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REVIEW

The Safety of Device Registries for Endovascular Abdominal Aortic Aneurysm Repair: Systematic Review and Meta-regression

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WHAT THIS PAPER ADDS

The literature is full of papers examining outcomes for different types of stent grafts for repairing infrarenal abdominal aortic aneurysms. New stent grafts are released regularly with publications reporting their "safety" or superiority, but there is no consensus on how to report this. There is also no information on how many patients would be needed to prove non-inferiority to accepted devices. This is the first time that individual EVAR stent graft complication rates have been pooled in meta-analysis, a consensus performed, then the numbers of patients required for registry publications calculated from the results.

Objectives: New and re-designed stent grafts for endovascular aortic aneurysm repair (EVAR) are released regularly. Manufacturers use data from registries to assess stent graft performance, but little is known about the ability of such registries to detect rates of clinically relevant complications. The aim of this paper was to perform a systematic review and meta-analysis to determine pooled failure rates for EVAR stent grafts, to define an acceptable non-inferiority limit for these devices, and then to calculate the number of patients needed for a new device to achieve non-inferiority against published devices.

Data sources and review methods: MEDLINE and EMBASE were searched for studies reporting outcomes of specific EVAR grafts being used for intact infrarenal abdominal aortic aneurysms, from inception to November 2016. Meta-regression was performed to pool data and calculate the patient numbers needed to detect non-inferiority of a future graft performance. An expert consensus was performed to define adequate standards for device safety.

Results: One hundred and forty-seven moderate quality papers involving 27,058 patients were included. Multiple outcomes were pooled. Of these, the estimated rate (±standard error) of overall endoleak (excluding Type II) at 2 years was 5.7 ± 0.6%. The pooled re-intervention rate was 11.1 ± 0.7% at 2 years. There were differences in pooled endoleak rates between different stent graft types. Expert consensus defined non-inferiority as better performance than the worst performing 25% of stent grafts. The most popular outcome in the expert consensus was cumulative endoleak rate (excluding Type II). The number of patients who would need to be enrolled in a registry to demonstrate non-inferiority at this level was 525. Only two of 147 included studies achieved this. The second most popular choice in the expert consensus was re-intervention rate; 492 patients are required to demonstrate this.

Conclusions: Five hundred and twenty-five patients need to be entered into a registry to demonstrate non-inferiority to previous stent grafts. Almost all previous publications have captured lower patient numbers. With performance varying between devices, and new devices being introduced regularly, there is an urgent need to capture higher quality long-term data on EVAR stent grafts.

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INTRODUCTION

The incidence of abdominal aortic aneurysm (AAA) repair continues to increase in the western world.[1] Around 40,000 non-ruptured AAA are treated every year in the United States alone, with 80% being treated endovascularly. In the

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UK the proportion of AAA treated endovascularly has increased from less than 10% in 2005 to around 60% in 2012, and continues to grow.[1] An infrarenal stent graft for endovascular AAA repair (EVAR) costs around $7000.[2]

This creates a lucrative market for device manufacturers, and new stent grafts for performing EVAR are released regularly. Commonly used, established stent grafts are given regular iterative updates, which often retain the same name for marketing purposes but may alter the graft design and structure.[3,4] The regulatory requirements for stent graft use vary by country or territory, and while not always available for scrutiny comprise a mixture of bench testing and limited clinical data. The "safety" and marketing data for these devices is therefore usually based on post-market surveillance registry publications; a recent Cochrane review highlighted that no randomised trials exist comparing one stent graft type with another.[5] Stent graft fixation, material, and stent design all vary between manufacturers, and different devices have appeared to suffer from different types of failure historically.[6] Most devices fail after more than 5 years, meaning long-term follow-up of EVAR stent grafts is especially important.

These device failures lead to a significant late complication rate after EVAR, which includes treated AAAs rupturing, often leading to death.[7] Even though there is a perception that individual stent graft designs failed in different ways, these results have never been pooled and compared. The ability of stent graft registry publications to detect failures that could lead to patient death is unknown. Exactly which of these late failures is of most interest to surgeons and radiologists is also undefined. The aims of this paper were therefore threefold:

1. To perform a systematic review and meta-regression to determine pooled failure rates for EVAR stent grafts. As part of this process, to examine individual factors leading to stent graft failure where available.
2. To define an acceptable non-inferiority limit for EVAR stent grafts via expert survey.
3. To calculate the number of patients needed for a new device registry to achieve non-inferiority against previous devices.

MATERIALS AND METHODS

Systematic review and meta-regression

Search methods. A systematic review of published work was conducted as per the protocol specified by the Cochrane collaboration,[8] and reported in line with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement for the conduct of meta-analyses of intervention studies.[9] The following sources were searched: Medline via PubMed, Embase, and the Cochrane Library Database (Cochrane Central Register of Controlled Trials) for studies comparing stent graft types for endovascular repair of intact abdominal aortic aneurysms (AAAs). All studies describing results from more than 10 patients were included. Non-English language papers were excluded. Studies arising from duplicate publications and review articles were excluded. Studies were excluded if the subjects included non-degenerative AAAs, thoracic, thoraco-abdominal, or isolated iliac aneurysms. Studies of only emergency or complex aneurysms (fenestrated, extreme anatomy, e.g. angled neck, short neck) were excluded, though if these were case cohort studies, data from the control group (non-emergency, non-complicated) were extracted. Studies of endovascular sealing devices were excluded. As a result, stent grafts (and manufacturers) included were Zenith (Cook Medical, Bloomington, IN, USA); Zenith Low Profile (Cook Medical); Endurant (Medtronic, Minneapolis, MN, USA); Excluder (W.L. Gore, Newark, DE, USA); AFX (Endologix, Irvine, CA, USA); Anaconda (Vascutek, Inchinnan, Glasgow, UK); Aorfix (Lombard, Didcot, UK); Powerlink (LeMaitre, Burlington, MA, USA); Talent (Medtronic); AneuRx (Medtronic); Incraft (Cordis, Milpitas, CA, USA). For each stent graft the heading "Aneurysm" and the specific stent graft name, e.g. "Excluder", were used as search terms.

Articles were also identified by hand searching of references and extensive use of the related articles function in PubMed. The last search date was November 24, 2016.

Data extraction. Data were extracted independently by two authors (F.K. and D.B.). Data extraction was initially trialled on 10 papers, and then refined. Extracted demographic data included stent graft studied, company sponsored study, on- or off label use, years over which graft studied, study design, number of patients, and duration of follow-up.

Outcome data collected included endoleak rates and types, re-intervention rates, and late rupture rates. Data on Type IV and V endoleaks were initially collected, but due to the extremely low reported rates of Type IV leaks, and the heterogeneity inherent in Type V leak definition, results for these types of leaks were not further examined, though they are pooled within total cumulative endoleak rates. Study quality was assessed using the Newcastle—Ottawa scale.[10] Further details of extracted data are given in Appendix 1. Where short and long-term results from the same patient cohort were published separately, relevant data were retrieved from both publications preferentially using the latest.

Statistical analysis

Type I—III endoleaks were modelled using weighted linear regression modelling, with constant term representing initial "failure to seal" and linear term representing subsequent development of leak over time: leak rate = late leak rate × mean follow-up time + failure to seal.

Terms were weighted in the regression analysis according to the number of patients in the study. Overall endoleak rates, re-intervention rates, and rupture rates were modelled in the same way. The reason that meta-regression was chosen over fixed point meta-analysis was that different studies included different follow-up times, so attempting to consider these rates at one or more time

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