A preoperative supervised exercise programme potentially improves long-term survival after elective abdominal aortic aneurysm repair

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A preoperative supervised exercise program potentially improves long-term survival after elective abdominal aortic aneurysm repair

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ABSTRACT

Objective: A preoperative supervised exercise program (SEP) improves cardiorespiratory fitness and perioperative outcomes for patients undergoing elective abdominal aortic aneurysm (AAA) repair. The aim of this study was to assess the effect of a preoperative SEP on long-term survival of these patients. A secondary aim was to consider long-term changes in cardiorespiratory fitness and quality of life.

Methods: Patients scheduled for open or endovascular AAA repair were previously randomized to either a 6-week preoperative SEP or standard management, and a significant improvement in a composite outcome of cardiac, pulmonary, and renal complications was seen following SEP. For the current analysis, patients were followed up to 5 years post-surgery. The primary outcome for this analysis was all-cause mortality. Data were analyzed on an intention to treat (ITT) and per protocol (PP) basis, with the latter meaning that patients randomized to SEP who did not attend any sessions were excluded. The PP analysis was further interrogated using a complier average causal effect (CACE) analysis on an all or nothing scale, which adjusts for compliance. Additionally, patients who agreed to follow-up attended the research center for cardiopulmonary exercise testing and/or provided quality of life measures.

Results: ITT analysis demonstrated that the primary endpoint occurred in 24 of the 124 participants at 5 years, with eight in the SEP group and 16 in the control group ($P = .08$). The PP analysis demonstrated a significant survival benefit associated with SEP attendance (4 vs 16 deaths; $P = .01$). CACE analysis confirmed a significant intervention effect (hazard ratio, 0.36; 95% confidence interval, 0.16-0.90; $P = .02$). There was no difference between groups for cardiorespiratory fitness measures and most quality of life measures.

Conclusions: These novel findings suggest a long-term mortality benefit for patients attending a SEP prior to elective AAA repair. The underlying mechanism remains unknown, and this merits further investigation. (J Vasc Surg 2024;79:15-23.)

Keywords: Abdominal aortic aneurysm; Supervised exercise therapy; Prehabilitation

An abdominal aortic aneurysm (AAA) is the abnormal expansion of the abdominal aorta to a diameter of ≥3 cm or 1.5 times its normal anteroposterior diameter.[1,2] National screening data from the United Kingdom (UK) in 2019 showed that approximately 1% of screened men had an AAA,[3] although the true incidence is likely to be higher, as many AAAs are identified incidentally on imaging.

Most AAAs are asymptomatic and grow insidiously, and there is a direct relationship between aneurysm size, growth rate, and rupture rate.[4] Mortality rates of up to 68% are reported following AAA rupture, and consequently most international guidelines recommend regular monitoring of AAA expansion.[5-7]

When an AAA reaches ≥5.5 cm or is >4.0 cm and growing rapidly, repair is indicated, if the patient is suitably fit for surgery.[1,8] Major vascular surgery increases metabolic demand, and patients require adequate cardiovascular fitness to withstand this in the intraoperative and perioperative phase.[9] Patients' potential capability to

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Presented at the 2023 Vascular Annual Meeting of the Society for Vascular Surgery, National Harbor, Maryland, June 14-17, 2023; Presented at the 2020 Annual Scientific Meeting [virtual] of the Vascular Society of Great Britain and Ireland, November 24-27, 2020.

Additional material for this article may be found online at www.jvascsurg.org.

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The editors and reviewers of this article have no relevant financial relationships to disclose per the JVS policy that requires reviewers to decline review of any manuscript for which they may have a conflict of interest.

0741-5214

https://doi.org/10.1016/j.jvs.2023.09.004

handle this stress can be measured via the gold-standard method of cardiopulmonary exercise testing (CPET). Indeed, certain CPET parameters are predictive of both short- and long-term outcomes for patients undergoing AAA repair, namely peak oxygen uptake ($\dot{V}O_{2Peak}$), oxygen uptake at the anaerobic threshold (AT), and the ventilatory equivalents for carbon dioxide at the AT.[10,11] CPET is advocated by the National Institute for Health and Care Excellence in the preoperative period if it will inform decision-making about whether a patient is fit for major vascular surgery.[1] In addition, participation in a supervised exercise program (SEP) prior to AAA repair can improve these parameters and further reduce the risk of complications.[12,13] A 6-week SEP infers significant improvements in $\dot{V}O_{2Peak}$ and AT,[12] and a randomized controlled trial (RCT) confirmed that SEP reduces short-term postoperative complications and length of hospital stay after AAA repair.[13] However, SEP had no impact on short-term mortality.

The longer-term mortality impact of a preoperative SEP is yet to be established in patients undergoing AAA repair, and, given that AAA repair is undertaken when patients are mostly asymptomatic, with the aim of prolonging life, this is an important prospect.

Should SEP participation infer a long-term survival benefit, the drivers of this may be related to maintained levels of increased cardiorespiratory fitness and/or quality of life. Therefore, the aim of this study was to conduct a long-term follow-up of the aforementioned RCT to ascertain whether a preoperative SEP provides a long-term survival benefit for patients undergoing elective AAA repair. A secondary aim was to consider whether patients who attended a preoperative SEP had higher levels of cardiorespiratory fitness and quality of life at long-term follow-up, when compared with the control group.

ARTICLE HIGHLIGHTS

- **Type of Research:** Randomized controlled trial, long-term follow-up
- **Key Findings:** In a randomized controlled trial of 124 patients, attending a preoperative supervised exercise program was associated with a 5-year mortality benefit, following elective abdominal aortic aneurysm repair.
- **Take Home Message:** Attending a preoperative supervised exercise program prior to elective abdominal aortic aneurysm repair is associated with a 5-year mortality benefit, compared with standard treatment.

METHODS

Study design and procedures. This study is a long-term follow-up of a previously published single-center prospective RCT performed at a UK tertiary vascular unit.[13]

In 2019, institutional research and development approval was gained so that data from the preliminary RCT database could be utilized alongside electronic hospital systems, to establish whether those enrolled in the trial were still alive. Additionally, General Practices were contacted to provide any missing information for patients that had no recorded cause of death or notable changes in health.

Further ethical approval was obtained from a local NHS research ethics committee (North East—Tyne & Wear South; 21/NE/0086) to contact patients who were still alive to invite them to attend for a one-off visit to complete quality of life (QoL) questionnaires and undergo a repeat CPET. Those who declined this visit were asked to complete the QoL questionnaires either by return mail or over the telephone. All patients provided informed consent and those who completed the questionnaires telephonically or via mail were sent a copy of the consent form, which was completed and returned. In some cases, consent was provided verbally.

CPETs were performed in accordance with published guidance,[14,15] using an individualized ramp-based cycle protocol. Participants were initially screened for contraindications to CPET and were continuously monitored for any indications for termination. Each test was preceded by a 3-minute rest period, followed by a 3-minute onloaded phase. This was followed by a progressive individualized ramp protocol designed to induce volitional exhaustion within 8 to 12 minutes, concluding with a recovery period. Patients were encouraged to maintain 65 to 70 rpm throughout and were encouraged to give a maximal effort, until volitional fatigue was reached. Monitoring continued from the beginning of the rest period to the end of recovery via 12-lead electrocardiogram (ECG), blood pressure, oxygen saturation, and rating of perceived exertion. Breath-by-Breath gas analysis was also performed (MedGraphics Ultima2 Medgraphics) to allow determination of cardiorespiratory fitness parameters.

All tests were performed by the lead author (S.S.) and supervised by an experienced, registered clinical exercise physiologist who leads a CPET service for this patient population (S.P.).

Patients and interventions. Full details of the recruited patients and allocated interventions have been reported previously.[13] Briefly, participants undergoing elective open or endovascular AAA repair were recruited and randomized to a thrice weekly, 6-week SEP or standard management (non-SEP; control).

Outcomes and analysis. The primary endpoint was all-cause mortality. Secondary outcomes included measures of cardiorespiratory fitness, specifically peak oxygen uptake ($\dot{V}O_{2peak}$), both relative to bodyweight ($mL \cdot kg^{-1} \cdot min^{-1}$) and as a percentage of the predicted value and oxygen uptake at the anaerobic threshold. $\dot{V}O_{2peak}$ was defined as the highest value achieved during exercise or early in recovery, using 30-second averaging. The ventilatory anaerobic threshold was determined using the V-slope and ventilatory equivalents methods.[16,17]

Other secondary outcomes included QoL, measured using the Medical Outcomes Study Short-Form 8 (SF-8) and the EuroQoL EQ-5D-3 L instruments. The SF-8 uses an eight-question tool to provide a score for eight domains with additional physical and mental component summary scores also generated. The EQ-5D-3 L assesses health-related quality of life across five dimensions (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression) using three levels of severity (no problems, some problems, extreme problems). The responses were used to generate single summary index scores by applying the UK value sets. These sets have been obtained via a standardized valuation exercise, whereby a representative sample of the UK general population placed a value on health states using the time trade-off (TTO) and visual analogue scale (VAS) valuation techniques.[18] Therefore, a summary index score was calculated based on both the TTO and VAS value sets. Additionally, patients were asked to rate their overall health on the EQ-5D VAS that ranges from 0 (worst imaginable health state) to 100 (best imaginable health state).

All data was inputted into a dedicated Microsoft Excel database and analyzed using SPSS statistics (IBM, Version 27). Survival was analyzed using Kaplan-Meier survival curves with log rank testing. A *P* value of $< .05$ was deemed statistically significant. Analyses were performed using both an intention to treat (ITT) and per protocol (PP) analysis. PP analysis was used as some patients were randomized to the SEP group but did not attend any sessions, which may have unfairly biased the results. In the PP analysis, these patients were excluded. To further interrogate this, a complier average causal effect (CACE) analysis was performed. For this, the compliance-adjusted intervention effect was calculated with compliance measured on an all-or-nothing scale.[19] That is, for patients in the intervention group, those who did not take on any exercise were regarded as non-compliant, whereas all others were regarded as fully compliant. The output was in the form of a hazard ratio (HR) (with confidence intervals [CIs] and two-sided *P* value) for the effectiveness of the intervention, adjusted for the observed compliance in the SEP group. This analysis was conducted through a Stata command, stcomply, in Stata 16. Technique details on this analysis can be found in Kim and White (2004).[19]

Secondary outcomes are presented as mean $\pm$ standard deviation (SD) with mean change scores $\pm$ SD also presented for differences in QoL scores from baseline and post-surgery to long-term follow-up. Mean difference between groups for these change scores are also presented with 95% CIs. Differences between groups for the absolute long-term follow-up values and the change scores over time were analyzed using independent samples *t*-tests with the significance values set at $< .05$. As these analyses were considered exploratory in nature, adjustment was not made for multiple testing.

RESULTS

All patients included in the analysis of the original RCT were followed-up for the primary endpoint in this study. Therefore, the previously reported baseline characteristics are still relevant [see[13]]. An updated CONSORT diagram is shown in Fig 1.

SEP attendance was variable. Of the 62 participants randomized to SEP, 11 participants did not attend, two participants attended six sessions, eight participants attended nine sessions, two participants attended 10 sessions, eight attended 12 sessions, one attended 14 sessions, four attended 15 sessions, seven attended 16 sessions, one attended 17 sessions, and the remaining 18 patients attended all 18 sessions. The ITT analysis showed that the primary endpoint occurred in 24 of the 124 participants at 5 years, with eight in the exercise group and 16 in the non-exercise group ($P = .08$) (Fig 2).

The PP analysis demonstrated a significant survival benefit for those that were allocated to and attended the SEP. Four of 51 compliant participants in the exercise group died compared with 16 of 62 participants in the non-SEP group ($P = .01$) (Fig 3). The CACE analysis, which adjusts for non-compliance, also showed a significant intervention effect (HR, 0.36; 95% CI, 0.16-0.90; $P = .02$), and there was a clear inverse relationship between the number of exercise sessions attended and mortality (Supplementary Table, online only).

When the analysis was performed based on the type of repair, the ITT analysis demonstrated no significant survival benefit for patients undergoing either open repair or endovascular aneurysm repair (EVAR). For open repair, three of 39 patients died in the exercise group compared with six of 39 patients in the non-exercise group ($P = .29$) (Supplementary Fig 1, online only). For EVAR, five of 23 patients died in the exercise group, compared with 10 of 23 in the non-exercise group ($P = .14$) (Supplementary Fig 2, online only).

However, there remained a trend for a benefit with the PP analysis. For open repair, one of 32 patients died in the exercise group compared with six of 39 patients in the non-exercise group ($P = .09$) (Supplementary Fig 3, online only). For EVAR, three of 16 patients died in the exercise group, compared with 10 of 23 in the non-exercise group ($P = .06$) (Supplementary Fig 4, online only).

We investigated the potential drivers of the benefit demonstrated within the PP analysis, although only a small minority of participants agreed to attend for further CPET (16 total; 11 in the exercise group, and five

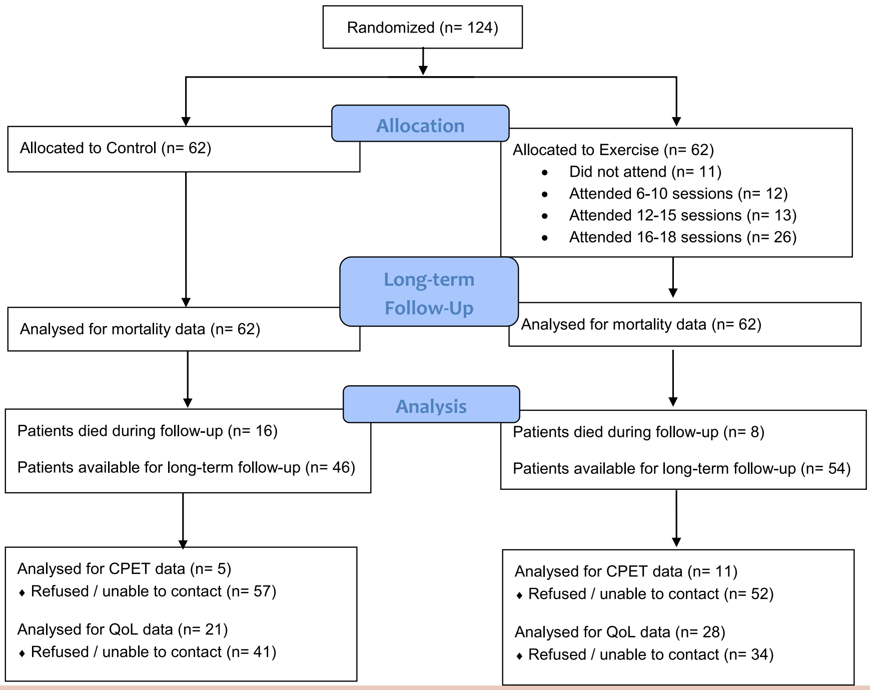

Fig 1. Consolidated Standards of Reporting Trials (CONSORT) diagram. *CPET*, Cardiopulmonary exercise testing; *QoL*, quality of life.

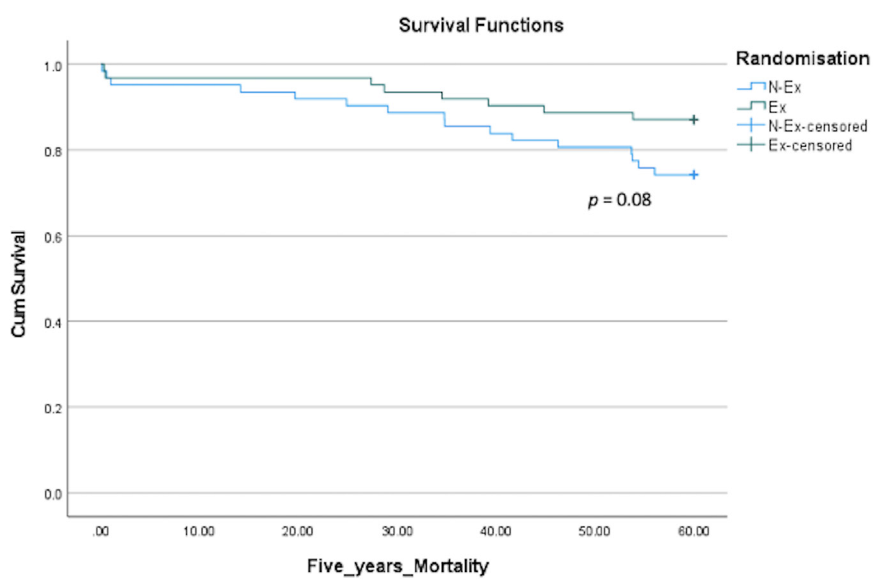

Fig 2. Kaplan-Meier curves for the intention-to-treat (ITT) analysis. *Ex*, Exercise; *N-Ex*, no exercise.

in the control group, 16% of those still alive). A greater proportion (49%) of participants provided QoL data. At long-term follow-up, the exercise group had generally higher absolute SF-8 and EQ-5D-3 L values than the control group (Tables I and II). They also had a lesser decline from baseline in four of the SF-8 domains (physical functioning, role physical, general health, and the physical component summary) and both the EQ-5D-3 L index values, when compared with the control group. However, the control group had a lesser decline in four other SF-8 domains (vitality, role emotional, mental health, and the mental component summary) and in the EQ-5D-3 L patient reported VAS when compared with the exercise group. For the final two domains of the SF-8, the decline was similar between groups (bodily pain and social functioning). Importantly, there was no significant difference between groups for the level of decline across any of the quality of life measures. Only the absolute general

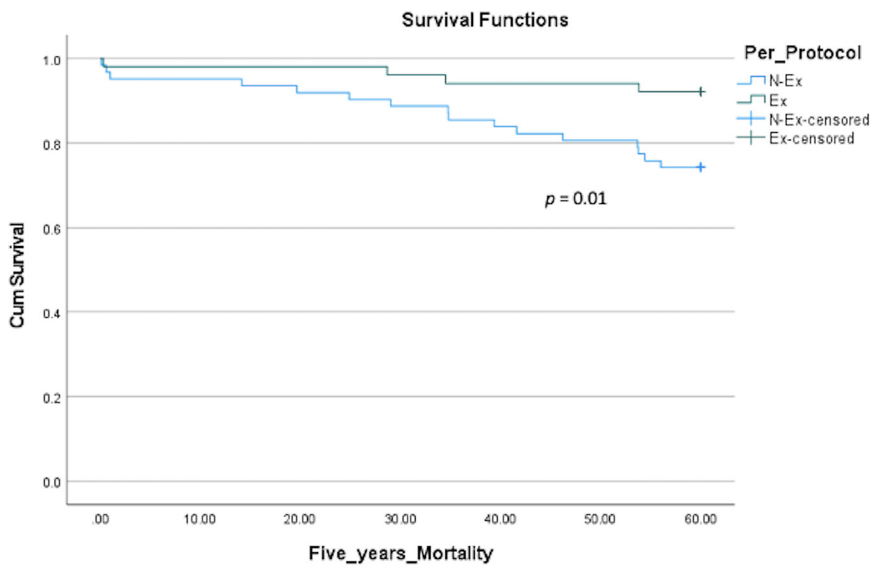

Fig 3. Kaplan-Meier curves for the per-protocol (PP) analysis. *Ex*, Exercise; *N-Ex*, no exercise.

Table I. Changes in quality of life measured by the SF-8 questionnaire, by intervention group, from baseline to long-term follow-up

	Baseline		Long-term follow-up						
	Exercise group (n = 28)	Control group (n = 21)	Exercise group (n = 28)	Change from baseline	Control group (n = 21)	Change from baseline	*P* value (between groups for long-term follow-up value)[a]	Mean difference in change (between groups)	*P* value (change between groups)[a]
Physical functioning	46.1 ± 8.7	47.2 ± 5.7	40.6 ± 8.3	−5.5 ± 8.4	38.7 ± 8.3	−8.5 ± 8.8	.45	3.0 (−2.0 to 8.0)	.23
Role physical	49.4 ± 6.3	48.3 ± 8.0	43.2 ± 10.5	−6.3 ± 9.9	37.9 ± 10.7	−10.4 ± 13.2	.09	4.1 (−2.5 to 10.8)	.21
Bodily pain	53.8 ± 8.9	53.4 ± 8.4	47.1 ± 10.8	−6.6 ± 12.5	46.4 ± 9.9	−7.0 ± 12.3	.81	0.4 (−6.9 to 7.6)	.92
General health	47.7 ± 6.5	46.8 ± 6.2	44.3 ± 9.1	−3.4 ± 9.5	38.7 ± 6.8	−8.1 ± 7.6	**.02**[b]	4.7 (−0.4 to 9.8)	.07
Vitality	52.4 ± 6.8	49.3 ± 6.8	43.4 ± 9.4	−9.0 ± 8.5	43.7 ± 8.7	−5.5 ± 8.7	.91	3.5 (−1.5 to 8.5)	.16
Social functioning	51.0 ± 6.8	51.4 ± 4.6	44.9 ± 9.5	−6.1 ± 9.5	45.7 ± 9.7	−5.7 ± 9.3	.77	0.4 (−5.0 to 5.9)	.88
Role emotional	49.2 ± 4.9	49.0 ± 6.0	45.8 ± 7.1	−3.4 ± 8.3	48.7 ± 6.0	−0.3 ± 8.6	.14	3.1 (−1.8 to 8.0)	.21
Mental health	50.4 ± 8.3	48.8 ± 7.2	49.4 ± 9.8	−1.0 ± 11.0	48.6 ± 9.1	−0.3 ± 9.9	.77	0.8 (−5.4 to 6.9)	.80
Physical component summary	50.0 ± 8.2	49.6 ± 6.0	41.4 ± 10.8	−8.5 ± 9.9	37.3 ± 9.9	−12.3 ± 9.4	.17	3.8 (−1.9 to 9.4)	.18
Mental component summary	52.2 ± 8.4	50.2 ± 7.6	48.7 ± 10.4	−3.5 ± 11.4	50.6 ± 8.6	0.3 ± 10.3	.51	3.8 (−2.5 to 10.2)	.23

Data are presented as mean ± standard deviation or 95% confidence intervals.
Boldface *P* values indicate statistical significance.
[a]Independent sample *t*-test.
[b]$P < .05$.

health value at long-term follow-up was significantly different between groups, favoring the SEP group ($P = .01$).

For post-surgery, the exercise group again had generally higher absolute SF-8 and EQ-5D-3 L values than the control group (Tables III and IV). However, the control group had a lesser decline in a number of SF-8 domains (physical functioning, vitality, role emotional, mental health, and the mental component summary) and the EQ-5D-3 L patient-reported VAS when compared with the exercise group. For the remaining domains (role physical, bodily pain, general health, social functioning, and the physical component summary) and EQ-5D-3 L index scores, the decline was similar between groups.

There was no significant difference between groups for the level of decline across nine of the 10 SF-8 domains or EQ-5D-3 L values, with only the role emotional domain of the SF-8 being significant, favoring the non-SEP group ($P = .03$).

With regards to markers of cardiorespiratory fitness, there were no statistically significant differences between groups at long-term follow-up for $\dot{V}O_{2peak}$ or oxygen uptake at the anerobic threshold, though the values were generally higher for the exercise group (Table V).

Table II. Changes in quality of life measured by the EQ-5D questionnaire, by intervention group, from baseline to long-term follow-up

	Baseline		Long-term follow-up						
	Exercise group (n = 28)	Control group (n = 21)	Exercise group (n = 28)	Change from baseline	Control group (n = 21)	Change from baseline	*P* value (between groups for long-term follow-up value)[a]	Mean difference in change (between groups)	*P* value (change between groups)[a]
EQ-5D index TTO score	0.82 ± 0.21	0.84 ± 0.16	0.68 ± 0.28	−0.13 ± 0.34	0.63 ± 0.30	−0.20 ± 0.26	.57	0.07 (−0.10 to 0.25)	.41
EQ-5D index VAS score	0.80 ± 0.19	0.82 ± 0.17	0.68 ± 0.22	−0.12 ± 0.28	0.63 ± 0.23	−0.19 ± 0.20	.45	0.07 (-0.08 to 0.21)	.37
EQ-5D patient reported VAS	79.39 ± 12.88	74.66 ± 13.63	65.7 ± 21.67	−13.68 ± 22.45	64.76 ± 17.49	−9.52 ± 23.01	.87	−4.15 (−17.33 to 9.02)	.53

TTO, Time trade off; *VAS*, visual analogue scale.
Data are presented as mean ± standard deviation or 95% confidence intervals.
[a]Independent sample *t*-test.

Table III. Changes in quality of life measured by the SF-8 questionnaire, by intervention group, from post-surgery to long-term follow-up

	Post-surgery		Long-term follow-up					
	Exercise group (n = 28)	Control group (n = 21)	Exercise group (n = 28)	Change from post-surgery	Control group (n = 21)	Change from post-surgery	Mean difference in change (between groups)	*P* value (change between groups)[a]
Physical functioning	47.6 ± 7.5	44.1 ± 7.8	40.6 ± 8.3	−7.0 ± 7.6	38.7 ± 8.3	−5.3 ± 10.9	1.7 (−3.6 to 7.0)	.52
Role physical	47.7 ± 8.0	42.6 ± 9.9	43.2 ± 10.5	−4.5 ± 8.4	37.9 ± 10.7	−4.7 ± 13.9	0.2 (3.4 to 7.2)	.96
Bodily pain	52.3 ± 7.1	51.2 ± 9.9	47.1 ± 10.8	−5.1 ± 11.1	46.4 ± 9.9	−4.8 ± 14.8	0.3 (−7.1 to 7.7)	.94
General health	50.9 ± 6.6	45.2 ± 8.5	44.3 ± 9.1	−6.5 ± 8.9	38.7 ± 6.8	−6.5 ± 8.7	0.0 (−5.1 to 5.2)	.99
Vitality	50.4 ± 7.8	49.3 ± 7.4	43.4 ± 9.4	−7.0 ± 8.9	43.7 ± 8.7	−5.6 ± 10.5	1.4 (−4.1 to 7.0)	.61
Social functioning	49.2 ± 8.1	49.2 ± 5.7	44.9 ± 9.5	−4.3 ± 11.4	45.7 ± 9.7	−3.6 ± 11.3	0.8 (−5.8 to 7.4)	.81
Role emotional	49.0 ± 6.9	45.7 ± 9.3	45.8 ± 7.1	−3.2 ± 8.6	48.7 ± 6.0	+3.0 ± 10.6	6.3 (0.7 to 11.8)	**.03**[b]
Mental health	52.2 ± 8.7	49.1 ± 8.1	49.4 ± 9.8	−2.8 ± 11.7	48.6 ± 9.1	−0.5 ± 10.9	2.3 (−4.3 to 8.9)	.48
Physical component summary	48.9 ± 8.0	44.5 ± 10.3	41.4 ± 10.8	−7.4 ± 8.5	37.3 ± 9.9	−7.2 ± 13.6	0.2 (−6.1 to 6.6)	.94
Mental component summary	52.7 ± 10.2	50.3 ± 8.9	48.7 ± 10.4	−4.0 ± 12.6	50.6 ± 8.6	0.3 ± 11.0	4.3 (−2.7 to 11.2)	.22

Data are presented as mean ± standard deviation or 95% confidence intervals.
Boldface *P* values indicate statistical significance.
[a]Independent sample *t*-test.
[b]$P < .05$.

Additionally, a greater number of participants in the exercise group[11] agreed to attend for CPET compared with the control group.[5]

DISCUSSION

The primary aim of this study was to identify whether attending a preoperative SEP is associated with a long-term survival benefit for patients undergoing elective AAA repair, an important prospect, given that the aim is to prolong life. On the ITT analysis, there were eight more deaths in the control group at 5 years, although this did not reach statistical significance. However, when considering the PP and CACE analyses, patients who were assigned to the SEP and actually attended had a significantly lower mortality rate at 5 years, suggesting there may be a long-term survival benefit associated with attending a preoperative SEP. There was also a supporting trend for this to be the case, regardless of whether patients underwent open repair or EVAR, and this subgroup analysis may have reached statistical significance with a larger sample.

This finding, although novel in the AAA population, has been identified previously in those with peripheral arterial disease (PAD). Sakamoto et al found that the cardiovascular event-free and death-free rate was significantly higher for patients with PAD who completed a SEP when compared with those that discontinued it, with a mean follow-up of 6 years.[20] The authors postulate that this survival benefit may be due to changes in cardiovascular risk factors associated with exercise such as improvements in blood pressure, lipid profile, glycemic control, and central adiposity.[20] Other possible mechanisms for this survival benefit for patients with PAD include improvements in endothelial functional, altered

Table IV. Changes in quality of life measured by the EQ-5D questionnaire, by intervention group, from post-surgery to long-term follow-up

	Post-surgery		Long-term follow-up					
	Exercise group (n = 28)	Control group (n = 21)	Exercise group (n = 28)	Change from post-surgery	Control group (n = 21)	Change from post-surgery	Mean difference in change (between groups)	*P* value (change between groups)[a]
EQ-5D index TTO score	0.83 ± 0.24	0.79 ± 0.24	0.68 ± 0.28	−0.14±0.32	0.63 ±0.30	−0.16±0.37	−0.02 (−0.18 to 0.21)	.88
EQ-5D index VAS score	0.82 ± 0.78	0.79 ± 0.23	0.68 ± 0.22	−0.14±0.28	0.63 ±0.23	−0.15±0.31	0.01 (−0.15 to 0.18)	.86
EQ-5D patient reported VAS	81.07 ± 12.27	72.57 ± 18.59	65.7 ± 21.67	−15.85 ± 25.85	64.76 ± 17.49	−7.8 ± 24.71	−7.54 (−22.3 to 7.2)	.30

TTO, Time trade off; *VAS*, visual analogue scale.
Data are presented as mean ± standard deviation or 95% confidence intervals.
[a]Independent sample *t*-test.

Table V. Long-term cardiorespiratory fitness values

Variable	Exercise group (n = 11)	Control group (n = 5)	*P* value[a]
$\dot{V}O_{2Peak}$ (mL·kg^{-1}·min^{-1})	16.8 ± 3.3	16.0 ± 2.0	.62
$\dot{V}O_{2Peak}$ (% of predicted)	72.2 ± 10.1	80.1 ± 21.5	.45
AT (mL·kg^{-1}·min^{-1})	10.5 ± 2.2	9.8 ± 0.7	.18

AT, Anaerobic threshold; $\dot{V}O_{2Peak}$, peak oxygen uptake.
[a]Independent sample *t*-test.

hemorheology, and improvements in fitness associated with improved walking distance.[20]

The latter was considered pertinent for the current study, especially as in the original RCT, improvements in cardiorespiratory fitness were demonstrated in the SEP group immediately following the 6-week program, with no changes evident in the control group.[13] It was postulated that this improvement in cardiorespiratory fitness, over and above the control group, may have been maintained, driving the long-term survival benefit demonstrated here. Alternatively, a reduction in the level of deconditioning post procedure may have led to an improved recovery and allowed maintenance of physical performance status and thus cardiorespiratory fitness.

This suggestion that increases in fitness may have led to improved survival was also supported by previous research. In men referred for clinical exercise testing, each metabolic equivalent increase in cardiorespiratory fitness measured during treadmill testing was associated with a 12% improvement in survival.[21] Similarly, in patients with coronary artery disease, each 1 mL·kg^{-1}·min^{-1} increase in $\dot{V}O_{2Peak}$ was associated with an approximately 15% decrease in the risk of death.[22]

However, this notion could not be confirmed, as the data demonstrated no significant difference between groups for cardiorespiratory fitness parameters. This finding may, however, have been limited by the small sample of participants who agreed to attend for repeat CPET, and thus a lack of power, especially as the data did show that those in the SEP group did appear to have higher values for $\dot{V}O_{2Peak}$ and oxygen uptake at the anerobic threshold. Furthermore, the SEP group had a mean anerobic threshold value that exceeded the 'at risk' value identified for those undergoing AAA repair. This suggests that even at long-term follow-up, those in the SEP group would be fit enough to undergo elective AAA repair, whereas those in the control group would not.[10,11]

QoL has also been shown to be a predictor for outcomes, with lower QoL scores being associated with increased mortality risk, both in the general population and in patients with coronary artery disease and heart failure.[23-25] It was therefore anticipated that QoL would be significantly lower in the control group when compared with the SEP group, although this was not demonstrated in the data. However, this may be due to the natural long-term QoL trajectory that has been demonstrated in those undergoing AAA repair. Following repair, it appears that QoL returns to baseline after approximately 3 to 6 months and is maintained at this level, which is comparable to a matched population, for up to 3 years.[26] However, in the longer term, it appears that QoL does decline to a level that is lower than the general population.[27] This may suggest that both SEP and control groups have reduced QoL when compared with a matched population. Therefore, the margin for a difference between groups may be small, and smaller than that detectable with our sample size. It is therefore possible that this study was underpowered to detect a difference, as was the case with cardiorespiratory parameters. Consequently, further long-term data is needed from a larger cohort of patients to determine whether there is a significant difference between groups in terms of cardiorespiratory fitness and QoL.

This data needs to be generated via new, well-designed RCTs that are of high methodological quality and include large sample sizes with planned and appropriate long-term follow-up, as recommended in a recent Cochrane review.[28]

Limitations. We were unable to collect specific data on complications for several patients. As such, the role of a preoperative SEP on long-term complications remains unknown. In addition, the use of a PP analysis may weaken the findings, although this effect should be minimized by the additional CACE analysis. We should note that for this study, the CACE analysis is used as a triangulation to the results from ITT and PP analyses, and it only provides a certain extent of evidence on the intervention effect from compliers. With regards to CPET and QoL data, only a small proportion of participants who were still alive provided this data, which is a clear limitation. However, we attempted to contact all patients to maximize the available data. Finally, it is possible that unmeasured confounding events could have occurred during the follow-up period, affecting the results. However, as these are not known, they could not be accounted for.

CONCLUSIONS

These novel findings suggest a long-term mortality benefit for patients who were randomized to, and attended, a SEP prior to elective AAA repair. However, we were unable to establish the drivers behind this. Further well-designed RCTs considering the role of preoperative SEP for patients undergoing AAA repair are required.

AUTHOR CONTRIBUTIONS

Conception and design: JL, GS, DC, TW, IC
Analysis and interpretation: SS, BR, RG, CH, TW, SI, SP
Data collection: SS, BR, RG, SI, SP
Writing the article: SP
Critical revision of the article: SS, BR, JL, RG, CH, GS, DC, TW, SI, IC
Final approval of the article: SS, BR, JL, RG, CH, GS, DC, TW, SI, IC, SP
Statistical analysis: SS, BR, RG, CH, TW, SI, SP
Obtained funding: Not applicable
Overall responsibility: SP

DISCLOSURES

None.

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Submitted Jul 19, 2023; accepted Sep 3, 2023.

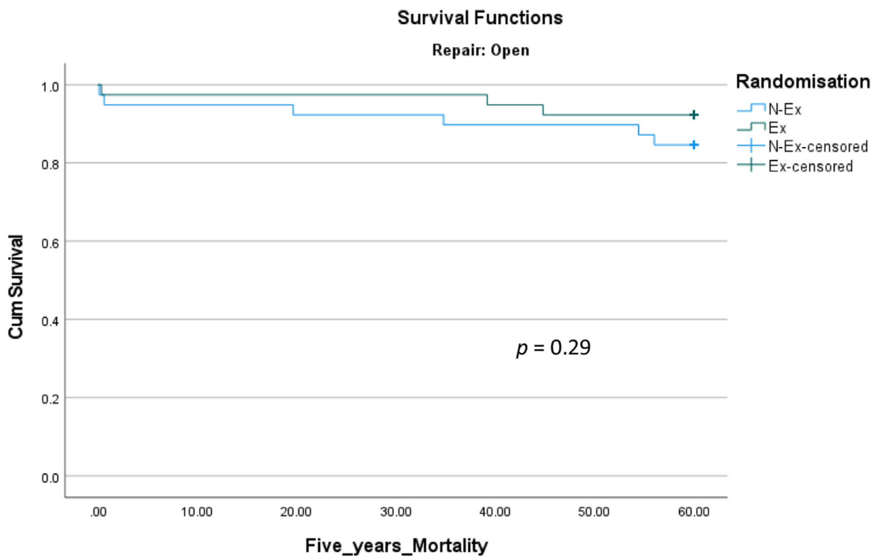
Additional material for this article may be found online at www.jvascsurg.org.

Journal of Vascular Surgery
January 2024

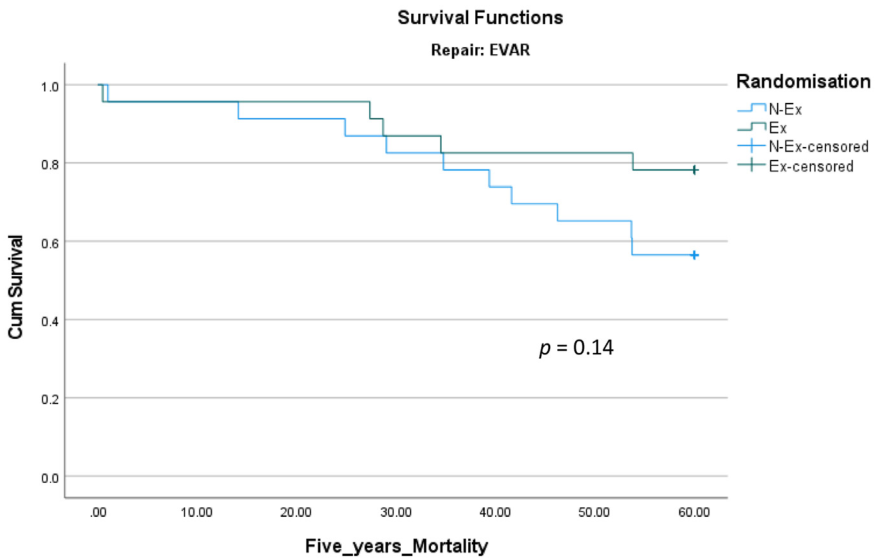
Supplementary Table (online only). Number of events stratified by the number of sessions attended

Sessions attended	No. of participants	Events recorded (deaths)
Did not attend	11	4 (36)
EVAR	4	2
Open	7	2
6-12 sessions	20	2 (10)
EVAR	6	1
Open	14	1
13-18 session	31	2 (6.5)
EVAR	13	2
Open	17	0

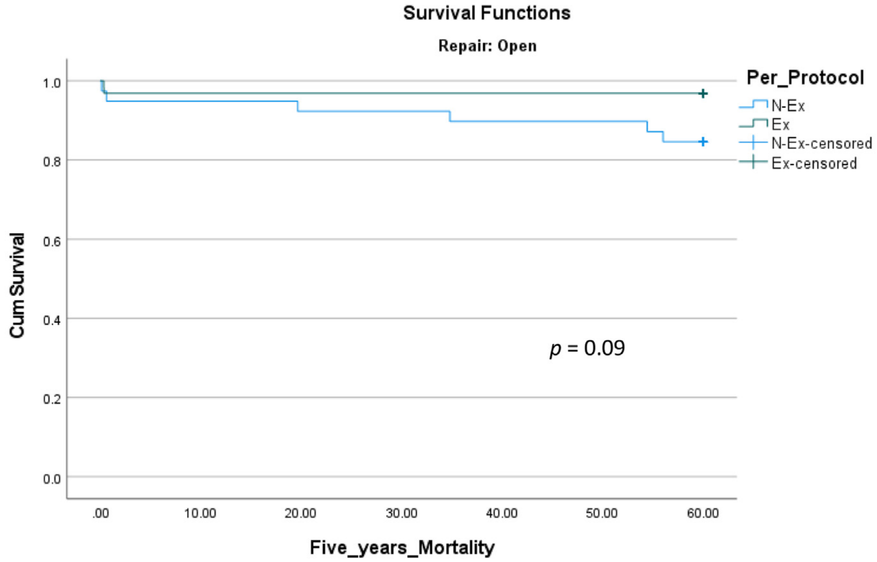
Data are presented as number or number (%).
EVAR, Endovascular aneurysm repair.



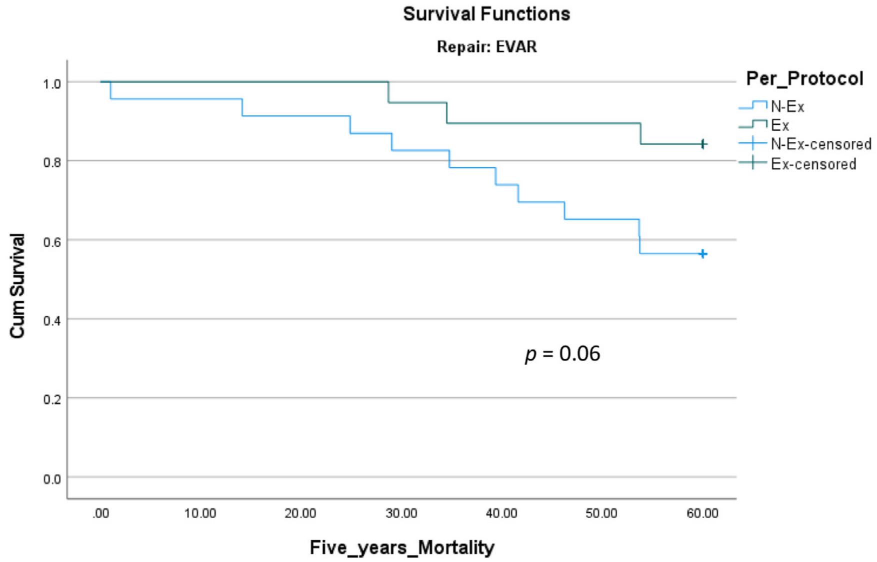
Supplementary Fig 1 (online only). Kaplan-Meier curve for the intention-to-treat (ITT) analysis for patients undergoing open repair. *Ex*, Exercise; *N-Ex*, no exercise.



Supplementary Fig 2 (online only). Kaplan-Meier curve for the intention-to-treat (ITT) analysis for patients undergoing endovascular aneurysm repair (*EVAR*). *Ex*, Exercise; *N-Ex*, no exercise.



Supplementary Fig 3 (online only). Kaplan-Meier curve for the per protocol (PP) analysis for patients undergoing open repair. *Ex*, Exercise; *N-Ex*, no exercise.



Supplementary Fig 4 (online only). Kaplan-Meier curve for the per protocol (PP) analysis for patients undergoing endovascular aneurysm repair (*EVAR*). *Ex*, Exercise; *N-Ex*, no exercise.