

## REVIEW

## Incidence of Stroke Following Thoracic Endovascular Aortic Repair for Descending Aortic Aneurysm: A Systematic Review of the Literature with Meta-analysis<sup>☆</sup>

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### WHAT THIS PAPER ADDS

This is a comprehensive review including a meta-analysis looking specifically at the stroke risk of patients undergoing thoracic endovascular aortic repair (TEVAR) for descending thoracic aortic aneurysm, thus eliminating heterogeneity regarding patient selection as effectively as possible. There is an indication that stroke risk is increased if the left subclavian artery (LSA) is covered without revascularisation during the procedure. Such data are important for informing patients of procedure risks and to increase research efforts towards stroke prevention.

**Objective:** Stroke is an increasingly recognised complication following thoracic endovascular aortic repair (TEVAR). The aim of this study was to systematically synthesise the published data on perioperative stroke incidence during TEVAR for patients with descending thoracic aneurysmal disease and to assess the impact of left subclavian artery (LSA) coverage on stroke incidence.

**Methods:** A systematic review of English and German articles on perioperative (in-hospital or 30 day) stroke incidence following TEVAR for descending aortic aneurysm was performed, including studies with  $\geq 50$  cases, using MEDLINE and EMBASE (2005–2015). The pooled prevalence of perioperative stroke with 95% CI was estimated using random effect analysis. Heterogeneity was examined using  $I^2$  statistic.

**Results:** Of 215 studies identified, 10 were considered suitable for inclusion. The included studies enrolled a total of 2594 persons (61% male) between 1997 and 2014 with a mean weighted age of 71.8 (95% CI 71.1–73.6) years. The pooled prevalence for stroke was 4.1% (95% CI 2.9–5.5) with moderate heterogeneity between studies ( $I^2 = 49.8\%$ ,  $p = .04$ ). Five studies reported stroke incidences stratified by the management of the LSA, that is uncovered versus covered and revascularised versus covered and not-revascularised. In cases where the LSA remained uncovered, the pooled stroke incidence was 3.2% (95% CI 1.0–6.5). There was, however, an indication that stroke incidence increased following LSA coverage, to 5.3% (95% CI 2.6–8.6) in those with a revascularisation and 8.0% (95% CI 4.1–12.9) in those without revascularisation.

**Conclusion:** Stroke incidence is an important morbidity after TEVAR, and probably increases if the LSA is covered during the procedure, particularly in those without revascularisation.

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### INTRODUCTION

Thoracic endovascular aortic repair (TEVAR) is regarded as a lower-risk treatment for a variety of thoracic aortic conditions,

and, thus, is the preferred treatment approach over open repair in many cases.<sup>1,2</sup> Its minimal invasiveness compared with open repair means that TEVAR has gained widespread adoption and has also been propagated in official guidelines to be applied at an even lower diameter aneurysm threshold than open repair.<sup>3</sup> The endovascular aortic repair technique appears more likely to meet the wish of patients for a rapid recovery. Associated neurological complications, however, interfere considerably with this wish; first, neurological events may be fatal in up to 33%,<sup>4</sup> and, second, the consequences of

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neurological events, that is long-term disability and handicap are highly correlated with impaired physical health related quality of life.<sup>5</sup> The most severe neurological complications are paraplegia and stroke. The incidence of spinal cord ischaemia following TEVAR varies considerably across studies between 0 and more than 10%,<sup>6–11</sup> and a considerable body of research has led to a reduction in the paraplegia rate.<sup>12</sup> So far, the reduction of stroke during endovascular aortic interventions has attracted less interest, apart from differential revascularisation strategies when left subclavian artery (LSA) coverage is needed. The risk of stroke during TEVAR is not surprising; atherosclerotic disease of the aortic arch is not only a recognised risk factor for unprovoked stroke,<sup>13</sup> but also for neurological events after open heart surgery or during carotid artery stenting.<sup>14</sup> A recent study looking at mid-term outcomes after TEVAR in relation to aortic pathology reported a more than twofold higher early stroke incidence among thoracic aortic aneurysm patients compared with those with an aortic dissection.<sup>15</sup> This may be a reflection of more advanced atherosclerotic disease among the aneurysm patients. Therefore, new therapies might focus on plaque stabilisation, for example the use of high dose statins, to prevent stroke and on the evolution of technical adjuncts (i.e. further development of fusion imaging techniques), which would lead to a reduction in the time the endograft dangles within the aortic arch causing plaque dislocation. However, before designing any such studies, it is essential to know the exact magnitude of the problem, the stroke incidence.

Therefore, the aim of this study was to synthesise the published data on stroke incidence following TEVAR for descending thoracic aortic aneurysm in a systematic review.

## METHODS

### *Systematic review and protocol*

The systematic review followed quality reporting guidelines set by the PRISMA (Preferred Reporting Items for Systematic reviews and Meta-Analysis) group (<http://www.prisma-statement.org/>).<sup>16</sup> A review protocol including every step of the systematic review was developed and approved by all authors.

### *Search strategy*

MEDLINE and EMBASE were initially searched up to February 16, 2015, and subsequently updated up to June 30, 2016 using the following search terms in different combinations; “Aorta, Thoracic/surgery” [Mesh], “Aorta, Thoracic/therapy” [Mesh], “stroke”, “neurologic deficit”. Filters were used to restrict studies to human studies only and to articles in English and German published from 2005 onwards, to focus on procedures with technologically more advanced devices. In addition, reference lists of reviews were also searched for further studies to be included.

### *Eligibility criteria, study selection*

Potential studies were reviewed according to a set of eligibility criteria. The study participants (minimum

$n = 50$ , men or women) must have undergone TEVAR with indications being separable among descending thoracic aortic aneurysms, traumatic aortic lesions, and aortic dissections. Studies were not excluded if penetrating aortic ulcers were not separable from aneurysms. Studies on patients with connective tissue disease were excluded, as well as studies involving ascending aortic aneurysms. In addition, the following were also excluded: review articles, studies where patient data were duplicated (in which case the most recent or comprehensive study was used), editorials, letters, and case reports. Study authors were contacted in cases where outcome data could not easily be separated according to underlying aortic pathology.

### *Data collection process*

A data extraction form was designed to identify variables in the eligible studies. The following were extracted: the study design (prospective, retrospective, case series, observational studies with or without comparison group, registries, multicentre or single centre), author affiliation, date of publication, country (where study was undertaken), year of publication, recruitment period, inclusion and exclusion study criteria, baseline data including age, sex, and other cardiovascular risk factors (e.g. blood pressure, history of smoking, drugs [i.e. statins], ischaemic heart disease, diabetes), type of endograft, information on coverage of the LSA and on revascularisation strategies, outcomes (stroke incidence in hospital or within 30 days of intervention, and mortality rate in hospital or within 30 days of intervention). Two authors (RSvA, JTP) independently extracted the data from the potentially eligible primary studies and cross-checked their results. Any disagreements between the two reviewers were discussed and settled by agreement.

For studies that failed to provide baseline variables (age separable by aortic pathology, stroke incidence according to coverage of LSA), study authors were contacted for completion and if these variables were not available the studies were excluded for these specific analyses.

### *Estimation of perioperative stroke incidence*

The reported overall mean stroke incidence either within 30 days or in-hospital (if 30 day outcome was not reported) was extracted from each study. In studies that reported on LSA coverage, stroke incidences were extracted according to revascularisation strategy of the LSA (uncovered versus covered and revascularised versus covered and non-revascularised).

### *Study quality*

The Newcastle–Ottawa Scale was used to assess the quality of the included studies using a “star system” based on three broad perspectives: the selection of the study groups; the comparability of the groups; and the ascertainment of either the exposure or outcome of interest for cohort studies. The different items were adapted to the study

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