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ORIGINAL ARTICLE – OBSERVATIONAL STUDY

Semi-Conservative Treatment Versus Radical Surgery in Abdominal Aortic Graft and Endograft Infections

Hamid Gavali [a,*], Kevin Mani [a], Mia Furebring [b], Karl Wilhelm Olsson [a], David Lindström [a], Karl Sörelius [c], Birgitta Sigvant [a,d], Gustav Torstensson [e], Manne Andersson [f,g], Claes Forssell [h], Håkan Åstrand [g], Tobias Lundström [i], Shahzad Khan [j], Björn Sonesson [j], Otto Stackelberg [k,l], Peter Gillgren [k,m], Jon Isaksson [n], Björn Kragsterman [a,o], Khatereh Djavani Gidlund [p], Tal Horer [p], Mitra Sadeghi [p], Anders Wanhainen [a,n]

[a] Department of Surgical Sciences, Section of Vascular Surgery, Uppsala University, Uppsala, Sweden
[b] Department of Medical Sciences, Section of Infectious Diseases, Uppsala University, Uppsala, Sweden
[c] Department of Vascular Surgery, Rigshospitalet, Copenhagen, Denmark; and Faculty of Health and Medical Sciences, University of Copenhagen, Copenhagen, Denmark
[d] Department of Vascular Surgery, Karlstad Central Hospital, Karlstad, Sweden
[e] Department of Surgery, Helsingborg Regional Hospital, Helsingborg, Sweden
[f] Department of Clinical and Experimental Medicine, Linköping University, Linköping, Sweden
[g] Department of Surgery, County Hospital Ryhov, Ryhov, Jönköping County, Sweden
[h] Department of Cardiovascular Surgery, Division of Vascular Surgery, Linköping University Hospital, Linköping, Sweden
[i] Department of Surgery and Urology, Eskilstuna Hospital, Eskilstuna, Sweden
[j] Department of Surgery, Malmö University Hospital, Lund University, Malmö, Sweden
[k] Department of Clinical Science and Education, Karolinska Institutet, Stockholm, Sweden
[l] Unit of Cardiovascular and Nutritional Epidemiology, Institute of Environmental Medicine, Karolinska Institutet, Stockholm, Sweden
[m] Department of Vascular Surgery, Södersjukhuset, Stockholm, Sweden
[n] Department of Surgical and Peri-operative Sciences, Umeå University, Umeå, Sweden
[o] Department of Surgery, Västerås Central Hospital, Västerås, Sweden
[p] Department of Cardiothoracic and Vascular Surgery and Department of Surgery, Faculty of Medicine and Health, Örebro University, Örebro, Sweden

WHAT THIS PAPER ADDS

The optimal surgical treatment for abdominal aortic graft and endograft infections (AGIs) is still not fully elucidated. As endovascular development continues, the treatment of more complex primary aortic pathologies in elderly and more frail patients is possible. This ultimately greatly increases the complexity of the traditional radical surgical resection approach in the future cohort at risk of developing an AGI. This paper explores and compares the survival and re-infection outcomes of a semi-conservative, graft preserving strategy *vs.* a conventional radical surgery approach in a large, nationwide, multicentre, retrospective cohort.

Objective: Abdominal aortic graft and endograft infections (AGIs) are rare complications following aortic surgery. Radical surgery (RS) with resection of the infected graft and reconstruction with extra-anatomical bypass or in situ reconstruction is the preferred therapy. For patients unfit for RS, a semi-conservative (SC), graft preserving strategy is possible. This paper aimed to compare survival and infection outcomes between RS and SC treatment for AGI in a nationwide cohort.
Methods: Patients with abdominal AGI related surgery in Sweden between January 1995 and May 2017 were identified. The Management of Aortic Graft Infection Collaboration (MAGIC) criteria were used for the definition of AGI. Multivariable regression was performed to identify factors associated with mortality.
Results: One hundred and sixty-nine patients with surgically treated abdominal AGI were identified, comprising 43 SC (14 endografts; 53% with a graft enteric fistula [GEF] in total) and 126 RS (26 endografts; 50% with a GEF in total). The SC cohort was older and had a higher frequency of cardiac comorbidities. There was a non-significant trend towards lower Kaplan—Meier estimated five year survival for SC *vs.* RS (30.2% *vs.* 48.4%; *p* = .066). A non-significant trend was identified towards worse Kaplan—Meier estimated five year survival for SC patients with a GEF *vs.* without a GEF (21.7% *vs.* 40.1%; *p* = .097). There were significantly more recurrent graft infections comparing SC with RS (45.4% *vs.* 19.3%; *p* < .001). In a Cox regression model adjusting for confounders, there was no difference in five year survival comparing SC *vs.* RS (HR 1.0, 95% CI 0.6 − 1.5).
Conclusion: In this national AGI cohort, there was no mortality difference comparing SC and RS for AGI when adjusting for comorbidities. Presence of GEF probably negatively impacts survival outcomes of SC patients. Rates of recurrent infection remain high for SC treated patients.

INTRODUCTION

Abdominal aortic graft and endograft infections (AGIs) are rare complications following aortic surgery. A lifetime incidence of 0.3 — 3% after aortic repair has been reported.[1–4] The exact frequency is difficult to assess due to a historic lack of a consistent definition.

Current European Society for Vascular Surgery (ESVS) guidelines recommend a diagnosis based on a criteria oriented scoring system according to the Management of Aortic Graft Infection Collaboration (MAGIC) criteria.[5,6] This system includes an assessment of clinical, laboratory, microbiological, and radiological findings.

The ESVS guidelines recommend radical surgy (RS) with resection of the infected aortic prosthesis and restoration of distal perfusion as the primary treatment of AGI.[5] The latter aspect is preferably achieved by means of an in situ reconstruction (ISR) with an autologous vein [i.e., a neo-aorto-iliac system (NAIS)], bovine pericardium, antibiotic soaked, or homologous aortic graft. If not feasible, an extra-anatomical bypass (EAB) by means of an axillobifemoral bypass remains a valid option.[7–14]

Despite improvements in surgical management and critical care, the mortality rate following RS for AGI remains high, with the 30 day mortality rate reported to be 10 — 20%.[10,13,14] Recurrent infections in the new conduit develop in up to 10% during follow up.[11] Due to the presence of comorbidities or complicated graft anatomy, a cohort of AGI patients will never be considered for RS. In some of these patients, a semi-conservative (SC), graft preserving strategy is applied. This includes endovascular adjuncts, surgical debridement of adjacent infected tissue and fistulae, as well as in some cases partial resection of the infected conduit combined with antimicrobial treatment. Small single centre studies have reported inferior results of a SC strategy with an overall mortality rate of 30 — 50% during one year follow up.[15,16]

The purpose of this study was to compare patients selected for SC treatment with patients selected for RS treatment (EAB and ISR) in a large, nationwide, multicentre cohort in terms re-infection and survival outcomes.
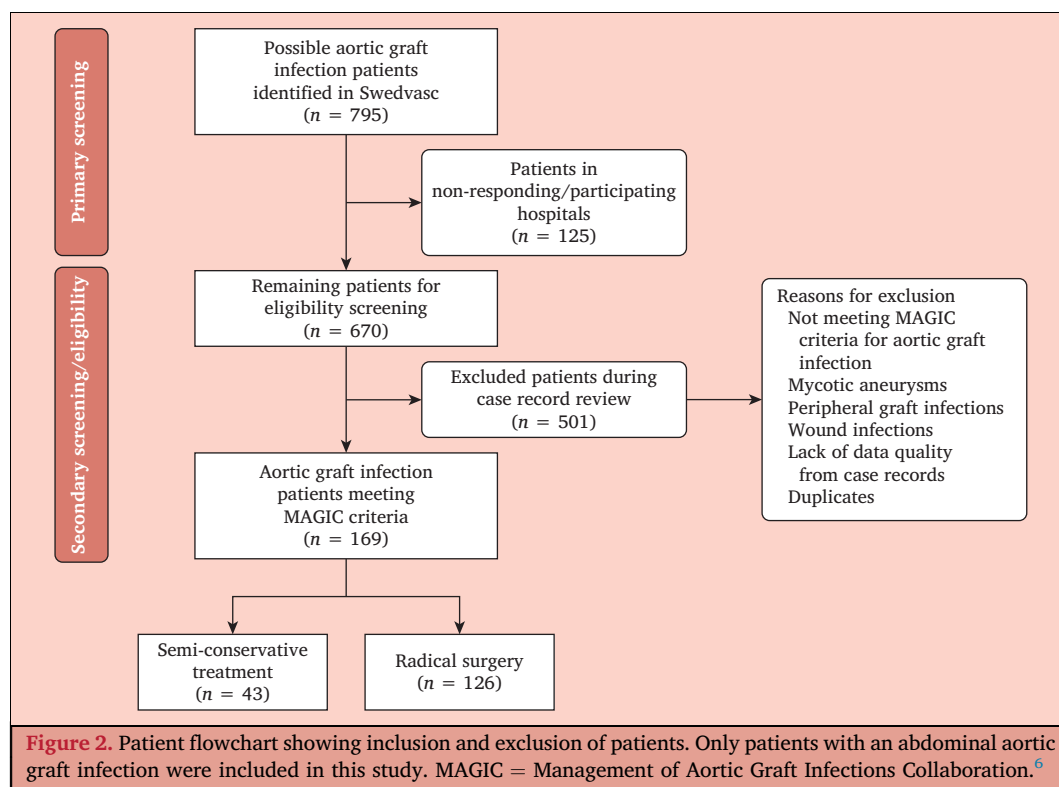
MATERIALS AND METHODS

Design and study population

The methods for patient identification and statistical analysis have been described elsewhere.[17] Briefly, all patients undergoing surgical treatment for an abdominal graft or endograft AGI between January 1995 and May 2017 in Sweden were identified using the prospective Swedish National Registry for Vascular Surgery (Swedvasc).[18] Patients fulfilling the MAGIC criteria of a diagnosed AGI were included in the study (Fig. 1). Figure 2 shows a flowchart for patient identification and selection. The vast majority of

	Clinical/surgical	Radiology	Laboratory
Major criteria	Pus (confirmed by microscopy) around graft or in aneurysm sac at surgery Open wound with exposed graft or communicating sinus Fistula development e.g. aorto-enteric or aortobronchial Graft insertion in an infected site e.g. fistula, mycotic aneurysm or infected pseudoaneurysm	Peri-graft fluid on CT scan ≥ 3 months after insertion Peri-graft gas on CT scan ≥ 7 weeks after insertion Increase in peri-graft gas volume demonstrated on serial imaging	Organisms recovered from an explanted graft Organisms recovered from an intra-operative specimen Organisms recovered from a percutaneous, radiologically guided aspirate of peri-graft fluid
Minor criteria	Localised clinical features of AGI e.g. erythema, warmth, swelling, purulent discharge, pain Fever ≥ 38 °C with AGI as most likely cause	Other e.g. suspicious peri-graft gas, fluid, soft tissue inflammation; aneurysm expansion; pseudoaneurysm formation; focal bowel wall thickening; discitis or osteomyelitis; suspicious metabolic activity on FDG PET/CT; radiolabelled leucocyte uptake	Blood culture(s) positive and no apparent source except AGI Abnormally elevated inflammatory markers with AGI as most likely cause e.g. ESR, CRP, white cell count

Figure 1. Management of Aortic Graft Infection Collaboration (MAGIC) criteria for aortic graft infection diagnosis. CT = computed tomography; AGI = abdominal aortic graft and endograft infection; FDG PET = fluorodeoxyglucose-positron emission tomography; ESR = erythrocyte sedimentation rate; CRP = C reactive protein. Reproduced with the permission from Lyons *et al.*[6]

Figure 2. Patient flowchart showing inclusion and exclusion of patients. Only patients with an abdominal aortic graft infection were included in this study. MAGIC = Management of Aortic Graft Infections Collaboration.[6]

cases in the primary screening were excluded due to being either wound or peripheral graft infections.

Pre- and post-operative data, including results of microbiological cultures, were retrieved through retrospective case record review using a predetermined protocol.

Objectives and definitions

The main objective was to compare overall survival and re-infection outcomes between RS and SC treatment of abdominal AGI. Secondary objectives were to identify risk factors associated with the overall mortality rate after surgical AGI treatment as well as to map the microbiological aetiology involved. Short and long term survival or mortality was defined as 90 days and five years, respectively.

Due to the retrospective nature of the study, no case selection criteria for the choice of RS vs. SC could be identified. RS was defined as an attempted complete graft excision, including the majority of the infected main body, followed by either EAB or ISR. The RS cohort was used as the comparator and has previously been described in detail and compared in terms of EAB vs. ISR, with similar survival and re-infection outcomes.[17] SC was defined as a graft preserving operation with surgical debridement and or percutaneous drainage of the adjacent infected tissue, and or any endovascular adjunct, with or without partial resection of the aortic graft while leaving at least the majority of one of the limbs, or the main body, of the infected conduit in situ. For endograft infections, patients were categorised to the RS group if any bare metal fixation system was left in situ as long as the endograft fabric was removed.

Graft enteric fistula (GEF) was defined as either a radiological, endoscopic, or peri-operative finding of suspected bowel erosion with connection between the intestinal tract and the graft or stent graft fabric, with or without an aorto-enteric fistula with communication with the aortic lumen.

The definition of pre-operative comorbidities is provided in Supplementary File 1. Post-operative complications were divided into circulatory complications ($>$ 24 hours of vasopressor treatment), respiratory complications ($>$ 24 hours of invasive ventilation), acute kidney injury (dialysis), amputation (above the ankle), multi-organ dysfunction syndrome (progressive organ dysfunction in at least two major organs as well as a documented diagnosis from a critical care physician), myocardial infarction (elevated troponins and chest pain or ischaemic electrocardiogram changes), abdominal compartment syndrome (intra-abdominal pressure $>$ 20 mmHg and associated new organ dysfunction), sepsis (Sepsis II criteria — systemic inflammatory response syndrome due to suspected infection[19]), lower extremity compartment syndrome (need for fasciotomy), stroke (cerebrovascular event with neurological deficit lasting $>$ 24 hours), mesenteric ischaemia (clinical diagnosis and or need for bowel resection), and pulmonary embolism (radiological evidence).

As neither MAGIC, nor any other criteria, covers the diagnosis of recurrent infection in the aortic graft left in situ, this diagnosis was left at the discretion of the physician reviewing the case records using laboratory, microbiological, radiological, and clinical data.

Survival outcomes were assessed through cross matching of unique patient identifiers with the Swedish population registry, ensuring a 100% survival follow up index for

Swedish residents. Deaths were not censored for any analysis unless specifically specified.

Microbiology

Microbiological findings from blood and graft cultures were identified through retrospective culture review. Possible contaminants were defined as normal skin flora according to the MAGIC criteria (e.g., coagulase negative staphylococci). Polymicrobial growth was defined as more than two identified species. For the feasibility of retrospective data collection, only antimicrobial treatments used after hospital discharge or 30 days post-operatively were included. Prolonged antimicrobial therapy was defined as sustained therapy for more than three months.

Statistical analysis

Data were assessed for normality using histograms and the Shapiro—Wilk test. Comparisons were made using the χ^2 test of homogeneity for dichotomous variables and one way analysis of variance (ANOVA) for continuous variables. If the respective test assumptions were not met, Fisher's exact test and Mann—Whitney U test were used when appropriate.

Overall survival was assessed using Kaplan—Meier survival curves, and differences in survival were analysed using the log rank test. Statistical analyses were truncated at the time when the standard deviation reached > 10%, or when the number of remaining cases fell to < 10.

Factors associated with death after surgery for AGI were analysed in binary logistic regression and Cox regression models. Binary logistic regression was used for 90 day survival owing to the follow up being restricted to the same period with a dichotomous outcome without any censored events. Some continuous variables, including age and renal function, were dichotomised due to non-proportional distribution of the hazard ratio (HR) and to aid clinical interpretation. Effect size was measured using odds ratio (OR) or HR with 95% confidence interval (CI).

Three regression models were created with the following aims. (1) To determine the impact of choice of operative method (SC vs. RS) on overall survival. A Cox regression was used adjusting for pre-operative confounders only. (2) To assess factors associated with early mortality, deaths within 90 days of surgery were included. Peri-operative and post-operative factors were included to identify possible risk factors. (3) To assess factors associated with long term mortality (5 years), deaths occurring within 90 days were excluded to avoid diluting long term risk factors with factors associated with early death. Peri-operative and post-operative factors were included.

In the Cox regression models, date of surgery for AGI (RS or SC) was used as baseline. Clinical follow up data were collected up to 31 January 2018. Mortality data were re-evaluated during the study, and participants could accrue survival follow up time until date of death or 31 December 2022, whichever occurred first. Factors included in multi-variable models were pre-specified according to clinical reasoning, and an attempt was made to limit the number of factors to one per five events analysed to reduce over-fitting.[20] Time trends were analysed by dividing the study period into early (1995 — 2008) and late (2009 — 2017) phases.

A two sided p value of < .05 was considered statistically significant. IBM SPSS Statistics versions 26.0 and 27.0 (IBM Corp., Armonk, NY, USA) were used for data processing and statistical analyses.

The study was approved by the regional ethics committee in Uppsala, Sweden [Dnr 2014/078].

RESULTS

Population and time trends

One hundred and sixty-nine patients, including 129 (76.3%) with graft infections and 40 (23.7%) with endograft infections, who met the MAGIC criteria with a surgically treated abdominal AGI were identified during the study period. An RS strategy was used in 126 patients and a SC strategy in 43 patients. Among the 40 endograft infections, 14 (35%) were treated with SC and 26 (65%) with RS.

In the RS group, 71 patients were treated with EAB and 55 with ISR [24 NAIS, 10 silver impregnated grafts, 10 antibiotic soaked grafts, four arterial autografts, and 7 miscellaneous (mainly untreated standard grafts)]. Six patients were treated with an emergency endovascular bridge prior to the radical treatment. Data on suprarenal metal or fixation left in situ were available for 19/26 of the RS treated endograft AGIs. Among these 19 cases, three patients had suprarenal metal or fixation left in situ. The RS cohort has previously been described in detail elsewhere.[17]

Within the SC treated group, 19 patients (44%) were treated with surgical debridement of infected peri-prosthetic tissue and/or percutaneous drainage alone without any partial graft resection, 19 patients (44%) were treated with a partial graft or endograft resection (no main body resections were recorded), and five patients (12%) were treated with an endovascular adjunct alone.

There was no difference in treatment strategy comparing the early study period (SC 22.5% vs. RS 77.5%) with the later study period (SC 28.1% vs. RS 71.9%) ($p = .40$).

Median clinical follow up was 5.1 years for the SC cohort and 3.9 years for the RS cohort ($p = .18$).

Baseline characteristics

Baseline characteristics and symptoms are presented in Table 1. The pathology preceding the primary AGI treatment in the total cohort was primary aneurysmatic disease (62.7%), aorto-iliac occlusive disease (21.7%), mycotic aneurysm (9.6%), inflammatory aneurysm (5.4%), and unknown (0.6%). Some 22.0% of the entire cohort had a ruptured aortic or iliac aneurysm as the indication for primary aortic repair. The median time from primary aortic surgery to the AGI intervention was longer in the SC group (SC 4.3 years vs. RS 2.4 years; $p = .049$).

Table 1. Comparison of baseline characteristics and comorbidities between semi-conservative (SC) and radical surgery (RS) repair among 169 aortic graft infection patients included in the study

Baseline characteristic	SC (n = 43)	RS (n = 126)	p value
Median age (IQR) − y	73.6 (67.1, 78.4)	70.0 (65.3, 75.7)	.039
Male sex	35 (81.4)	104 (82.5)	.98
Hypertension	28 (65.1)	79 (65.3)	1.0
Smoking	7 (16.3)	48 (40.3)	.005
Chronic kidney disease	9 (20.9)	13 (10.6)	.092
Diabetes	8 (18.6)	10 (8.1)	.062
Heart failure	10 (23.3)	9 (7.4)	.010
Coronary artery disease	26 (60.5)	37 (30.6)	<.001
Lung disease	8 (18.6)	13 (10.7)	.19
Circulatory shock	7 (16.3)	11 (8.7)	.19
ASA score >3 *	22 (53.7)	33 (27.3)	.002
Graft enteric fistula	23 (53.5)	62 (50.4)	.73

Data are presented as n (%) unless otherwise stated.
Data are incomplete or missing for some of variables, so the total number of patients in each cohort is not always the denominator.
IQR = interquartile range.
* American Society of Anaesthesiologists Physical Status Classification System score.

Table 2. Comparison of post-operative (30 day) complications between 169 patients treated with semi-conservative (SC) or radical surgery (RS) repair for aortic graft infections

Complication	SC (n = 43)	RS (n = 126)	p value
Mesenteric ischaemia	4 (10.0)	9 (8.1)	.71
Acute limb ischaemia	5 (12.5)	9 (8.1)	.53
Multi-organ dysfunction syndrome	8 (18.6)	25 (21.9)	.75
Acute kidney injury	3 (7.5)	17 (14.8)	.21
Respiratory	11 (27.5)	32 (28.3)	.90
Circulatory	11 (27.5)	28 (25.2)	.71
Myocardial infarction	2 (5.0)	7 (6.1)	.78
Abdominal compartment	1 (2.3)	3 (2.5)	.95
Sepsis	8 (18.6)	13 (11.7)	.32
Lower extremity compartment syndrome	0 (0)	4 (3.5)	.57
Stroke	0 (0)	2 (1.7)	1.0
Pulmonary embolism	0 (0)	3 (2.7)	.57
Median ICU stay (IQR) − h	30 (13−119)	60 (24−107)	.074
Median hospital stay (IQR) − d	25 (14−37)	24 (15−37)	.58

Data are presented as n (%) unless otherwise stated.
Data are incomplete/missing for some of variables, so the total number of patients in each cohort is not always the denominator.
ICU = intensive care unit; IQR = interquartile range.

Patients undergoing SC had a higher frequency of heart failure (SC 23.3% *vs.* RS 7.4%; *p* = .010) and coronary artery disease (SC 60.5% *vs.* RS 30.6%; *p* < .001). Additionally, the frequency of an ASA score > 3 was higher in the SC group (SC 53.7% *vs.* RS 27.3%; *p* = .002). The presence of a GEF was similar between the groups (SC 53.5% *vs.* RS 50.4%; *p* = .73).

The clinical presentation at the time of AGI intervention is presented in Supplementary File 2. Groin infections (SC 34.9% *vs.* RS 16.4%; *p* = .011) and deep abscesses (SC 30.2% *vs.* RS 14.9%; *p* = .027) were more common in the SC group.

Outcomes and survival

Thirty day post-operative complication rates are shown in Table 2. The complication rates as well as median intensive care unit and hospital length of stay were similar comparing SC with RS.

Uncensored data for at least one year survival were available for all patients. No difference in unadjusted survival was noted comparing the two groups (Table 3; Fig. 3). There was, however, a non-significant trend towards inferior unadjusted Kaplan−Meier estimated five year survival for the SC cohort (SC 30.2% *vs.* RS 48.4%; *p* = .066).

In a subgroup analysis of SC patients, there was a trend towards worse Kaplan−Meier estimated five year overall survival (SC with GEF 21.7% *vs.* SC without GEF 40.1%; *p* = .097) in patients with a GEF (Fig. 4). No overall survival difference was observed when comparing SC patients with *vs.* without partial graft resection (Supplementary File 3).

When adjusting for pre-defined peri-operative confounders, choice of treatment with RS compared with SC did not impact overall five year mortality in a Cox regression model (HR 1.0, 5% CI 0.6 − 1.5; *p* = .94) (Table 4).

Table 5 shows a binary logistic regression identifying risk factors for 90 day mortality, while including post-operative events. Advanced age defined as ≥ 75 years (OR 3.0, 95% CI 1.3 − 7.0) and a high ASA score > 3 (OR 4.1, 95% CI 1.7 − 10.2) were independent risk factors associated with 90 day death. SC *vs.* RS did not have an impact on 90 day death (OR 0.4, 95% CI 0.2 − 1.3; *p* = .14).

Table 6 shows a Cox regression identifying risk factors for overall late death, including post-operative events, while excluding 90 day death. Advanced age defined as ≥ 75 years (HR 2.0, 95% CI 1.2 − 3.2) and chronic kidney disease (HR 2.0, 95% CI 1.0 − 3.8) were independent risk factors associated with overall five year mortality. Once again, the choice of SC *vs.* RS was not associated with long term mortality.

Crude long term recurrent or persistent graft infection was more common in the SC group (SC 45.4% *vs.* RS 19.3%; *p* < .001). The frequency of recurrent infections in the GEF *vs.* no GEF subgroups was similar both for the SC (50.0% *vs.* 43.5%; *p* = .67) and RS (17.2% *vs.* 21.4%; *p* = .57) cohorts. The frequencies of amputation above the ankle and of overall re-interventions were similar (Table 7). Only two patients in the SC group had an attempted salvage RS performed during follow up.

In a binary logistic analysis, adjusting for advanced age, presence of GEF, graft *vs.* stent graft infection, and SC *vs.* RS, the choice of SC treatment was the only identified independent risk factor for recurrent or persistent graft

Table 3. Overall survival after aortic graft infection repair for 169 patients comparing semi-conservative (SC) with radical surgery (RS) repair

Survival	Survival rate		p value
	SC (n = 43)	RS (n = 126)	
30 day	83.7 (72.2−95.2)	79.4 (72.2−86.5)	.53
90 day	76.7 (63.6−89.9)	75.4 (67.8−83.0)	.86
1 year	58.1 (42.8−73.5)	69.1 (60.9−77.2)	.19
5 year *	30.2 (16.5−43.9)	48.4 (29.7−47.1)	.066

Data are presented as percent survival rate (95% confidence interval).
* Unadjusted Kaplan−Meier estimated 5-year survival.

No. at risk
— Semi-conservative   43   25   21   18   15   13
— Radical surgery   126   87   81   72   65   60

Figure 3. Cumulative Kaplan−Meier estimate of overall survival of 169 aortic graft infection patients comparing semi-conservative repair with radical surgical repair using log rank test.

infection (OR 4.1, 95% CI 1.8 − 9.2; *p* < .001) (Supplementary File 4). Repeating the analysis for the SC cohort alone, advanced age was independently associated with recurrent or persistent infection (OR 5.2, 95% CI 1.2 − 23.0; *p* = .031) (Supplementary File 5).

In a qualitative analysis of the cohort with a recurrent or persistent graft infection, albeit not systematically collected, 10/42 patients (SC, 7; RS, 3) with a recurrent or persistent graft infection had additional reported information about inadequate debridement at the time of surgery and 7/42 (SC, 3; RS, 4) had an antimicrobial switch after culture results during the inpatient stay owing to inadequate primary empirical treatment.

Microbiology and antimicrobial treatment

Microbiological data were obtained in 159/169 patients (94.1%). Excluding possible contaminants, 118 patients (74.2%) had positive cultures with a median number of pathogens of 1 (interquartile range [(IQR)] 0, 3). In the subgroup of patients with a GEF, 81.7% were culture positive with a median number of species of 2 (IQR 1, 3). On blood, peri-graft, or explanted graft cultures in the total cohort, the frequency of identified Gram positive species was 53.5% for SC *vs.* 47.6% for RS (*p* = .63). The frequency of polymicrobial growth, defined as more than two species identified, was 28.6% for SC *vs.* 23.9% for RS (*p* = .55).

In the total cohort, *Candida* or fungal species on blood, graft, or endograft cultures were more common in patients with a GEF (30.5%) *vs.* without a GEF (9.1%) (*p* < .001). The frequency of *Candida* positive cultures did not differ when comparing the cohort treated with SC (19.0%) *vs.* RS (20.5%) (*p* = .84). Supplementary File 6 shows detailed microbiological culture data of the SC cohort.

A total of 135 patients were alive at 30 days and were eligible for data collection on antimicrobial therapy. Data were obtainable in 109 (80.7%) of the patients. Among patients who survived the initial 90 days after surgery for AGI, the frequency of prolonged antimicrobial treatment (defined as > 3 months) was more common in the SC group (84.0%) than the RS group (50.0%) (*p* < .001). In a Cox regression model, prolonged antimicrobial therapy was not associated with any survival benefit when adjusting for surgical treatment method (Supplementary File 7).
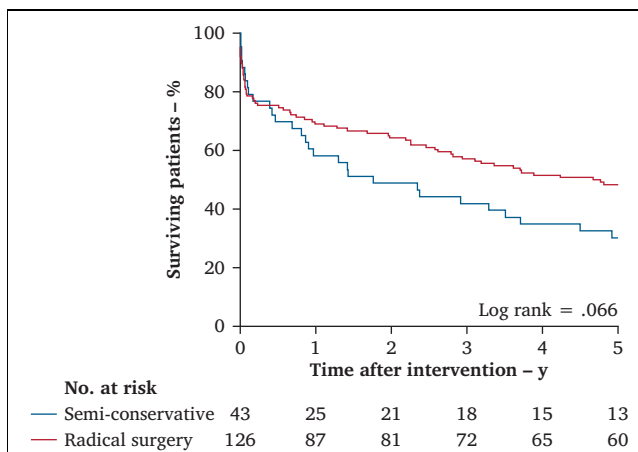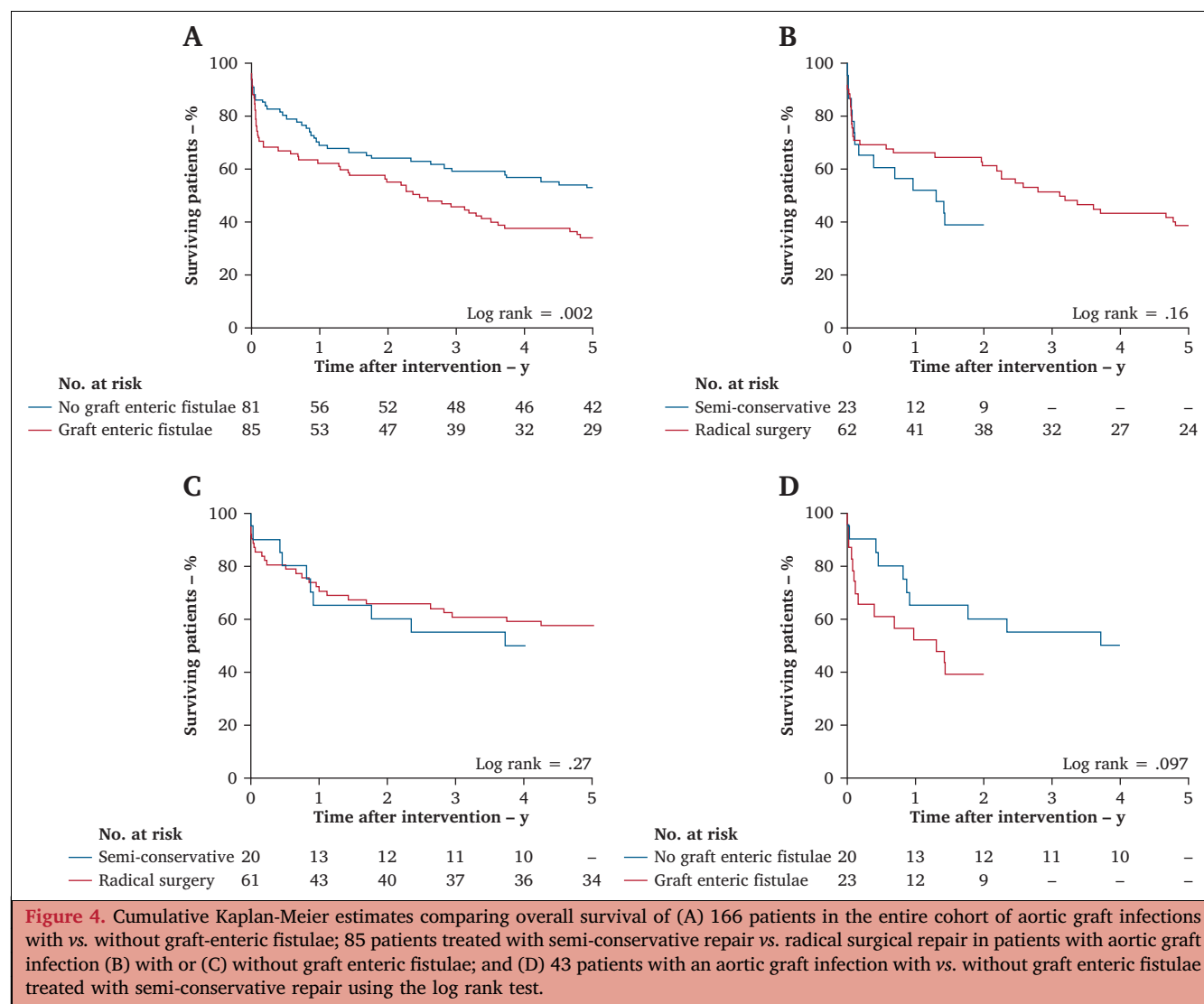
DISCUSSION

This study analysed the outcomes of a Swedish nationwide AGI cohort comparing patients selected for a semi-conservative (SC), graft preserving strategy *vs.* patients selected for traditional radical surgery (RS) with ISR or EAB. In the current cohort, adjusted long term survival was similar for patients undergoing SC treatment compared with RS, especially in patients without GEF. This suggest that the SC strategy may be an adequate choice in selected high risk surgical patients with AGI without GEF, at the cost of prolonged antimicrobial treatment and risk of re-infection.

The one year survival outcome of 58% after SC repair is consistent with the current literature.[21,22] However, few studies have reported long term outcomes beyond this. The major strength of the study is the national population based design, prospective registration, and a survival follow up index close to 100% resulting in a relatively large SC cohort with minimal loss to follow up compared with the case series in the literature.

There was a non-significant trend towards worse unadjusted short and long term survival and five year survival among patients treated with SC (30.2%) *vs.* RS (48.4%). This difference was, however, ameliorated when adjusting for baseline confounders in the Cox regression (Table 4). The difference in survival between SC and RS was numerically largest, to the disadvantage of SC, in the subgroup of patients with a GEF. Albeit non-significant, the large numerical difference indicates that there potentially can be an issue of power and risk of type II statistical error in some of the analyses. Additionally, the decision to include graft enteric erosions (enteric communication to the infected aortic graft or endograft without vascular lumen connection) in the GEF definition might have contributed both to the high frequency of observed GEFs and a reduced impact on survival outcomes. In those without a GEF, the overall unadjusted survival outcome was comparable (Fig. 4C). These trends are in line with recent findings from Janko *et al* showing worse overall survival in patients treated with partial

Figure 4. Cumulative Kaplan-Meier estimates comparing overall survival of (A) 166 patients in the entire cohort of aortic graft infections with *vs.* without graft-enteric fistulae; 85 patients treated with semi-conservative repair *vs.* radical surgical repair in patients with aortic graft infection (B) with or (C) without graft enteric fistulae; and (D) 43 patients with an aortic graft infection with *vs.* without graft enteric fistulae treated with semi-conservative repair using the log rank test.

resection of infected prosthesis, particularly in the context of a GEF.[21] Additionally, the observed 90 day survival of approximately 70% for patients with a GEF (both SC and RS) is similar to previous results from Kahlberg *et al* who reported a peri-operative survival of approximately 60% for both conservatively and surgically treated AGI patients with a GEF.[23]

The one and five year survival rates of the overall AGI cohort in this study of approximately 80% and 40%, respectively, highlight the adverse nature of the disease. In comparison, the survival rates are much more similar to that of primary ruptured abdominal aortic aneurysm (AAA) repair (one year, 65 — 75%; five year, 45 — 55%) compared with primary elective AAA repair (one year, 90 — 95%; five year, 75%).[24,25]

As expected, patients treated with SC were more prone to recurrent graft infections (SC 45.4% *vs.* RS 19.3%) (Table 7). This difference persisted when adjusting for potential confounders (OR 4.1) (Supplementary File 4). This

may have contributed to the observed increased frequency of prolonged antimicrobial therapy given to the SC cohort. Previous studies have shown an association with prolonged antimicrobial therapy and improved overall long term survival in AGI patients treated with EAB or ISR.[17,26] However, this was not observed in the current study including an SC cohort. A probable explanation is the high collinearity between SC treatment, recurrent graft infection, and the decision to prolong antimicrobial therapy. Lacking intention to treat data on antimicrobial therapy, this confounding cannot be adjusted for. Additionally, lacking data on time to diagnosis of recurrent infection following AGI repair, it was not possible to differentiate persistent *vs.* actual recurrent infections. The qualitative analysis of the recurrent or persistent infections is limited by the retrospective design and data protocol of the study, but given the reported numbers of inadequate debridement and empirical antimicrobial miss rate in the SC cohort with recurrent or persistent infections, it is likely that these factors are

Table 4. Multivariable Cox regression of 169 patients identifying impact of operative method on overall (5 year) mortality after radical surgery repair for an aortic graft infection adjusting for predefined confounders

Factor	HR (95% CI)	p value
Age ≥ 75 years	2.0 (1.4–3.0)	<.001
Coronary artery disease	1.0 (0.7–1.5)	.97
Chronic kidney disease	1.3 (0.8–2.3)	.28
Pulmonary disease	0.8 (0.5–1.4)	.53
ASA score > 3 *	1.9 (1.2–2.9)	.006
Semi-conservative repair †	1.0 (0.6–1.5)	.94
Graft–enteric fistula	1.4 (1.0–2.0)	.087
Shock	0.9 (0.5–1.7)	.85
Time period, early vs. late ‡	0.8 (0.3–1.9)	.63

HR = hazard ratio; CI = confidence interval.
* American Society of Anaesthesiologists Physical Status Classification System score.
† Radical surgery used as index comparator.
‡ Time period 1995 − 2008 versus 2009 − 2017.

important to reduce the risk of recurrent infection. Appropriate antimicrobial treatment has previously been shown by Sixt et al to be associated with reduced mortality in patients with vascular graft infections.[27]

The presence of *Candida* species on blood, graft, or endograft cultures was more common in patients with a GEF and occurred in 30%. Similar frequencies have been reported in recent AGI studies.[28] It is reasonable to assume the presence of a GEF when *Candida* species are identified on blood cultures in a patient with a suspected AGI. When a GEF is identified, a low threshold should be maintained to start systemic antifungal treatment with echinocandins. Additionally, only blood or peri-operative tissue or graft samples were included in the microbiological analysis, and there were no data on the use of 16S ribosomal ribonucleic acid polymerase chain reaction (16S rRNA-PCR). The

Table 5. Multivariable binary logistic regression of 169 patients to identify risk factors for 90-day mortality after aortic graft infection repair adjusting for predefined confounders

Factor	OR (95% CI)	p value
Age ≥ 75 years	3.0 (1.3–7.0)	.011
Coronary artery disease	2.1 (0.9–5.0)	.11
Chronic kidney disease	0.7 (0.2–2.5)	.58
Pulmonary disease	0.4 (0.1–1.5)	.19
ASA score > 3 *	4.1 (1.7–10.2)	.002
Semi-conservative repair †	0.4 (0.2–1.3)	.14
Graft–enteric fistula	1.4 (0.6–3.3)	.48
Post-operative dialysis	2.3 (0.7–7.8)	.17
Time period, early vs. late ‡	0.9 (0.4–2.0)	.74

OR = odds ratio; CI = confidence interval.
* American Society of Anaesthesiologists Physical Status Classification System score.
† Radical surgery used as index comparator.
‡ Time period 1995 − 2008 versus 2009 − 2017.

frequency and aetiology of pathogens identified islikely to differ with the implementation of such adjuncts.

Limitations

The major limitation of the study is the partial retrospective data collection and persistent heterogeneity in the SC cohort. For feasibility reasons, data acquisition had to be simplified and thus some data were not retrievable, such as case selection criteria for RS vs. SC, the anatomical features of a diagnosed GEF, frequency of adverse events associated with prolonged antimicrobial treatment as well as anatomical AGI staging according to Samson et al or Szilagyi et al.[29,30] Additionally, the rarity of the disease, even in a nationwide setting with a long study period, introduces issues with statistical power. Type II errors are possible in the survival analyses given the large confidence intervals and borderline event per-variable ratios. The power issues restricted further subgroup analyses, such as additional comparisons of the impact of different microbiological agents on re-infection, and SC vs. RS in the limited endograft AGI subgroup.

Additionally, the generalisability of the study results could be affected by geographic practice bias. Currently > 70% of the elective annual abdominal aortic caseload in Sweden is treated with endovascular strategies.[31] The overall decreased open repair volume over time could potentially negatively impact the outcome of complex aortic AGI repair, more so in the presence of a GEF.

It is expected that there is great heterogeneity between the SC and RS cohorts in terms of baseline comorbidities, as SC treatment of an AGI is in general seen as a secondary treatment option in the sick patient not fit for RS. Lacking intention to treat data, it was not possible to discern whether some SC interventions were planned as bridging treatments to future RS that ultimately failed. This, together with the higher frequency of comorbidities, could partly explain the unexpected similarity in the early (90 day) mortality rate comparing SC and RS. However, as the frequency of SC did not change over the study period, the decision making process is likely to have been consistent over time. Additionally, the definition of SC treatment ranging from endovascular adjuncts alone to partial (non-main body) resection introduces significant treatment heterogeneity in this cohort. Partial (non-main body) resection is an invasive treatment strategy. However, it differs greatly from RS both in terms of prosthetic material left in situ at risk of recurrent infection and the surgical stress on the patient. As such, a decision was made to include partial resection in the SC definition. Due to the small cohort size, a more detailed subgroup analysis of the SC cohort was not possible.

One potential source of bias is the lack of data on time from symptom onset to AGI intervention. The difference in median time from index surgery to AGI intervention (SC 4.3 years vs. RS 2.4 years) could imply some delay to surgical intervention in the SC group. While speculative, this could introduce lead time bias affecting the outcome of the SC

Table 6. Multivariable Cox regression, with 90-day mortality excluded, of 169 patients identifying risk factors associated with overall (5 year) mortality after radical surgical repair for an aortic graft infection adjusting for predefined confounders

Factor	HR (95% CI)	p value
Age $\geq$ 75 years	2.0 (1.2−3.2)	.009
Coronary artery disease	1.2 (0.7−1.9)	.55
Chronic kidney disease	2.0 (1.0−3.8)	.040
Pulmonary disease	1.0 (0.5−1.9)	.92
ASA score > 3 *	1.5 (0.9−2.6)	.13
Semi-conservative repair †	0.6 (0.4−1.0)	.055
Graft−enteric fistula	1.3 (0.8−2.0)	.29
Post-operative dialysis	1.6 (0.8−3.5)	.19
Time period, early vs. late ‡	1.6 (0.8−3.0)	.32

HR = hazard ratio; CI = confidence interval.
* American Society of Anaesthesiologists Physical Status Classification System score.
† Radical surgery used as index comparator.
‡ Time period 1995 − 2008 versus 2009 − 2017.

patients. Furthermore, there was a higher frequency of observed heart failure, coronary artery disease, and high ASA score in the SC cohort, suggesting that frailty and comorbidities were the main contributors in the decision making. While these factors were accounted for in the Cox regression, residual confounding is likely, ultimately negatively impacting the outcome of SC compared with RS.

In the current dataset, it was not possible to elucidate the time resolution in terms of when the GEF was diagnosed within the SC group. Many GEFs were likely to exist at the time of diagnosis and or primary surgical SC therapy, some may have developed during follow up as a consequence of re-infection or failed SC therapy. Future studies are needed to clarify the frequency of secondary development of GEFs in SC therapy failure.

While recurrent AGI was more common in the SC group, the diagnosis and comparison of frequencies is made difficult by the lack of a uniform definition. Currently, the MAGIC criteria do not cover this area. Moving forward, there is a need for a homogeneous and structured definition of treatment success or infection resolution as well as recurrent infection.

Despite these limitations, the study adds important data on the outcome of SC treated AGI patients, which is currently limited. SC treatment appears to be a reasonable choice, with acceptable outcomes in a comorbid AGI cohort unfit for RS, especially in the absence of a GEF. This is an important finding as, on a global scale, more and more complex thoraco-abdominal aortic aneurysm disease is being treated by fenestrated and branched endograft solutions, ultimately being the conduit at risk of future infections.[32] It is likely that many of these future endograft AGI patients will be unfit for RS repair given the extent of surgery needed. Given the rarity of the disease, the expected need for more SC based treatment in the future, and scarcity of available evidence, it is important to make all current data available. In the future, more research is needed on SC treated endograft AGI to guide treatment strategies.

Conclusion

In this nationwide, multicentre AGI cohort, there was a trend towards worse unadjusted overall survival for SC compared with RS, particularly in the presence of a GEF. This was largely explained by higher age and the presence of more comorbidities, including a higher frequency of high peri-operative ASA score in the SC group. When adjusting for these confounders, there was no significant difference in long term survival between SC and RS, suggesting that SC may be a reasonable treatment strategy in selected patients without a GEF. The frequency of recurrent infections remained high among SC treated patients, which warrants the need for close surveillance and prolonged or lifelong antimicrobial therapy.

CONFLICT OF INTEREST STATEMENT AND FUNDING

None.

APPENDIX A. SUPPLEMENTARY DATA

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ejvs.2023.06.019.

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Table 7. Comparison of crude rates of long term complications of 169 aortic graft infection patients during clinical follow up after semi-conservative (SC) versus radical surgery (RS) repair

Complication	SC (n = 43)	RS (n = 126)	p value
Median follow up (IQR) − y *	5.1 (3.9, 14.6)	3.9 (3.2, 9.5)	.18
Recurrent graft infection	45.4	19.3	<.001
Anastomosis dehiscence or stump blowout	2.3	10.5	.10
Amputation	9.3	4.3	.23
Re-intervention	23.3	26.3	.70

Data are presented as percentage unless stated otherwise.
IQR = interquartile range.
* Clinical follow up among survivors (in years).

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