Research Article

Infra-Renal Endovascular Abdominal Aortic Aneurysm Repair Outcomes in Octogenarians - A Systematic Review and Meta-Analysis

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Abstract

Background: The safety and durability of endovascular aortic aneurysm repair (EVAR) in Octogenarians is a topic of debate. The purpose of this review is to assess the post-operative 30-day outcomes as well as mid -term mortality in octogenarians undergoing EVAR.

Methods: We followed the standard PRISMA guidelines and qualitatively evaluated relevant studies. Meta-analysis was conducted using Mantel – Haenszel and weighted summary proportions, and meta-regression was utilised. The primary outcome was identified as 30-day mortality after EVAR, while secondary outcomes included early post-EVAR endoleaks, cardiac, pulmonary, stroke, renal, and access complications as well as mid mortality.

Results: A total of 25 observational studies, comprising 40,641 octogenarians with an average age of 83.5 years, were included in the meta-analysis. Females were more frequent among octogenarians (19.5% vs 11.8%, p<0.0001). Octogenarians suffered from more comorbidities as coronary artery disease (CAD) (50.1% versus 47.5%, OR 1.2, 95% CI 1.04-1.39, p=0.01), renal disease (47.9% versus 25.87%, OR 1.69, 95% CI 1.30-2.21, p<0.0001), and an ASA score ≥3 (85.6% versus 78.3%, OR 1.49, 95% CI 1.35-1.64, p<0.0001).

30-day pooled complication included cardiac complications 5.2%, pulmonary 2.9, renal 3.5%, stroke 1.3%, access complications 8.5%, any complications 27.5%. 19.8% had evidence of endoleak at 30 days, only 3.1% of octogenarians required re-intervention at 30 days. Octogenarians had similar rates of post-operative re-intervention, sac diameter increase and rupture as non-octogenarians.

The pooled perioperative 30-day mortality for octogenarians was 2.5%, increasing to 9.1% and 52.9% at 1 and 5 years, respectively. Meta-regression analysis suggests an all-cause mortality rate of approximately 10.6% per year (10.58, R 0.86).

Conclusions: EVAR in octogenarians carries a 30-day perioperative mortality of 2.5% with annual all-cause mortality of 10.6% With appropriate patient selection and shared decision-making, EVAR provides a safe and effective option for AAA repair in this age group.

Keywords: Infra-renal Aortic Aneurysm; EVAR; Octogenarians

Introduction

Abdominal Aortic Aneurysm (AAA) is diagnosed when the aortic diameter is more 50.0% of its normal diameter [1] AAA Repair is considered when the risk of rupture outweighs the mortality risk associated with the repair for which the current diameter threshold for elective AAA repair is >5.5cm [2] following randomised evidence provided by the UK Small Aneurysm Trial (UKSAT) [3] and the American Aneurysm Detection and Management study (ADAM) [4]. Beyond this, the rupture risk increases and although there is some recent debate regarding precisely how much, the 30-day mortality of ruptured AAA repair remains high, with a rate of 34.5% in 2021 [5,6]. Therefore, it is crucial to identify and repair AAA in a timely and appropriate manner [8].

Since 1990, Endovascular aneurysm repair (EVAR) has provided an additional surgical option for patients undergoing AAA repair with over half of all elective AAA repairs in the UK now being done through an endovascular approach rising to over 80.0% of AAA repair in Octogenarians [6,7]. The number of individuals aged over 80 years and over is expected to triple between 2020 and 2050 globally from 142 million to 426 million [8]. Potentially leading to an increase in the number of elderly patients reaching the treatment threshold for abdominal aortic aneurysms (AAA) [9].

Whilst previous studies have shown that both open surgical repair (OSR) and EVAR in octogenarians are associated with increased mortality, and postoperative complications compared to non-octogenarians, EVAR offers a potential treatment option in those who are either unsuitable or unfit to undergo major OSR for which octogenarians as a more co-morbid subgroup are more likely to fall within [10-13].

In 2017, Han et al systematic review compared EVAR in octogenarians vs non-octogenarians [14], however, there have since been additional studies published in the literature. Therefore, offering an up-to-date assessment of infra-renal EVAR outcomes in octogenarians is essential. This can provide a comprehensive analysis of mid-term EVAR outcomes among octogenarians.

Methods

Protocol and registration: This review followed standard reporting guidelines and was registered with the International Prospective Register of Systematic Reviews (PROSPERO) [15] and adhered to the Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) [16] guidelines.

The eligibility criteria for the studies included in the systematic review were as follows:
1.   The studies must report on elective non-ruptured infra-renal EVAR
2.   The studies must compare the outcomes of octogenarians to non-octogenarians.
3.   The study size must be 30 or greater.
4.   The studies must report post-procedural outcomes and mortality at any specified point.
The exclusion criteria for the studies were:
1.   Studies that reported complex EVAR procedures such as branched, fenestrated, or thoracic or did not differentiate between the types of AAA.
2.   Studies that reported solely on ruptured AAA.

3.   Studies that did not differentiate between OSR and EVAR.
4.   Studies that contained unpublished, non-peer-reviewed data, such as abstracts, small case series, reviews, or expert opinions.
5.   Studies that reported data in a non-comparable fashion, such as single-arm studies.

Literature review and search: A comprehensive and systematic literature search was conducted by two independent reviewers, CDH and KN. The search was performed using the Medline and Embase databases, which were accessed through the Healthcare Databases Advanced Search (HDAS) interface. A comprehensive list of keywords and Medical Subject Heading (MeSH) terms were used to retrieve relevant articles from the literature. The search criteria were not limited by language and covered articles published from January 1991 (when the results of the first use of Elective Infra-renal EVAR were reported by Parodi et al [7] to February 2021. In addition, the reference lists of selected articles were screened for any additional studies. The search was initially run over a period of two weeks from 8/02/2021 – 21/02/2021 and updated over a period of one week from 20/02/2023-26/02/2023. The 2023 update used OVID Technologies Inc. due to the closure of the HDAS interface [12]. Details of the search strategy are provided in **Appendix 1**.

Study selection: Pre-defined eligibility criteria were set as described Titles and abstracts of articles were screened and the full text reviewed of studies that appeared to meet the inclusion criteria. Any discrepancies were resolved by a third review author (YY).

Data Collection: Data collection was carried out by two authors (IMO and KN) and was cross-checked by a third author (CDH). Data collection included details of study design, patient demographics, aneurysm anatomy, procedural details, postoperative outcomes, and follow-up. Data was collected for both octogenarian and non-octogenarian populations to facilitate comparison where required.

Study outcomes: Primary outcome: 30-day mortality after EVAR.

Secondary outcomes: early post-EVAR complications including endoleaks, cardiac, pulmonary, stroke, renal, and endovascular access complications as well as midterm mortality.

Risk of Bias in individual studies and across studies: The quality of the selected studies was evaluated by two authors (KN and IMO) using the Newcastle-Ottawa Scale (NOS) [17]. A score of seven or above out of a maximum of nine was considered to be indicative of a high-quality study. To assess the risk of publication bias, funnel plots were utilised as a visual representation of the distribution of effect sizes in the studies. The asymmetrical inverted V shape in the data points on the funnel plot indicates the absence of publication bias.

Statistical analyses: The primary outcomes were analysed using either Odds Ratio (OR) for dichotomous data or Weighted Mean Difference (WMD) for continuous data, both with a 95% Confidence Interval (CI). Statistical significance was established with a p-value less than 0.05. The Mantel-Haenszel

Appendix

1.   Literature Search terms for HDAS database and update search through OVID platform.

EMBASE, Medline	(((((aortic aneurysm).ti,ab OR (abdominal*).ti,ab OR (AAA*).ti,ab) AND ((aged, 80 AND over*).ti,ab OR (octogenarians).ti,ab OR (80*).ti,ab OR (elderly).ti,ab)) AND ((endovascular repair).ti,ab OR (endovascular procedures).ti,ab OR (EVAR).ti,ab)) AND (mortality).ti,ab) [DT 1991-2021]

2. Supplementary table showing Study definitions were defined for pre-operative characteristics.

Study Author	CAD	Pulmonary Disease	Renal Disease	PVD
Alberga et al [14]	Use of diuretic or digoxin, antianginal, antihypertensive, peripheral oedema, warfarin therapy, raised JVP, cardiomegaly or abnormality on ECG	Dyspnoea on exertion, limiting dyspnoea, dyspnoea at rest or visible consolidations or fibrosis on chest imaging	e G F R < 6 0 m l / min/1,73m2	N/A
Garcia et al [1]	History of angina pectoris, myocardial infarction or coronary revascularisation	COPD under medical treatment or requiring previous hospitalisation	N/A	Absence of distal pulses
Benveniste et al [15]	N/A	N/A	N/A	N/A
Rueda-Ochoa et al [16]	Myocardial infarction, coronary artery bypass graft or percutaneous transluminal angioplasty confirmed by ECG or medical records.	N/A	N/A	Symptomatic, not based solely on ankle brachial index and confirmed from GP records
Hye et al [17]	History of MI, coronary artery disease, bypass graft, congestive heart failure, cardiac chest pain, angina, EF <50%	N/A	N/A	N/A
Lagergren et al [5]	N/A	Diagnosis of COPD	N/A	N/A
Varkevisser et al [7]	N/A	Diagnosis of COPD	e G F R < 6 0 m l / min/1,73m2	History of peripheral arterial bypass or stenting procedure or a previous major amputation
Trenner et al [18]	N/A	N/A	N/A	N/A
Crespy et al [8]		Chronic respiratory failure (defined by Pa02 lower than 70mm Hg or in the absence of precise data, diagnosis reported by the patient or mentioned in medical file)	Creatinine clearance of less than 90mL/min	N/A
Endicott et al [19]	Angina or ACS Congestive heart failure	Diagnosis of COPD	N/A	N/A
Hicks et al [20]	N/A	Diagnosis of COPD	Pre-operative creatinine of >1.78 mg/dL	Patients with history of arterial bypass, peripheral vascular intervention or carotid endartectomy)
Machado et al [21]	N/A	N/A	N/A	N/A

De Leur et al [22]	N/A	COPD	N/A	N/A
Debus et al [23]	N/A	N/A	N/A	N/A
Pol et al 2014 [24]	N/A	N/A	N/A	N/A
Visser et al [25]	N/A	N/A	N/A	N/A
Pol et al [26]	N/A	N/A	N/A	N/A
Tsilimparis et al [27]	Previous PCI/ Cardiac surgery	Severe COPD	N/A	Rest pain/ gangrene
Geisbuch et al [28]	N/A	Diagnosis of COPD	e G F R < 6 0 m l / min/1,73m2	N/A
Fonseca et al [29]	N/A	Diagnosis of COPD	N/A	N/A
Schermerhorn et al [30]	Myocardial infarction within last 24 months, con-gestive heart failure, valvu-lar heart disease	Diagnosis of COPD	N/A	N/A
Leon et al [31]	N/A	N/A	N/A	N/A
Lange et al [32]	N/A	N/A	N/A	Ankle-brachial index <0.87
Biebl et al [33]	N/A	N/A	Serum creatinine c o n c e n t r a t i o n >1.5mg/dL	N/A
Sicard et al [34]	N/A	Diagnosis of COPD	Preoperative serum creatinine level 2.0mg/dL or more	N/A

method was employed to compare the odds of outcomes between octogenarians and non-octogenarians, with an OR greater than 1 indicating that the event was more frequent among the octogenarians group. Weighted summary proportions were utilised to assess events within individual study populations. The degree of heterogeneity among studies was calculated using the I-squared (i^2) test. In cases where significant heterogeneity was identified, a random-effects model was used. Conversely, a fixed-effects model was applied in the absence of significant heterogeneity.

To assess publication bias, 30-day mortality was selected as this was the most consistently reported outcome across the studies included.

All statistical analysis was conducted using Review Manager (RevMan), Windows 10 Version 5.4, The Cochrane Collaboration 2020, and MedCalc Statistical Software version 19.2.6 (MedCalc Software bv, Ostend, Belgium; https://www.medcalc.org; 2020).

Results
Study Selection and Characteristics: After conducting an initial screening to exclude duplicates, 914 articles were initially assessed. Of these, 130 articles were considered for potential inclusion in the review. Of these, 42 were abstracts only, 33 were missing post-procedural outcomes data or had incorrect age comparisons, 13 had no comparison by age, 8 were non-original data (such as review articles or meta-analyses), 5 could not be retrieved, 3 included complex or ruptured AAA repair, 2 had fewer than 30 patients and 2 had duplicate data with no additional parameters reported.

As a result, 21 studies met the pre-defined inclusion criteria, and four further studies were identified from reviewing the references of the included studies. The updated 2023 search iden-

tified a further 145 articles of which 15 were considered for potential conclusion but all were eventually excluded. **Figure 1** provides a detailed illustration of the study selection, inclusion, and exclusion process is presented in the PRISMA diagram.

The studies included in this review were conducted from 1994 to 2019 and published between 2005 and 2021. The studies originated from the USA (8 studies), Europe (9 studies), 4 international studies (data collected from 2 or more countries) and Australia (1 study). Although there was some overlap in the data sources used between studies, only unique data was extracted for this review. The total number of patients undergoing infra-renal AAA repair was 40,641 octogenarians and 119,858 non-octogenarians. **Table 1** provides individual study characteristics. The quality of the studies was evaluated using the NOS, with scores ranging from 5 to 8. Most studies were rated as medium or high quality, as shown in **Table 2**. All studies were observational and there were no randomised controlled trials.

Bias and quality within studies: Funnel plots for 30-day mortality in **Figure 2** showed an even distribution within the accepted limits, indicating a low likelihood of publication bias.

Patient demographics: The total number of patients undergoing infra-renal AAA repair was 40,641 octogenarians and 119,858 non-octogenarians. Patient demographics and comorbidities are summarised in **Table 3**. Significantly more non-octogenarians were male (88.2%) compared to the octogenarians (80.5%) (OR 0.53, 95% CI 0.56-0.61, p <0.0001).
Octogenarians had more co-morbidities compared to non-octogenarians as coronary artery disease (CAD) (50.1% versus 47.5%, OR 1.2, 95% CI 1.04-1.39, p=0.01), renal disease (47.9% versus 25.9%, OR 1.69, 95% CI 1.30-2.21, p<0.0001), and an ASA score ≥3 (85.6% versus 78.3%, OR 1.49, 95% CI 1.35-1.64, p<0.0001).
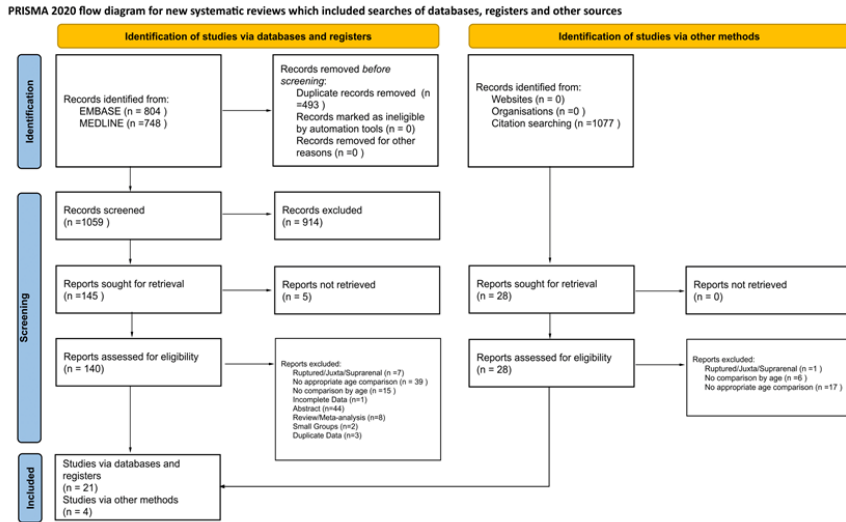
Figure 1: PRISMA flow diagram of study selection process.
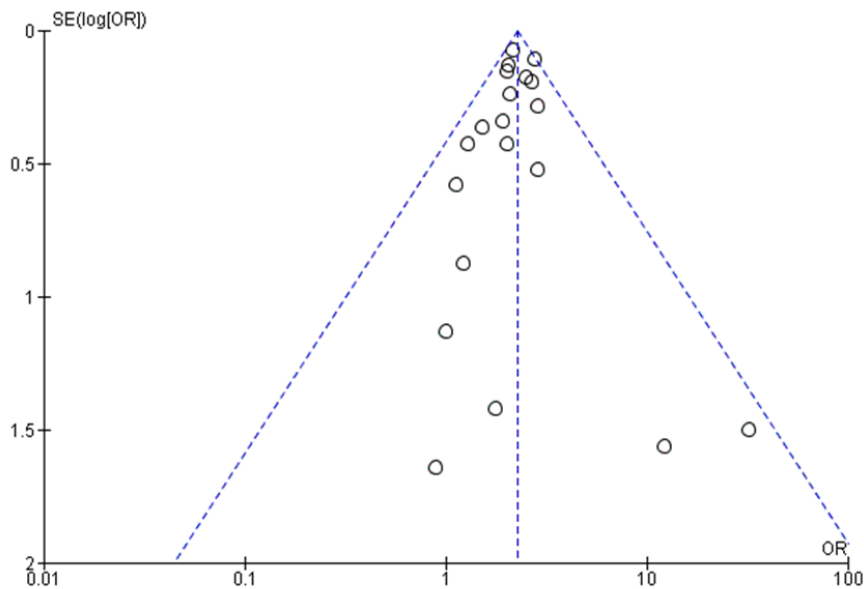

Figure 2: Funnel Plot for 30 Day mortality of Octogenarians compared to non-Octogenarians.
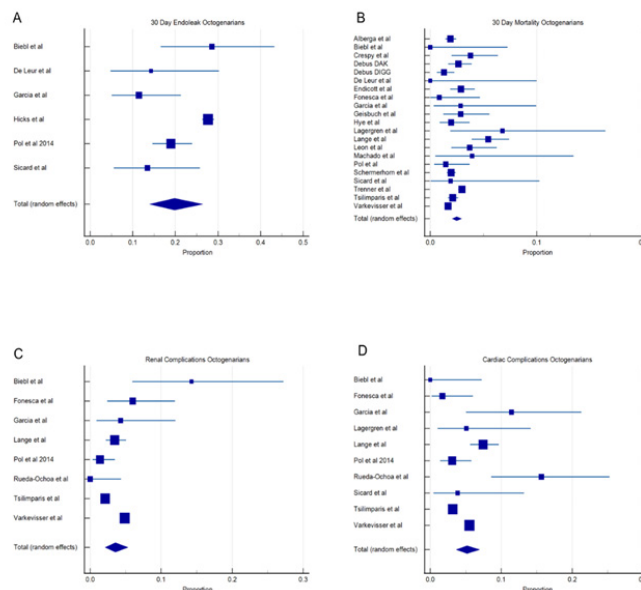

Figure 3: Single arm forest plots to represent the Octogenarian cohort (Single arm forest plots within the Octogenarian cohort showing individual studies proportion and overall total effect. A = 30-day endoleak, B = 30-day mortality, C = cardiac complications and D = renal complications.)

Table 1: Summary of Included Studies.

Study Author	Year	Study Location	Total Number	Octogenarians	Non-Octogenarians	Data Base	Study	Data Collection Period
Alberga et al [18]	2021	Netherlands	12054	3015	9039	DSAA*	R	2013-2018
Garcia et al [19]	2021	Spain	241	70	171	Local Hospital	R	2000-2017
Benveniste et al [20]	2020	Australia	180	67	113	Local Hospital	P	2008-2019
Rueda-Ochoa et al [21]	2020	Netherlands	558	83	475	Local Hospital	R	2000-2015
Hye et al [22]	2019	USA	1967	458	1509	KPSGR*	R	2010-2014
Lagergren et al [10]	2019	USA	255	59	196	Local Hospital	R	2008-2015
Varkevisser et al [12] #	2019	North America + Singapore	37078	9502	27576	VQI*	R	2003-2018
Trenner et al [23]	2018	Germany	45608	9773	35835	German Federal Statistical Office	R	2005-2013
Crespy et al [13]	2017	France	684	345	339	Four French Hospitals	R	1998-2011
Endicott et al [24]	2017	USA	4822	902	3920	VASQIP*	R	2002-2010
Hicks et al [25]#	2016	North America + Singapore	16109	4074	12035	VQI*	R	2002-2012
Machado et al [26]	2016	Portugal	171	51	120	Local Hospital	R	2001-2013
De Leur et al [27]	2015	Netherlands	120	35	85	Local Hospital	R	2005-2012
Debus et al [28]	2015	Germany	3686	860	2825	DIGG*	R	2013-2014
Debus et al [28]	2015	Germany	3681	912	2769	DAK*	R	2008-2015
Pol et al [29]	2014	International	1263	290	973	ENGAGE*	P	2009-2011
Visser et al [30]	2014	Netherlands	193	97	96	Local Hospital	P	1996-2011
Pol et al [31]'	2012	International	1200	274	926	ENGAGE*	P	2009-2011
Tsilimparis et al [32] ~	2012	USA	12390	3590	8800	ACSNSQIP*	R	2005-2010
Geisbuch et al [33]	2011	Germany	985	279	688	Local Hospital	R	1994-2011
Fonseca et al [34]	2010	USA	322	117	205	Local Hospital	R	2003-2008
Schermerhorn et al [35]	2008	USA	22830	4566	18264	Medicare	R	2001-2004
Leon et al [36]	2005	USA	1679	351	1328	COMPdata database	R	1995-2003
Lange et al [37]	2005	Europe	4888	697	4191	EUROSTAR*	R	1996-2004
Biebl et al [38]	2004	USA	182	49	133	Local Hospital	R	1999-2003
Sicard et al [39]	2001	USA	260	52	208	Local Hospital	R	1997-2000

R - Retrospective study, P - Prospective Study, *VQI - Vascular Quality Initiative, ENGAGE - Endurant Stent Graft Natural Selection Global Post-market Registry, KPSGR - Kaiser Permanente Endovascular Stent Graft Registry, DSAA - Dutch Surgical Aneurysm Audit, DAK - German Employees' Health Insurance Fund, DIGG - German Institute for Vascular Health Care Research, EUROSTAR - The EUROpean collaborators *on Stent–graft Techniques for abdominal aortic Aneurysm Repair, ACSNSQIP - American College of Surgeons National Surgical Quality Improvement Programme, # Both Studies use the VQI database, ' Both studies use ENGAGE registry, ~ Figures for total number, number of octogenarians and non-octogenarians not given and back calculated from mortality percentages, ^ Study includes two different databases DIGG and DAK.*

Table 2: Quality of Study Assessment using Newcastle Ottawa Scale.

Paper	Study	Selection (Max 4)	Comparability (Max 2)	Exposure/Outcome (Max 3)	Total (Max 9)
Alberga et al [18]	Cohort	4	0	2	6
Garcia et al [19]	Cohort	3	1	2	6
Benveniste et al [20]	Cohort	4	1	2	7
Rueda-Ochoa et al [21]	Case-Control	4	2	2	8
Hye et al [22]	Cohort	3	2	3	8
Lagergren et al [10]	Cohort	3	1	2	6
Varkevisser et al [12]	Cohort	3	1	2	6
Trenner et al [23]	Cohort	3	2	2	7
Crespy et al [13]	Cohort	3	1	2	6
Endicott et al [24]	Cohort	2	2	2	6
Hicks et al [25]	Cohort	3	1	2	6
Machado et al [26]	Cohort	4	2	2	8
De Leur et al [27]	Cohort	3	2	2	7
Debus et al [28]	Cohort	3	1	2	6
Pol et al 2014 [29]	Cohort	4	2	2	8
Visser et al [30]	Case - Control	2	2	2	6
Pol et al [31]	Cohort	4	1	2	7
Tsilimparis et al [32]	Cohort	4	2	2	8
Geisbuch et al [33]	Cohort	3	1	3	7
Fonseca et al [34]	Cohort	2	1	3	6
Schermerhorn et al [35]	Cohort	3	1	2	6
Leon et al [36]	Cohort	3	1	1	5
Lange et al [37]	Cohort	4	2	2	8
Biebl et al [38]	Cohort	2	1	2	5
Sicard et al [39]	Cohort	2	1	2	5

Colour coded by Green/Yellow/Red. Green for high scoring papers and Red for low scoring papers and Yellow for intermediate.

Table 3: Patient characteristics and comorbidities.

Pre-op Characteristic	No of Studies	Octogenarians			Non - Octogenarians			OR	95% CI	p value
		Total (n)	Events (n)	(%)	Total (n)	Events (n)	(%)			
Male	14	24607	19814	80.52	80946	71413	88.22	0.53	0.56,0.61	**<0.0001**
Hypertension	10	10618	8892	83.74	30396	24852	81.76	1.18	0.91,1.52	0.22
Diabetes	11	11076	657	5.93	31905	2122	6.65	1.02	0.8,1.3	0.88
Hyperlipidaemia	7	11004	7250	65.89	33503	17798	53.12	0.83	0.48 - 1.45	0.52
Smoking All	12	11773	8051	68.39	36096	28799	79.78	0.5	0.38,0.67	**<0.0001**
Smoking Active	4	10081	1257	12.47	29376	10704	36.44	0.25	0.23 - 0.26	**<0.0001**
Smoking Previous	4	10081	6415	63.63	29376	15782	53.72	1.27	0.98 - 1.65	0.07
CAD	12	14729	7375	50.07	44939	21340	47.49	1.2	1.04,1.39	**0.01**
Pulmonary Disease	11	14279	4105	28.75	43506	14213	32.67	0.95	0.76,1.19	0.66
Renal Disease	10	14584	6984	47.89	44369	11478	25.87	1.69	1.3,2.21	**0.0001**
PAD	7	10799	1187	10.99	31163	3695	11.86	1.15	0.88 - 1.5	0.3
ASA ≥ 3	9	5483	4693	85.59%	18084	14162	78.31%	1.49	1.35,1.64	**<0.0001**

CAD = Coronary artery disease, PAD = Peripheral arterial disease, ASA = American Society of Anaesthesiology. (For further definitions of CAD, Pulmonary disease, renal disease and PVD please see supplementary table 1)

Procedural data: The patients' aneurysm morphology and peri-operative data are reported in **Table 4**. The mean diameter of AAA was significantly larger among octogenarians (58.9mm) compared to non-octogenarians (56.7mm) (mean difference 2.99mm, 95% CI 2.01-3.93mm, p<0.0001). There was no difference in aneurysm neck length (mean difference 1.77mm, 95% CI -1.81-5.35, p 0.33) or neck diameter (mean difference 0.21mm, 95% CI -0.01-0.43, p 0.06) between the two groups. Operation time (146.2 minutes versus 137.6 minutes, mean difference 3.25 minutes, 95% CI -8.8-15.9, p 0.6) and length of ICU stay (1.03 days versus 1.14 days, mean difference -0.27 days, 95% CI -0.93—0.39, p 0.42) and overall hospital length of stay (mean 7.72 days versus 5.85 days, p 0.12) were comparable between the two groups. Octogenarians had a higher mean blood loss (278.9mL versus 255mL, mean difference 24.64mL, 95% CI 7.26-42.02, p 0.005).

30-Day Outcomes: The thirty-day mortality, endoleak and post-operative complications are summarised in **Table 5**. Thirty-day mortality was 2.5% among octogenarians with the weighted summary proportion of endoleak 19.8%. Cardiac complications were recorded as 5.2%, pulmonary complications in 2.9 %, renal complications in 3.6%, stroke in 1.3%, endovascular access complications in 8.5% and any complications of 27.5%. Technical success was 96.0% whilst conversion to open was 0.7% and the 30-day reintervention rate was 3.1%.

Midterm outcomes: The midterm outcomes are summarised in **Table 6**, Six studies reported 1-year mortality with a weighted summary proportion of 9.1%. Three studies reported on 2-year and 3-year mortality rates with 24.3% and 23.6% respectively. At 5-years a weighted summary proportion the mortality was 52.9%.

Table 4: Perioperative and Aneurysmal Data.

Procedural Characteristic	No of Studies	Octogenarians		Non- octogenarians		Mean Difference	95% CI	p value
		Number	Mean	Number	Mean			
Max AAA Diameter mm	8	5783	58.94	19758	56.72	2.99	2.01,3.93	**<0.0001**
Neck Length	2	339	27.8	1106	26.9	1.77	-1.81 - 5.35	0.33
Neck Diameter	3	1036	24.3	5297	24	0.21	-0.01 - 0.43	0.06
Operation Time	6	5525	146.2	17842	137.6	3.25	-8.8 - 15.9	0.6
Blood Loss	3	4413	278.9	13141	255	24.64	7.26 - 42.02	0.005
Intensive Care Unit admission duration	3	4709	1.03	13347	1.14	-0.27	-0.93 -0.39	0.42
Time to discharge	6	1510	7.72	6003	5.85	0.88	-0.23 - 1.99	0.12

Table 5: 30-day outcomes.

Post-operative Outcomes	No of Studies	Octogenarians				
		Total (n)	Events (n)	(Proportion%)	95% CI	Fixed/Random effects
30 Day Mortality	21	3595	827	2.484	2.058, 2.948	Random
30 Day Endoleak	6	4570	1217	19.81	13.925, 26.444	Random
Cardiac Complications	10	1450	729	5.182	3.655, 6.958	Random
Pulmonary Complications	8	1439	818	2.893	1.448, 4.814	Random
Renal Complications	8	1439	582	3.547	2.118, 5.325	Random
Stroke Complications	5	1223	15	1.338	0.773, 2.150	Fixed
Local Complications	7	1127	157	8.471	3.893, 14.598	Random
Any Complications	11	1757	3392	27.485	19.777, 35.937	Random
Technical Success	4	9892	9660	95.95	91.674, 98.739	Random
Conversion to open	6	8526	39	0.66	0.302, 1.154	Random
30 Day Reintervention	4	1371	420	3.118	2.224, 4.158	Random

Results from DIGG and DAK registries/databases have been counted as separate for 30 day mortality.

Table 6: Mid to Long-term mortality and outcomes.

| Long Term Outcome	No of Studies	Octogenarians				
		Total (n)	Events (n)	(Proportion%)	95% CI	Fixed/Random effects
1 Year Mortality	6	4578	417	9.136	8.317, 10.007	Fixed
2 Year Mortality	3	199	48	24.266	18.525, 30.780	Fixed
3 Year Mortality	3	157	38	23.637	10.326, 40.348	Random
5 Year Mortality	5	386	159	52.857	38.703, 66.780	Random
Rupture	4	1194	7	0.7	0.316, 1.337	Fixed
Endoleak	6	1141	238	21.289	13.903, 29.763	Random
Sac Diameter Increase	5	953	81	11.115	5.119, 19.042	Random
Re Interventions	9	1219	109	8.777	5.894, 12.169	Random
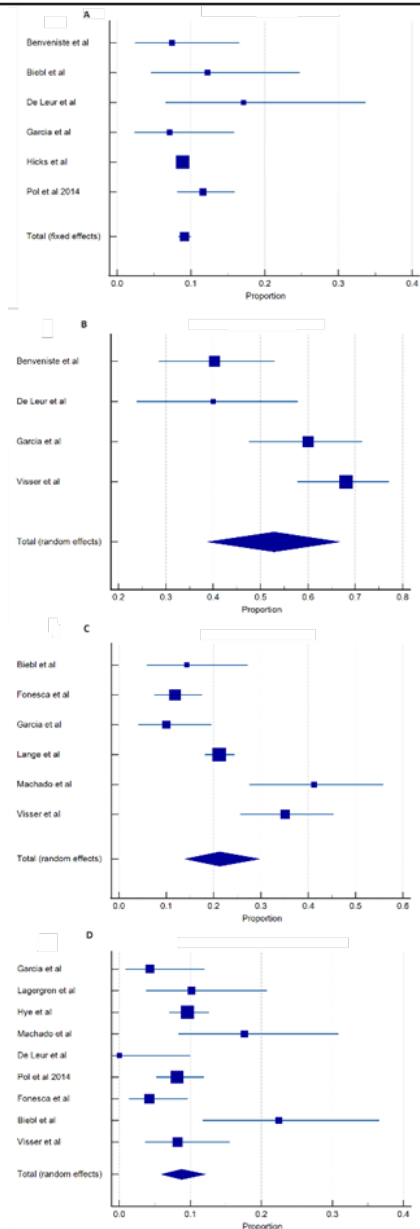
Figure 4: Mid to long-term outcomes (weighted summary proportions) for; A = 1 Year Mortality, B = 5 Year Mortality, C = Endoleak, D = Re-intervention (R3 Minor C3 - Please mention the time for the C & D estimates).

Four studies reported on the incidence of late rupture of 0.7%, six studies on endoleak 21.3%, five studies reported the incidence of sac diameter increase which was 11.1% and nine studies reported on incidence of re-intervention which was 8.8%.

Additional Analyses

Sensitivity Analysis: After conducting the initial meta-analysis, we noticed that one of the studies, Fonesca et al, had a substantially lower mortality at 5 years compared to the other studies. We therefore performed a sensitivity analysis on this to determine its impact on the results. The sensitivity analysis included data from five studies with a total 386 octogenarians. We systematically excluded each study in turn examining the resultant weighted mean proportion, and standard deviations. For this outcome Fonesca et al was found to lie more than 2 standard deviations away and as such the removal of this study offers a more representative outcome of the octogenarian population for 5-year mortality.

Meta-Regression: A meta-regression analysis was conducted to examine the all-cause mortality rates between 1- and 5 years post-EVAR.
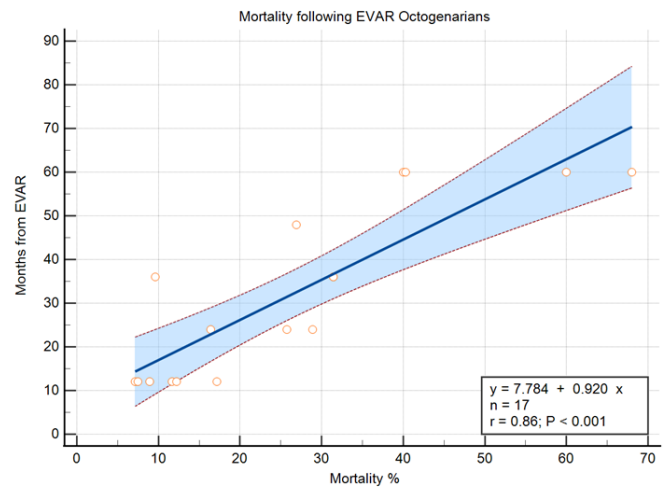

Figure 5: A = Linear meta-regression of mortality for octogenarians following EVAR.

The results of the analysis revealed that octogenarians had a yearly all-cause mortality rate of 10.6% with an R2 of 0.74. This indicates that the model as seen in **Figure 5** explains 74.0% of the variability in the mortality data.

Discussion

Octogenarians who require infra-renal AAA repair, pose a clinically challenging cohort considering their multiple co-morbidities and the yearly risk of rupture and the associated high mortality. With the expected increase in the octogenarian population over the coming years, EVAR is likely to be frequently used particularly within the octogenarian cohort.

Our meta-analysis and systematic review provide a thorough review of the differences in early postoperative outcomes observed in octogenarians undergoing infra-renal AAA repair as well as mid -term mortality. This complements a previous meta-analysis performed by Han et al in 2017 [2] where, following a rigours literature search and strict inclusion/ exclusion criteria 10 studies have been included which have been published since this data and an additional 5 studies identified for inclusion.

Our study primary outcome of 30-day mortality was noted to be 2.5% among octogenarians which appears acceptable when viewed in the context of the annual rupture risk of a AAA >5.5cm.
The increased 30-day mortality is consistent with the findings of increased rates of cardiac, renal, pulmonary, and endovascular access complications within the octogenarian population. Whilst the technical success was significantly higher in non-octogenarians this did not translate into a significant difference in re-intervention rate with Benveniste et al suggesting that re-intervention rates were higher in those with unfavourable anatomy and usage outside of instructions for use. Nor did the higher incidence of endoleak seen in octogenarians both in the early or late follow-up result in a significant difference in re-intervention rate between the age groups.

Biebl et al [38] found that the most common systemic complication in patients over 80 years old was renal dysfunction, whilst Saratzis et al [40] found that the incidence of Acute Kidney Injury (AKI) after EVAR is significant and is independently associated with medium-term mortality and morbidity [41]. Rueda et al [21] suggested that renal dysfunction with preoperative urea levels greater than 50 mg/dl identified a higher likelihood

of AKI indicating a need to identify the at-risk population to optimise pre-operative renal functions. Renal dysfunction following EVAR may be caused due to use of contrast and thromboembolism and vigilant monitoring of serum creatinine and urine output is warranted to allow for timely interventions to minimise post-operative complications. Both cardiac and pulmonary complications were observed to be significantly higher in octogenarians post-EVAR in our study. Pre-operatively octogenarians did not have a significantly higher incidence of pulmonary disease within our study population.

Within our study, we noted a lower proportion of males and active smokers in the octogenarian population however a higher proportion of ex-smokers with nicotine and gender well established risk factors for aneurysm formation [38]. The increase in co-morbidity with age was demonstrated with the significantly higher incidence of cardiac, pulmonary, and peripheral vascular disease within the octogenarian population correlating with the higher proportion of octogenarians considered ASA ≥ 3 as evidenced by Pol et al [29]. This increased co-morbidity in the octogenarian population may be one of the factors influencing the higher post-operative mortality and complication rates observed compared to the non-octogenarian population with Garcia et al [19] showing an ASA of 4 being an independent risk factor for lower mid-term survival rates. Lange et al also found an increased risk of systemic complications in octogenarians who underwent EVAR, they proposed that this may be due to octogenarians being more heavily comorbid, which could have led to them being deemed unfit for open repair [37].

Although previous studies suggested a higher likelihood of complex aortic anatomy in octogenarians with increased aneurysm tortuosity and max diameter than in non-octogenarians [29,37]. This study showed no significant difference in neck length or neck diameter. Both groups had comparable EVAR operative time, ICU duration, length of hospital stay, technical success or conversion to open. Whilst blood loss was found to be statistically significant between the two groups the small difference in volume is unlikely to be of clinical significance. This is discussed by Pol et al [29] suggesting the reasons the reason for the increased blood loss in the octogenarian group may be secondary to less favourable aneurysm anatomy although theirs did not reach statistical significance, however, they noted that this remained significantly less that blood loss from open surgical repair. Octogenarians with unrepaired large aortic aneurysms pose an increased risk of rupture as discussed by Lederle et al [41] with a 9.4% rupture risk in 1 year for aneurysms between 5.5-5.9cm. However, Hye et al [22] observed that although age >80 and AAA diameter >5.5cm were independent risk factors for survival post-AAA when combined the risk was not amplified.

Our analysis showed that whilst as expected midterm mortality rates were higher in octogenarians which is congruent with De Leur and Lagergren et al's findings [10,27]. De Leur's results however suggested this was not the case after open surgical repair and Fonesca et al [34] results showed comparable 5-year mortality between octogenarians and non-octogenarians. One explanation may be selection bias and a higher operative fitness among the octogenarians undergoing OSR as well as those selected for EVAR in the Fonesca study. This highlights the importance of considering patient selection when offering surgical intervention. The all-cause mortality in octogenarians following EVAR of 10.6% is acceptable and worth consider-

ation. De Leur et al reported an even poorer mid-term survival among octogenarians treated conservatively, again perhaps explainable by selection bias. This however contrasts with the findings of the EVAR 2 trial [40] which showed no benefit of EVAR over conservative management in those unsuitable for operative repair, but they reported a 30-day mortality of 7.3% compared to our study's findings of 2.5% at 30 days. Mortality due to rupture was low at 0.7% and is likely to be an underestimation when compared to previous trials such as the EVAR 2 trial.

The above findings support EVAR as a reasonable option for infra-renal aortic aneurysms, particularly in large aneurysms. With an all-cause mortality of 10.6% of which 0.7% was due to rupture this supports the importance of patient selection and the patient-shared decision when considering aneurysm repair.

Limitations

This systematic review has several limitations. Firstly, heterogeneity throughout the studies should be noted including follow-up periods, patient enrolment and patient characteristics, stent graft devices used and post-procedural outcomes. All the studies were observational in nature and only 11 papers considered to be of high quality reducing the quality of evidence available for review and analysis. This systematic review covers a wide period of 1994-2019, as a result the older generation of stent grafts as well as the learning curve previously associated with the delivery of EVAR may have influenced the outcomes of some of the older studies included. Loss to follow-up as well as lack of reporting on cause of death following aneurysm repair impacts the ability to assess the efficacy of EVAR in the octogenarian population as well as introducing potential selection bias.

Conclusion

Our findings support the usage of EVAR as a safe option for AAA repair in the octogenarian population demonstrating acceptable midterm mortality at 5 years as well as mortality within the early peri-operative phase at 30 days. Given the octogenarian's unique risk profile, we emphasize the importance of careful and appropriate patient selection based on a patient-centred multi-disciplinary approach. This must take into consideration the individual co-morbidities, rupture risk and quality of life markers. Careful patient selection may further reduce the peri-operative and mid-term mortality associated with EVAR repair in octogenarians and further studies are required to investigate prognostic indicators pre-EVAR repair.

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