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Clinical paper

Randomized trial of the i-gel supraglottic airway device versus tracheal intubation during out of hospital cardiac arrest (AIRWAYS-2): Patient outcomes at three and six months



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ABSTRACT

Aim: The AIRWAYS-2 cluster randomised controlled trial compared the i-gel supraglottic airway device (SGA) with tracheal intubation (TI) as the first advanced airway management (AAM) strategy used by Emergency Medical Service clinicians (paramedics) treating adult patients with non-traumatic out-of-hospital cardiac arrest (OHCA). It showed no difference between the two groups in the primary outcome of modified Rankin Scale (mRS) score at 30 days/hospital discharge. This paper reports outcomes to 6 months.

Methods: Paramedics from four ambulance services in England were randomised 1:1 to use an i-gel SGA (759 paramedics) or TI (764 paramedics) as their initial approach to AAM. Adults who had a non-traumatic OHCA and were attended by a participating paramedic were enrolled automatically under a waiver of

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consent. Survivors were invited to complete questionnaires at three and six months after OHCA. Outcomes were analysed using regression methods.

Results: 767/9296 (8.3%) enrolled patients survived to 30 days/hospital discharge and 317/767 survivors (41.3%) consented and were followed-up to six months. No significant differences were found between the two treatment groups in the primary outcome measure (mRS score: 3 months: odds ratio (OR) for good recovery (i-gel/TI, OR) 0.89, 95% CI 0.69–1.14; 6 months OR 0.91, 95% CI 0.71–1.16). EQ-5D-5L scores were also similar between groups and sensitivity analyses did not alter the findings.

Conclusion: There were no statistically significant differences between the TI and i-gel groups at three and six months. We therefore conclude that the initially reported finding of no significant difference between groups at 30 days/hospital discharge was sustained when the period of follow-up was extended to six months.

Keywords: Heart arrest, Airway management, Tracheal intubation, Laryngeal mask, Survival rate, Health-related quality of life

Introduction

Survival rates following out-of-hospital cardiac arrest (OHCA) remain disappointingly low. Of the nearly 30,000 people who receive resuscitation for OHCA in England annually, only 25% achieve a return of spontaneous circulation (ROSC), and 8% are discharged from hospital alive.¹

The earlier an intervention is provided in OHCA the greater its potential to increase survival.² If basic life support and initial defibrillation of a shockable rhythm does not result in ROSC, the attention of emergency medical services (EMS) clinicians (paramedics) turns to airway management and drug delivery.³ However, optimal airway management during OHCA has been an enduring area of uncertainty, with very little high-quality research on which to base treatment recommendations.⁴ Options range from basic airway intervention to advanced procedures such as the insertion of a supraglottic airway (SGA) or tracheal intubation (TI), which is considered the “gold standard” of advanced airway management.⁵

Large observational studies have shown an association between survival following OHCA and the use of basic airway management techniques, when compared with either SGA or TI.⁶ However these studies are prone to residual confounding and resuscitation time bias.^{7,8} As a result, methodologies to complete high-quality randomised controlled trials (RCTs) of alternative advanced airway management (AAM) strategies in the early stages of cardiac arrest have been developed.⁹

During 2018, two RCTs of AAM during OHCA were published. Both compared an SGA with TI as the initial AAM strategy adopted by paramedics treating non-traumatic OHCA in adults. The Pragmatic Airway Resuscitation Trial (PART) compared the laryngeal tube SGA with TI in 3004 patients and found a statistically significant benefit in survival to 72 h and hospital discharge, and a favourable neurological status at hospital discharge, for those patients randomised to the laryngeal tube.¹⁰ At the same time, we published the AIRWAYS-2 trial which showed no difference in good functional outcome (modified Rankin Scale (mRS) score of 0–3) at hospital discharge or 30 days between 9296 patients randomised to either the i-gel SGA or TI.¹¹

Whilst early outcomes are valuable measures in studies involving OHCA patients, there is an increasing recognition of the importance of longer-term outcomes and functional recovery following OHCA, including quality of life in survivors.¹² The aim of this paper was

therefore to compare the secondary outcomes of mRS score and EuroQol-5D (EQ-5D) at three and six months after OHCA between groups of patients in the AIRWAYS-2 trial managed by paramedics randomised to use either the i-gel or TI as their initial AAM strategy when treating adult patients following OHCA.

Methods

The AIRWAYS-2 trial methodology has been reported previously.^{11,13} In summary, we completed a cluster RCT of paramedics from four large EMS provider organisations (ambulance services) in England covering approximately 21 million people. 1523 paramedics volunteered to participate and were randomised 1:1 to use an i-gel SGA (759 paramedics) or TI (764 paramedics) as their initial AAM strategy when attending adult patients with non-traumatic OHCA.

Randomisation and case ascertainment

Individual patient randomisation was considered impractical due to the risk that research procedures would delay life-saving treatment. We therefore chose to designate paramedics as the unit of randomisation, thereby creating a relatively large number of clusters containing a relatively small number of patients on average. This had the benefit of minimising the intra-cluster correlation and more closely approximating individual patient randomisation than would be the case if larger clusters were used. It was not possible to blind paramedics to the treatment allocation. Therefore, it was necessary to enrol all eligible patients into the trial to avoid the risk of selection bias, (e.g. to avoid paramedics selectively enrolling patients on the basis of their predicted outcome).¹⁴ This complete case ascertainment was achieved by supplementing routine case reporting by participating paramedics with daily review of all cardiac arrests occurring in the four participating EMS provider organisations (ambulance services) and cross-referencing with routinely collected audit data that are submitted to a national OHCA registry.¹

Patient enrolment

Automatic patient enrolment proceeded under a waiver of consent provided by the Confidentiality Advisory Group (CAG: reference 14/CAG/1030). Ethics review and approval was provided by South Central - Oxford C Research Ethics Committee (REC: reference 14/SC/1219). This included a process of written informed consent for

participating paramedics and for surviving patients (or a personal consultee for surviving patients without mental capacity). The main disadvantage of automatic enrolment was that many enrolled patients did not receive any AAM. There was also an increased risk that eligible patients might not be recognised as such by the participating paramedic, leading to protocol deviations. Paramedics were given the clinical freedom to deviate from the trial protocol if they felt that a particular approach to airway management was in the patient's best interests.

Patient inclusion criteria

Patient inclusion criteria were: known or believed to be 18 years of age or older; non-traumatic OHCA; attended by a paramedic participating in the trial who was either the first or second paramedic to arrive at the patient's side; resuscitation commenced or continued by paramedics or EMS personnel. Patient exclusion criteria were: detained in the Prison Service; previously recruited to the trial (determined retrospectively); resuscitation deemed inappropriate (using guidelines based on those of the Joint Royal Colleges Ambulance Liaison Committee)¹⁵; advanced airway already in place (inserted by another paramedic, doctor or nurse) when a paramedic participating in the trial arrived at the patient's side; known to be already enrolled in another pre-hospital RCT; patient mouth opening <2 cm.

Intervention

The intervention was the insertion of a second generation SGA (i-gel: Intersurgical, Wokingham, UK), which is the SGA most commonly used by paramedics in England.¹⁶ This was compared with TI using direct laryngoscopy and an intubating bougie. A standard approach to airway management in the trial, from basic to advanced techniques, was agreed by participating ambulance services. This included the use of bag-mask ventilation and simple airway adjuncts before AAM. In all other respects care proceeded as usual, with resuscitation following standard international guidelines.¹⁷

Follow-up procedures

All enrolled patients who survived to hospital discharge were followed-up by a member of the local research team who consulted with the clinical staff caring for the patient to determine the optimal time to approach the patient and/or their family to seek consent. Consent was sought from the patient or from a personal consultee if the patient was judged to lack capacity. Each patient or consultee was able to choose either active follow-up (collection of routinely available data combined with telephone and/or postal contact at 30 days/hospital discharge, and three and six months after cardiac arrest), passive follow-up (collection of routinely available data only, with no further patient contact) or no further data collection. In cases where a consultee opinion was obtained, and active follow-up chosen, the patient's capacity was re-assessed at the three- and six-month follow-up. If an initially incapacitated patient regained capacity, consent to continue their involvement in the trial was sought from the patient. The mortality status of patients who consented to follow-up was ascertained from national record systems. The mortality status of all other survivors was obtained from Hospital Episode Statistics data provided by NHS Digital (under HRA CAG approval) where linkage was possible.

Outcomes

For patients who provided active consent, the mRS score was measured at three and six months after the index OHCA. The mRS score, which incorporates both functional outcome and survival, is widely used in OHCA research and comprises a seven-point scale (0–6) with lower scores representing better recovery.¹⁸ Patients who die are given a score of six. The mRS scores were dichotomised into good recovery (score 0–3) and poor recovery (score 4–6). The EuroQol (EQ-5D-5L) is a validated measure of health-related quality of life and has been used widely in OHCA survivors.¹⁹ The EQ-5D-5L descriptive system comprises 5 domains: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. The EQ-5D-5L visual analogue scale (VAS) records a person's self-rated health with a range of 0–100. The EQ-5D-5L descriptive system and VAS were measured at 30 days/hospital discharge (whichever comes first), three and six months after the index OHCA for patients who consented to active follow-up and had survived to these timepoints. The EQ-5D-5L index scores (index) were calculated from the descriptive system responses by mapping onto the EQ5D-3L value set.²⁰ Patients who had died were given a value of 0 for both the index and VAS scores.

Statistical analysis

The primary analysis included participants with outcome data (complete-case analysis). The effect of missing data was examined with two sensitivity analyses. The first ('worst-case' scenario) assigned the worst possible score to known survivors with missing data, whilst patients for whom the survival status was unknown were assumed to have died. The second sensitivity analysis ('imputed case' scenario), used multiple imputation (60 imputations). Imputations was performed using the ICE command in Stata v15.1 (StataCorp) and estimates were combined using Rubin's rules. The imputation model included the following variables: age, sex, length of intensive care unit (ICU) stay, treatment group, ambulance provider organisation, paramedic experience, distance from base ambulance station, and index, VAS and mRS scores at 30 days/hospital discharge, three months and six months timepoints (see supplement for further details).

Logistic regression was used to analyse the dichotomised mRS scores with paramedic fitted as a random effect. A two-part binomial-beta model was used to analyse the EQ-5D-5L index and VAS scores. The scores of survivors were transformed for the purposes of modelling using the following transformation:

$$y' = \frac{y - a}{b - a}$$

$$y^n = \frac{[y'(N - 1) + 1/2]}{N}$$

where y is the outcome (index or VAS score), b is the highest possible score (index: 1, VAS: 100), a is the smallest possible score (index: –0.59, VAS: 0), N is the total number of survivors with data and y^n is the transformed score. This transformation ensured that the transformed scores were between 0 and 1 (excluding 0 and 1) which is required for beta regression.²¹ The two-part binomial-beta model produces two treatment estimates.²² The first (binomial part) is the odds ratio for survival ('alive vs dead') with an estimate greater than 1

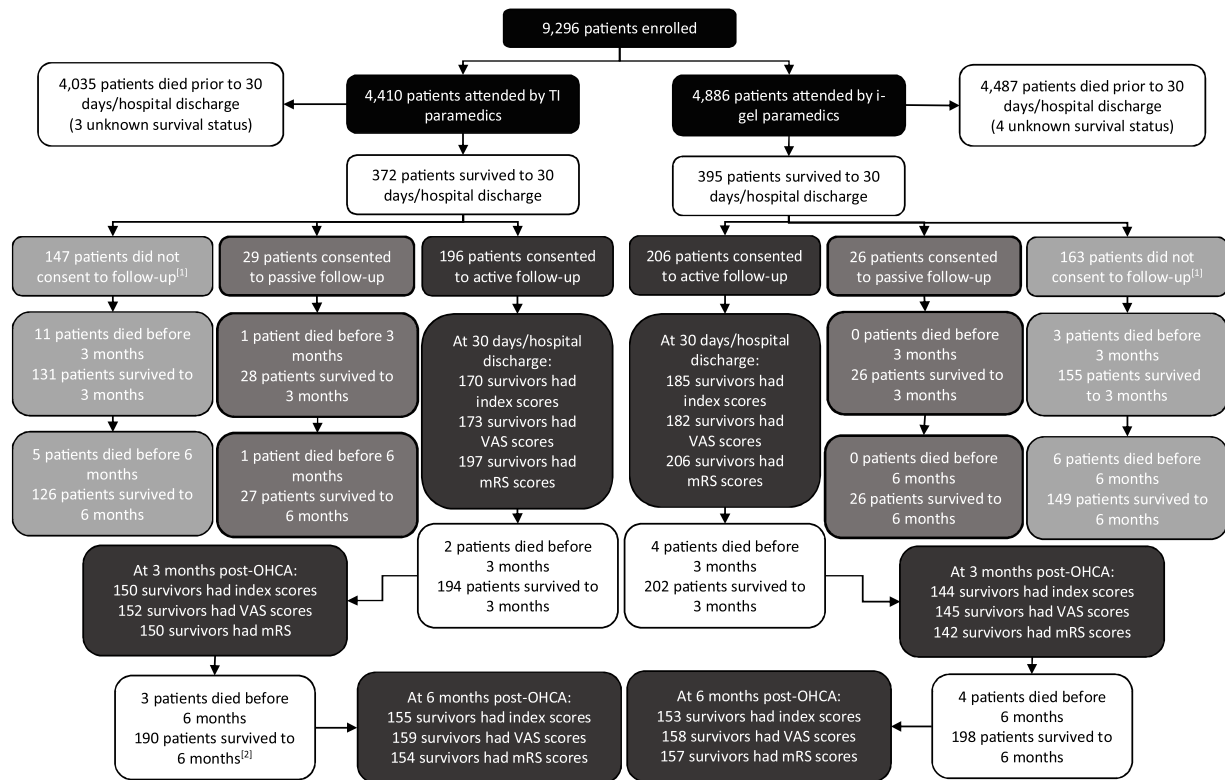


Fig. 1 – Flow of participants and data.

^[1] 10 patients (5 TI, 5 i-gel) who did not consent to follow-up have unknown survival status.

^[2] 1 patient (1 TI, 0 i-gel) who consented to active follow-up is known to have survived to 3 months but has unknown survival status between 3 months and 6 months follow-up.

favouring i-gel over TI. The second estimate (beta part) relates to the quality of life of survivors ('given patient survived'). Again, an estimate greater than 1 indicates a better quality of life in the i-gel group over the TI group.

All models were fitted to each timepoint separately as convergence issues prevented the fitting of longitudinal models. To allow for clustering of paramedics in the two-part binomial-beta models, confidence intervals were estimated using clustered bootstrapping (see supplement for further details). The clustered bootstrap and two-part binomial-beta model was performed in SAS v9.4. All other analyses were performed in Stata v15.1 (StataCorp).

Results

In total, 9296 patients were enrolled in the AIRWAYS-2 trial (4410 TI, 4886 i-gel). 767/9296 (8.3%) of patients survived to 30 days/hospital discharge and 402/767 (52.5%) consented to active follow-up. Of the 402 patients who consented to active follow-up, 388 (96.5%) were known to have survived to six months post-OHCA, 13 had died and the survival status at six months was unknown for 1 patient. All 402 patients who consented to active follow-up completed questionnaires at 30 days/hospital discharge. Completion rates at three months and six months were 300/396 (153/194 TI, 147/202 i-gel), and 317/388 (159/190 TI, 158/198 i-gel) respectively (Fig. 1).

In the period between 30 days/hospital discharge and six months post-OHCA, the proportion of patients with a mRS score of 0 (no

symptoms) increased whilst the proportion of patients with a mRS score of 5 (severe disability requiring constant nursing care) decreased (Table 1, Supplement Fig. 1). All patients with a score of 5 at six months also had a score of 5 at 30 days/hospital discharge (Supplement Fig. 2). Most patients with a mRS score of 0 at three and six months had improved since 30 days/hospital discharge (Supplement Figs. 2 and 3). Of patients who had a mRS score of 0 at six months, the majority also had a score of 0 at three months (Supplement Fig. 3). Of the 66 patients with a mRS score of 5 at 30 days/hospital discharge, 12/66 (18.2%) died before 3 months, 11/66 (16.7%) improved and 5/66 (7.6%) stayed the same; data were missing for the remaining 38 (57.6%) (Supplement Fig. 4).

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Table 1 – Complete case modified Rankin Scale analyses results.

Complete case modified Rankin Scale (0–3; good recovery)	Randomised to Tracheal Intubation (n = 4410)	Randomised to i-gel (n = 4886)	Odds Ratio estimate (95% CI)	p-Value	ICC	Risk difference estimate (95% CI)	p-Value
	n (%)	n (%)					
Hospital discharge/30 days (mRS 0–3; good recovery) ^a	300/4407 (6.8%)	311/4882 (6.4%)	OR = 0.92 (0.77, 1.09)	0.33	0.05	RD = -0.62% (-1.65%, +0.41%)	0.24
0 (no symptoms)	124/4407 (2.8%)	117/4882 (2.4%)					
1	48/4407 (1.1%)	41/4882 (0.8%)					
2	50/4407 (1.1%)	58/4882 (1.2%)					
3	78/4407 (1.8%)	95/4882 (1.9%)					
4	46/4407 (1.0%)	45/4882 (0.9%)					
5	27/4407 (0.6%)	39/4882 (0.8%)					
6 (deceased)	4034/4407 (91.5%)	4487/4882 (91.9%)					
Three months follow-up (mRS 0–3; good recovery) ^{a,b}	123/4199 (2.9%)	121/4636 (2.6%)	OR = 0.89 (0.69, 1.14)	0.35	<0.001	RD = -0.51% (-1.18%, +0.16%)	0.14
0 (no symptoms)	52/4199 (1.2%)	55/4636 (1.2%)					
1	6/4199 (0.1%)	4/4636 (0.1%)					
2	30/4199 (0.7%)	35/4636 (0.8%)					
3	35/4199 (0.8%)	27/4636 (0.6%)					
4	22/4199 (0.5%)	17/4636 (0.4%)					
5	5/4199 (0.1%)	4/4636 (0.1%)					
6 (deceased)	4049/4199 (96.4%)	4494/4636 (96.9%)					
Non-active consent patients who were not known to have died at three months	164/4407 (4.7%)	186/4882 (5.0%)					
Six months follow-up (mRS 0–3; good recovery) ^{a,c}	134/4212 (3.2%)	136/4661 (2.9%)	0.91 (0.71, 1.16)	0.43	<0.001	RD = -0.39% (-1.08%, +0.30%)	0.27
0 (no symptoms)	59/4212 (1.4%)	66/4661 (1.4%)					
1	4/4212 (0.1%)	5/4661 (0.1%)					
2	42/4212 (1.0%)	41/4661 (0.9%)					
3	29/4212 (0.7%)	24/4661 (0.5%)					
4	18/4212 (0.4%)	18/4661 (0.4%)					
5	2/4212 (0.1%)	3/4661 (0.1%)					
6 (deceased)	4058/4212 (96.3%)	4504/4661 (96.6%)					
Non-active consent patients who were not known to have died at six months	158/4407 (4.4%)	180/4882 (4.5%)					

^a 7 patients (3 Tracheal Intubation, 4 i-gel) were unable to be identified at 30 days/hospital discharge and were excluded from this analysis.

^b 104 patients (44 Tracheal Intubation, 60 i-gel) were missing mRS at 3 months follow-up and were excluded from the complete-case analysis at this timepoint.

^c 78 patients (37 Tracheal Intubation, 41 i-gel) were missing mRS at 6 months follow-up and were excluded from the complete-case analysis at this timepoint.

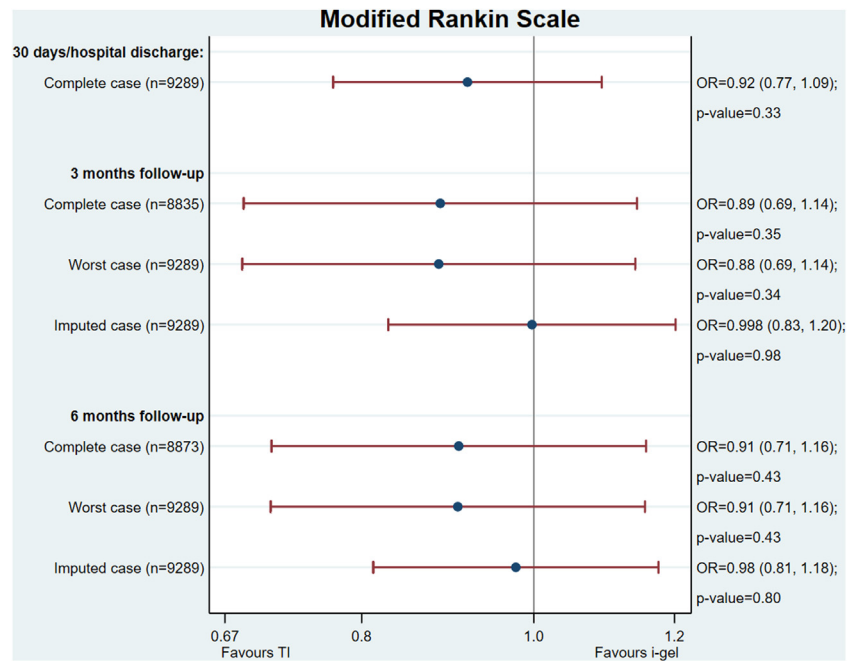


Fig. 2 – Main analyses of modified Rankin Scale scores.

Table 2 – Complete case EQ-5D-5L index and visual analogue scale analyses results.

	Randomised to Tracheal Intubation (N=4410)		Randomised to i-gel (N=4886)		'Alive vs dead' model		'Given patient survived' model	
	Survived (n (%))	Median (IQR)	Survived (n (%))	Median (IQR)	OR ^a (95% CI)	p-Value	OR ^b (95% CI)	p-Value
INDEX								
30 days/hospital discharge ^d	170/4205 (4.0%)	0.76 (0.50, 0.84)	185/4672 (4.0%)	0.71 (0.40, 0.84)	0.98 (0.79, 1.21)	0.86	0.92 (0.72, 1.18)	0.53
Three months post-OHCA ^e	150/4199 (3.6%)	0.80 (0.67, 0.91)	144/4638 (3.1%)	0.81 (0.68, 1.0)	0.86 (0.68, 1.09)	0.22	1.07 (0.83, 1.38)	0.63
Six months post-OHCA ^f	155/4213 (3.7%)	0.84 (0.70, 1.0)	153/4657 (3.3%)	0.84 (0.67, 1.0)	0.89 (0.70, 1.13)	0.33	0.92 (0.74, 1.15)	0.47
VISUAL ANALOGUE SCALE								
30 days/hospital discharge ^g	173/4208 (4.1%)	70 (50, 80)	182/4669 (3.9%)	65 (45, 80)	0.95 (0.76, 1.17)	0.63	0.81 (0.64, 1.03)	0.08
Three months post-OHCA ^h	152/4201 (3.6%)	80 (60, 90)	145/4639 (3.1%)	80 (65, 90)	0.86 (0.68, 1.08)	0.19	1.08 (0.86, 1.35)	0.53
Six months post-OHCA ⁱ	159/4217 (3.8%)	80 (65, 90)	158/4662 (3.4%)	80 (65, 90)	0.89 (0.70, 1.13)	0.35	1.01 (0.80, 1.27)	0.94

Notes:

^a Outcome is survivors vs non-survivors. Models were adjusted for ambulance service (4 levels), paramedic experience (2 levels: ≥ 5 years, < 5 years) and distance from base ambulance station (2 levels: ≥ 5 miles, < 5 miles). Confidence intervals were adjusted for paramedic clustering using a clustered bootstrap.

^b Outcome is either: (a) EQ-5D single summary index, or (b) EQ-5D visual analogue scale, conditional on surviving to the relevant timepoint. The outcomes were transformed to a scale between 0 and 1 non-inclusive. Models were adjusted for trust (4 levels: YAS, SWAST EMAS and EEAST), paramedic experience (2 levels: ≥ 5 years, < 5 years) and distance from base ambulance station (2 levels: ≥ 5 miles, < 5 miles). Confidence intervals were adjusted for paramedic clustering using a clustered bootstrap.

^d Missing for 205 Tracheal Intubation group patients and 214 i-gel group patients.

^e Missing for 211 Tracheal Intubation group patients and 248 i-gel group patients.

^f Missing for 197 Tracheal Intubation group patients and 229 i-gel group patients.

^g Missing for 202 Tracheal Intubation group patients and 217 i-gel group patients.

^h Missing for 209 Tracheal Intubation group patients and 247 i-gel group patients.

ⁱ Missing for 193 Tracheal Intubation group patients and 224 i-gel group patients.

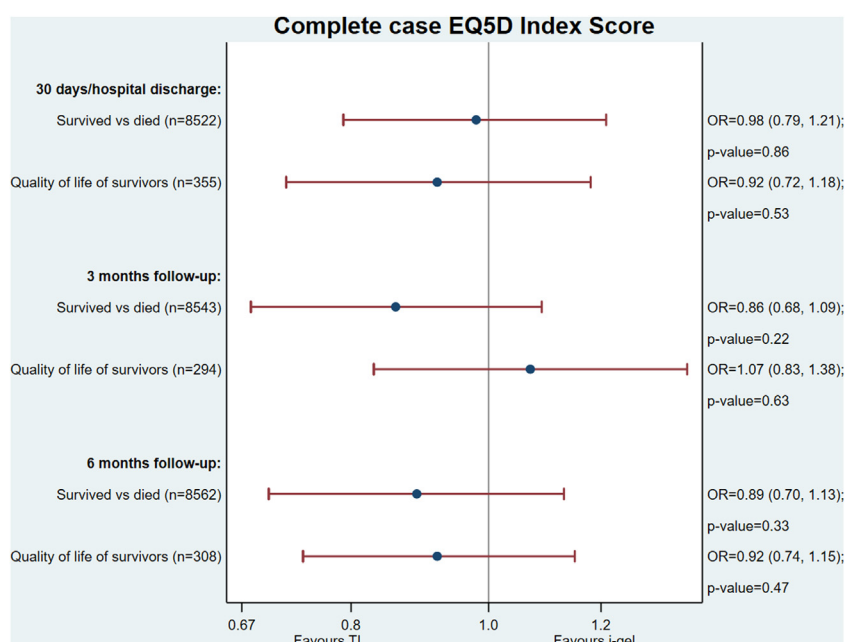


Fig. 3 – Main analyses of index scores.

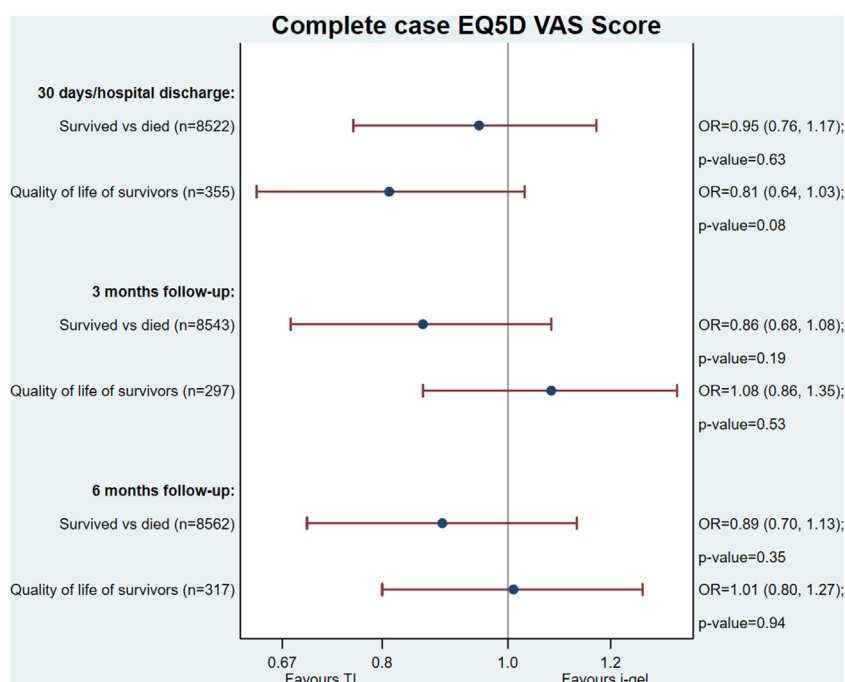


Fig. 4 – Main analyses of visual analogue scale scores.

The mRS scores at all three timepoints showed higher proportions of patients with a good recovery in the TI group compared to the i-gel group but these differences were not statistically significant [complete case analysis: 30 days/hospital discharge OR = 0.92 (95% CI 0.77-1.09); three months OR = 0.89 (95% CI 0.69-1.14); six months OR = 0.91 (95% CI 0.71-1.16)] (Table 1, Fig. 2). The 'worst-case' and 'imputed case' sensitivity analyses provided consistent results (Supplement Tables 1 and 2, Fig. 2).

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The EQ-5D domain scores are shown in Supplement Table 3. The data indicate higher median index and VAS scores at 30 days/hospital discharge in the TI group and similar median scores at the later timepoints (Table 2). The survival component of the two-part model showed no statistically significant difference in the odds of survival in the TI group compared to the i-gel group at all three timepoints (Table 2, Figs. 3 and 4). For the quality of life component in survivors, the outcomes were similar in the two groups at all timepoints for both index and VAS scores (Table 2, Figs. 3 and 4). The sensitivity analyses showed consistent findings with the complete case analyses (Supplement Tables 4 and 5, Supplement Figs. 5–8).

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Discussion

The functional outcomes (mRS scores) at 3 and 6 months for patients recruited to the AIRWAYS-2 trial were consistent with the primary outcome of mRS score measured at 30 days/hospital discharge.¹¹ The proportions of patients achieving a good recovery were not statistically different between the two treatment groups at all three timepoints. Quality of life measured using the EQ-5D-5L also revealed no significant differences between the two treatment groups across the three timepoints. The 'worst case' and 'imputed case' sensitivity analyses, designed to determine the potential impact of missing data, did not alter these conclusions.

The majority of RCTs in OHCA have reported only short-term outcomes, and even the most recent international advisory statement describing a core outcome set for RCTs in OHCA patients does not recommend data collection beyond 90 days, mainly because of the substantial resources required and the risk of attrition bias.¹² As a result, the natural history of survivor recovery following OHCA has been documented by only a few investigators,^{19,23–25} and there remains a need to examine the longer-term impacts of OHCA on functional status, cognition and quality of life.^{26,27}

Several studies have documented improvements in the functional status of OHCA survivors for at least the first three months and up to six months after cardiac arrest.^{25,26} Our data support this: we have shown a shift in the distribution of mRS scores consistent with improving functional status between hospital discharge and three months, and an attenuated shift in the same direction between three and six months. The decrease in the proportion of patients with an mRS score of 5 between hospital discharge and three months represents a combination of some patients dying and others improving their functional status.²⁸

Although the PART trial documented a significantly higher rate of favourable outcome among patients randomised to a strategy of initial laryngeal tube SGA compared with TI,¹⁰ longer-term outcomes were

not collected, so it is unknown whether this difference was sustained at three and six months after OHCA.

Our research has several limitations. In keeping with similar studies, our trial has relatively few survivors from which to gather longer-term outcomes. Furthermore, we were reliant on both active patient consent and the participant's willingness to complete and return the questionnaires at the follow-up timepoints. Despite considerable effort by the research teams, only 52.4% of survivors consented to active follow up and only 41.3% of survivors were followed up to six months. As a result, our analyses are undermined by missing data, with limited trial power and the risk of attrition bias. However, the proportion of missing data is very similar in the two groups, and there is no evidence that the availability of follow-up data was influenced by patient allocation. Furthermore, the sensitivity analyses reported did not alter our conclusions about the two treatment strategies. Other limitations relevant to the wider trial are described in a previous paper.¹¹ Importantly, the trial population included patients who did and did not receive AAM, and paramedics allocated to the i-gel group were more likely to use an advanced technique than those allocated to TI.

Conclusions

Longer term follow-up confirmed the results of the AIRWAYS-2 primary analysis. There were no significant differences in functional outcome or quality of life between the i-gel SGA and TI groups at three and six months after OHCA. This suggests that our initially reported findings are robust over time.

Authors' contribution

Guarantors: Bengner and Rogers had full access to all the data in the trial and take responsibility for the integrity of the data and the accuracy of the data analysis. Concept and design: Bengner, Black, Brett, Kirby, Nolan, Reeves, Robinson, Rogers, Scott, South, Taylor, Thomas, Voss, Wordsworth. Acquisition, analysis, and interpretation of data: All authors. Drafting of the manuscript: Bengner. Critical revision of the manuscript for important intellectual content: All authors. Statistical analysis: Lazaroo, Scott, Smartt, Rogers (Clinical Trials and Evaluation Unit, Bristol Medical School, University of Bristol, Bristol, UK). Technical and project support: Clout, Taylor.

Conflict of interest

All authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Rogers salary was funded by a grant from the British Heart Foundation until March 2017; part of Reeves salary was funded by grants from the National Institute for Health Research. All other authors declare no conflicts of interest.

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The funding organization had no role in the design and conduct of the trial; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at <https://doi.org/10.1016/j.resuscitation.2020.09.026>.

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