $\leq$ or $>$16.5 months. However, major differences in event rates could occur when follow up varies. The present study only included studies that reported at least the primary outcome (30 day mortality and one year survival). These primary outcomes have considered a certain time interval, thereby enhancing comparability of event rates between included studies.

The current ESVS guidelines recommend that stable patients with high virulence organisms with enteric fistula should receive a staged procedure with EAR followed by graft excision and debridement, aortic stump closure, omental flap coverage and closure or diversion of the intestinal defect.[2] Prosthetic ISR should be used when combined with silver and/or antibiotic binding.[2] Although the level of evidence used for these recommendations remains low, the recommendations are generally in accordance with the findings of the present study.[2]

The incidence of aortic graft infection is, with the worldwide adoption of EVAR as a first choice treatment for abdominal aortic aneurysms, declining. An incidence of 0.6% endograft infections was reported by a meta-analysis from 2017.[133] The authors also demonstrated a high pooled 30 day/in hospital mortality of 26.6%. This might, in part, be explained by the high proportion of patients (40%) treated as an emergency. The available data from this systematic review are insufficient to allow any comparison on the topic of emergency or elective treatment. A more recent meta-analysis demonstrated a somewhat lower, but still considerably high 30 day mortality of 17% for patients treated for infected endografts.[134] Survival was worse following TEVAR (compared with EVAR) and in patients presenting with an AEF.[134]

The present study has several features that improve the strength of its findings. First, it adhered to the PRISMA

guidelines in performing a systematic review of the literature with strict selection criteria for study design, patient inclusion and exclusion criteria, and outcome reporting. This contributed to comparability of the individual study data. Moreover, from 2006 many new studies have been performed and these are included in the systematic review. Strict definitions and outcome criteria were also used to improve comparability between the outcome data of the included studies.

However, there are some limitations that warrant careful interpretation of the present findings. First, only retrospective studies and two prospective non-randomised studies, all of moderate methodological quality, could be included. Thereby there is a considerable risk of selection bias. For example, the choice for the type of surgery might be dependent on the severity of the infection or condition of the patient, thereby also influencing important outcomes. For example, it is possible that ISR was performed preferably in patients with less extensive contamination and in better clinical condition. The available data did not allow any quantification or estimation of the impact of this form of bias. A shift in operative techniques used was noted over time. In the earlier reports EAR was the most frequently reported technique, whereas in the more recently reported studies *in situ* repair was performed more frequently. All the above might have played a role in the outcome of the techniques used.

There was also considerable heterogeneity of the inclusion criteria, operative techniques used, and outcomes reported. Some studies used a wide range of different techniques without reporting outcomes per type of technique. There was also high statistical heterogeneity, indicated by the high I^2 indices accompanying the majority of the pooled analyses performed. Both types of heterogeneity reduce comparability of the individual studies. Moreover, comparative studies were rare among the included studies and none of the comparisons included were available for more than one study. Thereby, the findings of different subgroup analyses cannot be compared directly and findings should be interpreted with care.

Some of the relevant outcomes, such as recurrent infection, were generally reported without a specified time interval. As the average follow up period varied between studies, comparisons of event rates for these outcomes are further hampered.

Most of included studies also included patients with AEF (median 26%, range 0—50% of included patients) and outcomes were not separately reported for patients with and without AEF. One exception was the study by O'Hara that reported a 30 day mortality for patients with and without AEF (53% vs. 14%, respectively).[6] As demonstrated by this study, outcomes can be dramatically influenced by the presence of AEF and also the choice of treatment might be biased by the presence of AEF.

More data are needed to identify the most appropriate treatment strategy for aortic graft infections and for different subgroups, such as patients with AEF, emergency cases, mycotic aneurysms, septic bleeding, highly virulent microorganisms, etc. Taking the prevalence of aortic graft infection into account, a prospective randomised controlled trial is probably not feasible. A prospective worldwide registry including sufficient parameters to allow case mix corrections in future analyses and including sufficient follow up for standardised outcome measures might be the most appropriate next step in obtaining reliable evidence on this topic, like the Management of Aortic Graft Infection Collaboration(MAGIC) from several English NHS hospitals.[135] Future studies should at least use uniform standardised diagnostic criteria, treatment modalities, and outcome parameters to improve comparability of studies and reliability of outcome data.

In conclusion, despite numerous studies, no definite answer can be formulated on how to manage aortic graft infections. There is a lack of well designed, high quality comparative studies, making conclusive recommendations impossible. The current best available data suggest that partial graft removal should be avoided and the lowest 30 day mortality and best one year survival are for *in situ* repair and prosthetic grafts. Initiatives such as the MAGIC database to collaboratively collect prospective data are an important step forward in obtaining more solid answers on this topic.

CONFLICT OF INTEREST

None.

FUNDING

None.

APPENDIX A. SUPPLEMENTARY DATA

Supplementary data related to this article can be found at https://doi.org/10.1016/j.ejvs.2019.03.013.

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Eur J Vasc Endovasc Surg (2019) 58, 281

COUP D'OEIL

Fatal Aortic Occlusion Due to Compression From Self Induced Acute Gastric Dilatation

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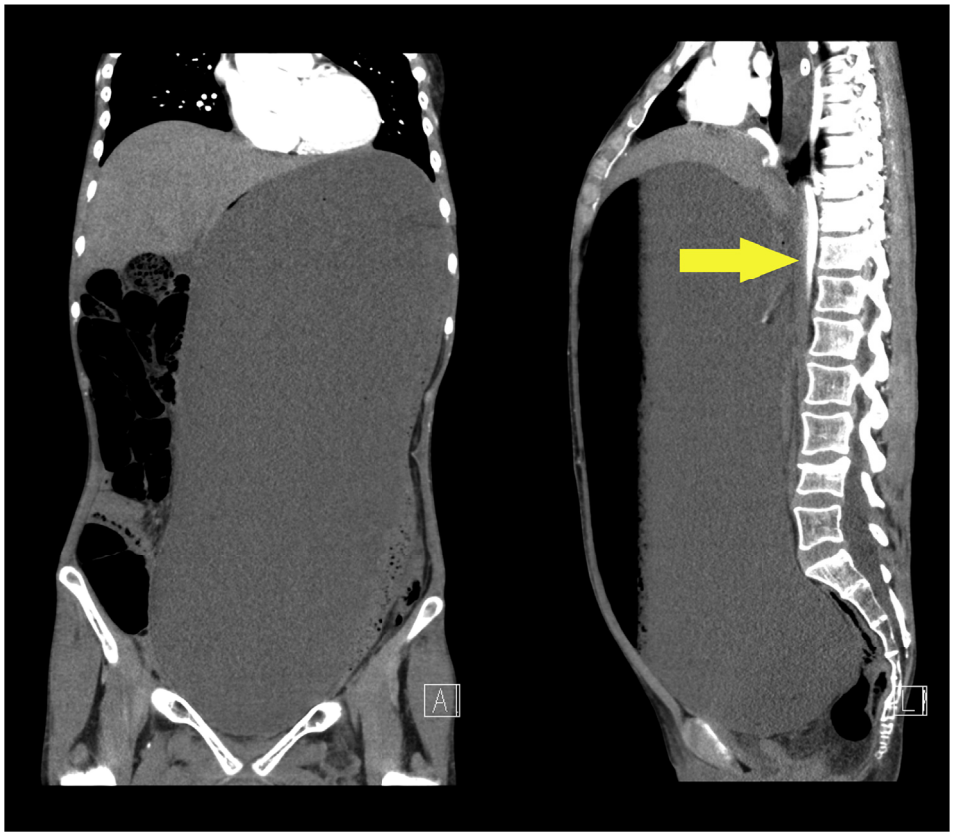

A 25 year old woman with bulimia presented with acute abdominal pain. She reported ingestion of 15 L water to present with sufficient weight to her psychiatrist. Subsequently, she developed severe ischaemia in both legs with missing femoral pulses. Computed tomography angiography showed extreme distension of a fluid filled stomach and occlusion of the abdominal aorta (arrow) and intestinal branches. Gastric fluid aspiration not only led to improved leg perfusion, but also to an acute drop of blood pressure. Acute exploratory laparotomy revealed multiple gastric perforations and ischaemia of the complete gastrointestinal tract. Increasing haemodynamic instability resulted in intra-operative death.

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https://doi.org/10.1016/j.ejvs.2019.02.025