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The Consequences of Real Life Practice of Early Abdominal Aortic Aneurysm Repair: A Cost-Benefit Analysis

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WHAT THIS PAPER ADDS

The 55 mm intervention threshold for abdominal aortic aneurysm (AAA) repair is uniformly accepted; however, vascular registry data show a high incidence of premature repair (i.e., earlier than indicated by the consensus guidelines) in clinical practice. To estimate the consequences of the practice of premature repair, a simulation on the basis of the Medicare data for endovascular aneurysm repair was performed. Conclusions of this simulation are that although premature AAA repair beneficially influences survival, it comes with considerable costs (approx. 1 million USD per prevented aneurysm related death) thereby negatively impacting EVAR cost effectiveness.

Background: The reported 54 mm median intervention diameter for endovascular aneurysm repair (EVAR) in the Vascular Quality Initiative and European data from the Pharmaceutical Aneurysm Stabilisation Trial (PHAST) implies that in real life the majority of abdominal aortic aneurysm (AAA) repairs occur at diameters smaller than the consensus intervention threshold of 55 mm. This study explores the potential consequences of this practice.

Methods: The differences between real life AAA repair and consensus based intervention threshold were explored in reported data from vascular quality initiatives and PHAST. The subsequent consequences of advancement of endovascular aneurysm repair (EVAR) were estimated using a multistate model based on life tables for the EVAR Medicare population.

Results: There appears an approximate 5 mm difference in AAA diameter between real life practice and consensus intervention threshold. Assuming a 2.5 mm annual growth rate, this results in an approximately 2 year advancement of AAA repair. According to the model used, early repair reduces overall small aneurysm patient mortality by 2.3%, it results in 21.9% more EVAR procedures, more EVAR related deaths, and 42.3% and 36.8% more open and endovascular re-interventions, respectively. Cost–benefit estimates imply 482 fewer AAA related deaths, but 140 extra EVAR related deaths for a population of more than 30,000 AAA patients, and a 300 million USD increase in health costs for the 8 year observation period in the Medicare population.

Conclusions: In the real life situation a large proportion of EVAR procedures appear to occur before reaching the consensus threshold. Although this reduces mortality, it comes at a cost of approximately 1 million USD per prevented rupture related death.

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INTRODUCTION

The United Kingdom Small Aneurysm Trial and Aneurysm Detection and Management (ADAM) trial reported no survival benefit for early elective open repair of abdominal aortic aneurysms (AAAs) measuring 40–54 mm.^{1–3} Similar

findings were reported for early elective endovascular aneurysm repair (EVAR) by the Comparison of surveillance versus aortic endografting for small aneurysm repair (CAESAR) and Positive Impact of Endovascular Options for Treating Aneurysms Early (PIVOTAL) trials.^{4,5} Consequently, current guidelines for AAA treatment recommend ultrasound follow-up for AAAs smaller than 55 mm for male patients, after which point surgical repair should be considered.⁶ This trade-off is reflected by the respective 59 and 65 mm mean intervention diameters in the Vascular Study Group of New England (VSGNE) database and the EVAR 1 trial.^{7,8}

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Remarkably, the reported 54 mm median intervention diameter for EVAR in the Vascular Quality Initiative suggests that in a real life setting AAA repair occurs earlier than indicated by prevailing guidelines.⁹ Similar observations in the Pharmaceutical Aneurysm Stabilisation Trial (PHAST), a nationwide study performed in the Netherlands, indicate that the majority of AAA repairs in patients under surveillance for a small (i.e., <55 mm) AAA occurred at diameters less than 55 mm.¹⁰

Although earlier repair may prevent rupture of small AAA in some patients, premature repair comes with potential clinical and financial consequences. To that end, a simulation on basis of a multistate model using real life data from the EVAR procedures performed in the Medicare population was established.¹¹

METHODS

Simulation model

A multistate model was applied,¹² which is used to model movement of patients among various states in order to analyse and compare (time to) events. This study is based on modeling data of 39,966 Medicare patients (22.3% female) who received elective EVAR between 2001 and 2009.¹¹ The 8 year life table for this Medicare EVAR population was used as a basis for the model.

In this report, the consequences of a 5 mm advancement of AAA repair for a “real life” setting are simulated. This 5 mm advancement is based on observations of the PHAST trial¹⁰ and on the data from the Vascular Quality Initiative⁹ and the VSGNE.⁷ More specifically, data from the PHAST trial show a 52 (2.7) mm mean (SD) intervention diameter for the 43 patients undergoing elective AAA repair. This number is close to the 54 mm median diameter for elective EVAR in the Vascular Quality Initiative.⁹ In contrast, data from the VSGNE indicate a 59 mm mean intervention diameter for elective AAA repair.⁷

Consequently, there appears to be a 5 mm difference in mean intervention diameters in the VSGNE and Vascular Quality Initiative^{7,9} and a 5 mm discrepancy between the local size readings and the protocolled trial readings in the PHAST trial,¹⁰ suggesting that AAA repair is often performed at a 5 mm lower diameter in real life settings. Assuming 2.5 mm as the average yearly growth rate for 50 mm AAAs,¹⁰ this 5 mm difference will result in an approximately 2 year earlier repair than indicated by the ultrasound based guidelines. On this basis, it was decided to model the consequences of 2 year premature AAA repair for a real life setting.

Primary outcome measures were the number of EVARs, deaths, and re-interventions. Data for the Medicare cohort¹¹ hold information on open and endovascular re-interventions. Open re-interventions were defined as AAA related secondary open surgical procedures (e.g., open repair of aneurysm, repair of false aneurysm, removal of graft, or graft infection). Endovascular re-interventions were defined as AAA related secondary endovascular procedures (e.g., stent graft extension, embolisation, aortic or iliac angioplasty).¹¹

The simulation model was constructed based on the following assumptions:

- (1) the proportion of deaths in the population remains equal and is not influenced by postponing repair;
- (2) the proportion of AAA rupture after EVAR is not influenced by postponing repair;
- (3) the AAA growth rate is 2.5 mm/year and remains stable over 2 years;¹⁰
- (4) throughout 8 years of follow-up, interventions related to the management of the AAA or its complications will shift 2 years, but the proportion will remain equal;
- (5) half of the patients who present with a ruptured AAA die before emergency repair and will be added to the number of deaths. The incidence of rupture for AAAs of 40–55 mm per year in the model was 1%.¹

Table 1. Life table with 8 year events of 39,966 Medicare patients who received EVAR.

| Interval start | Interval end | Number undergone repair/at risk ^a | Number of ruptures | % | Number of endovascular re-interventions | % | Number of open re-interventions | % | Number of deaths | % | Lost to follow-up | % |
|----------------|--------------|--|--------------------|------|---|------|---------------------------------|------|------------------|------|-------------------|-------|
| 0 | 0.5 | 39,966 | 166 | 0.42 | 787 | 1.97 | 65 | 0.16 | 1911 | 4.78 | 0 | 0 |
| 0.5 | 1.0 | 38,055 | 138 | 0.36 | 635 | 1.67 | 38 | 0.10 | 1220 | 3.21 | 0 | 0 |
| 1.0 | 1.5 | 36,835 | 106 | 0.29 | 477 | 1.29 | 38 | 0.10 | 1149 | 3.12 | 1458 | 3.96 |
| 1.5 | 2.0 | 34,228 | 77 | 0.22 | 380 | 1.11 | 34 | 0.10 | 1263 | 3.69 | 1306 | 3.82 |
| 2.0 | 2.5 | 31,659 | 84 | 0.27 | 342 | 1.08 | 35 | 0.11 | 1180 | 3.73 | 1595 | 5.04 |
| 2.5 | 3.0 | 28,884 | 62 | 0.21 | 275 | 0.95 | 37 | 0.13 | 1127 | 3.90 | 1530 | 5.30 |
| 3.0 | 3.5 | 26,227 | 51 | 0.19 | 242 | 0.92 | 26 | 0.10 | 1074 | 4.10 | 1807 | 6.89 |
| 3.5 | 4.0 | 23,346 | 49 | 0.21 | 198 | 0.85 | 21 | 0.09 | 1034 | 4.43 | 1732 | 7.42 |
| 4.0 | 4.5 | 20,580 | 46 | 0.22 | 143 | 0.69 | 16 | 0.08 | 939 | 4.56 | 2069 | 10.05 |
| 4.5 | 5.0 | 17,572 | 41 | 0.23 | 130 | 0.74 | 23 | 0.13 | 808 | 4.60 | 1870 | 10.64 |
| 5.0 | 5.5 | 14,894 | 40 | 0.27 | 106 | 0.71 | 18 | 0.12 | 741 | 4.98 | 2057 | 13.81 |
| 5.5 | 6.0 | 12,096 | 28 | 0.23 | 65 | 0.54 | 13 | 0.11 | 631 | 5.22 | 1772 | 14.65 |
| 6.0 | 6.5 | 9693 | 32 | 0.33 | 48 | 0.50 | 7 | 0.07 | 540 | 5.57 | 1622 | 16.73 |
| 6.5 | 7.0 | 7531 | 11 | 0.15 | 39 | 0.52 | 6 | 0.08 | 391 | 5.19 | 1578 | 20.95 |
| 7.0 | 7.5 | 5562 | 19 | 0.34 | 37 | 0.67 | 7 | 0.13 | 333 | 5.99 | 1440 | 25.89 |
| 7.5 | 8.0 | 3789 | 12 | 0.32 | 20 | 0.53 | 8 | 0.21 | 207 | 5.46 | — | — |
| Total | | | 962 | | 3924 | | 392 | | 14,548 | | | |

^a Number at risk = number at risk previous half year – (number of deaths + lost to follow-up).

Table 2. Simulation model: 2 year postponement of EVAR in the Medicare population. Model starts with 39,966 patients.

| Interval start | Interval end | Number undergone repair/at risk ^a | Rupture (1%/year) | Emergency repair (N) | Rupture (no repair) | Number of endovascular re-interventions | Number of open re-interventions | Number of deaths | Without repair | 30% repair patients | Population | Total number of deaths | Lost to follow-up | Patients remaining eligible for repair |
|----------------|--------------|--|-------------------|----------------------|---------------------|---|---------------------------------|------------------|----------------|---------------------|--------------|------------------------|-------------------|--|
| 0 | 0.5 | 39,966 | 100 | 100 | 100 | 0 | 0 | 100 | 100 | 30 | 1911 (4.78%) | 2040 | 0 | 37,926 |
| 0.5 | 1.0 | 37,926 | 95 | 95 | 95 | 0 | 0 | 95 | 95 | 28 | 1217 (3.21%) | 1341 | 0 | 36,585 |
| 1.0 | 1.5 | 36,585 | 91 | 91 | 91 | 0 | 0 | 91 | 91 | 27 | 1141 (3.12%) | 1260 | 1449 (3.96%) | 33,876 |
| 1.5 | 2.0 | 33,876 | 85 | 85 | 85 | 0 | 0 | 85 | 85 | 25 | 1250 (3.69%) | 1360 | 1294 (3.82%) | 31,222 |
| Total | | | 371 | 371 | 371 | 0 | 0 | 371 | 371 | 111 | 5519 | 6002 | | |

^a Number at risk = number at risk previous half year – (number of deaths + lost-to-follow up).

- (6) 30% of patients undergoing emergency repair will not survive and will be added to the number of deaths;¹³
 (7) the peri-operative mortality of EVAR is 1.6%.¹¹

Cost analysis was performed on the basis of data for procedural costs as reported in the EVAR trials (GBP) and OVER trial (USD).^{14,15} Both open and endovascular re-interventions in the Medicare database include a great variety of clinical procedures with varying degrees of invasiveness and technical complexity. Costs were conservatively estimated for open and endovascular re-interventions at 50% of the costs for respectively open repair and EVAR published in the OVER and EVAR trials.

Analyses

Outcomes in the alternative scenario of the model in which repair was delayed two years were calculated manually using the Medicare data as basis.¹¹ The chi-square test was used to calculate *p* values.

RESULTS

Life tables containing the events of 8 years for the Medicare cohort and model cohort are presented in Tables 1–3. Modeling suggested that 2 year advancement of AAA repair results in a 2.3% reduction in mortality (Table 4). Yet, this reduction came at the cost of 21.9% more EVAR procedures and a 0.96% increase in EVAR related deaths. Moreover, premature EVAR resulted in a 42.3% and 36.8% increase in open and endovascular re-interventions, respectively (Table 5).

A sensitivity analysis was performed for population mortality and rupture rates (results are presented in Tables S1-A and S1-B). Based on data from the United Kingdom Small Aneurysm Trial,¹ a 1% annual rupture risk for AAAs of 40–55 mm was imputed in the model. The influence of the annual rupture rate on model outcomes were tested by simulating annual rupture rates of 0.7% and 1.3%. It showed that an annual rupture rate of 0.7% resulted in fewer emergency repairs (–111) and deaths by AAA rupture (–145), in addition to more EVARs (+98). In contrast, an annual rupture rate of 1.3% increased the number of emergency repairs by 111 and AAA related deaths by 145, and reduced the number of EVARs by 97.

The first 2 year mortality rate of the small AAA patients in the Medicare cohort was 13.8%. The influence of different population specific mortality rates on model outcomes was estimated by simulating a first 2 year mortality of 10% and 18%. The lower population mortality rate increased the number of EVARs by 132, EVAR related deaths by 2, and open and endovascular re-interventions by 1 and 11 respectively. A higher mortality rate reduced the number of EVAR procedures by 145 and minimally reduced EVAR related mortality and the number of open and endovascular re-interventions.

Based on data from the Medicare population, it was estimated that 2 year advancement of repair resulted in extra costs of 324.1 million USD for EVAR procedures and

Table 3. Life table (events) for the model cohort (2 year postponement of EVAR).

| Start | End | Number at risk | Events rupture | | Endovascular re-interventions | | Open re-interventions | | Number of deaths | | Lost to follow-up | |
|-------|-----|----------------|----------------|------|-------------------------------|------|-----------------------|------|------------------|------|-------------------|-------|
| | | | N | % | N | % | N | % | N | % | N | % |
| 0 | 0.5 | 31,222 | 131 | 0.42 | 615 | 1.97 | 50 | 0.16 | 1165 | 3.73 | 1574 | 5.04 |
| 0.5 | 1.0 | 28,484 | 103 | 0.36 | 476 | 1.67 | 28 | 0.10 | 1111 | 3.90 | 1510 | 5.30 |
| 1.0 | 1.5 | 25,863 | 75 | 0.29 | 334 | 1.29 | 26 | 0.10 | 1060 | 4.10 | 1782 | 6.89 |
| 1.5 | 2.0 | 23,021 | 51 | 0.22 | 256 | 1.11 | 23 | 0.10 | 1020 | 4.43 | 1708 | 7.42 |
| 2.0 | 2.5 | 20,293 | 55 | 0.27 | 219 | 1.08 | 22 | 0.11 | 925 | 4.56 | 2039 | 10.05 |
| 2.5 | 3.0 | 17,328 | 36 | 0.21 | 165 | 0.95 | 23 | 0.13 | 797 | 4.60 | 1844 | 10.64 |
| 3.0 | 3.5 | 14,687 | 28 | 0.19 | 135 | 0.92 | 15 | 0.10 | 731 | 4.98 | 2028 | 13.81 |
| 3.5 | 4.0 | 11,928 | 25 | 0.21 | 101 | 0.85 | 11 | 0.09 | 623 | 5.22 | 1747 | 14.65 |
| 4.0 | 4.5 | 9558 | 21 | 0.22 | 66 | 0.69 | 8 | 0.08 | 532 | 5.57 | 1599 | 16.73 |
| 4.5 | 5.0 | 7426 | 17 | 0.23 | 55 | 0.74 | 10 | 0.13 | 385 | 5.19 | 1556 | 20.95 |
| 5.0 | 5.5 | 5485 | 15 | 0.27 | 39 | 0.71 | 7 | 0.12 | 329 | 5.99 | 1420 | 25.89 |
| 5.5 | 6.0 | 3736 | 9 | 0.23 | 20 | 0.54 | 4 | 0.11 | 204 | 5.46 | — | — |
| Total | | | 565 | | 2480 | | 226 | | 8883 | | | |

30.3 million USD for secondary re-interventions. These additional costs of premature EVAR were partially outweighed by a reduction in emergency repairs and rupture related deaths of 0.93% and 1.21%, respectively. Extrapolation of the data from the model, estimates the costs for one prevented AAA rupture by a 5 mm advancement of AAA repair at approximately 1 million USD.

Costs per prevented death from rupture were influenced by different annual rupture rates in the sensitivity analysis, as annual rupture rates of 0.7% and 1.3% resulted in approximately 1.7 million and 0.7 million USD per prevented AAA death respectively. Variations in the population mortality rates minimally influenced the price of one prevented death by AAA rupture, as this remained around 1 million USD.

DISCUSSION

The presented simulation model on the basis of the Medicare data shows that premature EVAR is associated with lower mortality but comes with considerable costs. It is estimated that the costs of one prevented death by rupture in the Medicare population is around 1 million USD, a price that may profoundly impact EVAR cost effectiveness. As large differences in procedural costs exist between geographical regions the actual consequences of premature repair for EVAR cost effectiveness may vary per region.

Prevailing guidelines for AAA management recommend ultrasound follow-up of the aneurysm until 5.5 cm (for males), at which point consideration for repair needs to be

made.⁶ Considering a delay in pre-operative work-up, it is anticipated that compliance with the guidelines will result in mean intervention diameters above 55 mm. This is reflected by the mean intervention diameters of 65 mm in the EVAR 1 trial and 59 mm in the Vascular Study Group of New England (VSGNE) database.^{8,7}

The reported 54 mm median intervention diameter for elective endovascular repair in the Vascular Quality Initiative shows that in general practice at least half of AAA repairs occurred at diameters below the consensus intervention threshold.⁹ Also, in evaluating the PHAST trial it was observed that a large part of AAA repairs in patients under surveillance for a small AAA were performed at diameters less than 55 mm.¹⁰ As AAA management in this trial was left to the discretion of the attending physician and patients’ preferences, this suggests that in real life the majority of AAA repairs in the participating centres were premature.

Based on the 2.5 mm of annual growth for aneurysms of 50–55 mm in 286 patients participating in the PHAST study, the above data imply that in the real life setting AAA repair occurs around 2 years earlier than would be expected based on practice guidelines.

The events leading to a premature decision for repair appear multifactorial, and presumably include patients’ and doctors’ variables, but also technical factors such as systematic discrepancy between ultrasound and computed tomography (CT) based AAA size estimates. Reportedly, even after correcting for different measuring protocols, CT

Table 4. Events during 8 years of follow-up in the CT based premature EVAR Medicare cohort and the simulation model of 2 year delayed repair.

| Outcomes Medicare cohort and model | | | | | | |
|------------------------------------|-----------------|--------|--------|---|-----------------------|--|
| Events in 8 years | Medicare cohort | Model | p | Difference between Medicare and model Absolute difference | 95% CI* (lower–upper) | |
| EVAR repairs | 39,966 | 31,222 | — | — | — | |
| Total mortality | 14,548 | 14,884 | <.0001 | 336 | (306–378) | |
| Open re-interventions | 392 | 226 | .0003 | 166 | (145–184) | |
| Endovascular re-interventions | 3924 | 2480 | <.0001 | 1444 | (1373–1491) | |

*CI: Confidence interval.

Table 5. Comparison of events and costs after 8 years of follow-up between the Medicare cohort and the 2 years delayed repair simulation model.

| Differences in costs and benefits between Medicare cohort and model | | | | |
|---|---|---------|----------------|-----------------|
| Events in 8 years | Differences between Medicare cohort and model | | Costs per unit | |
| | Cohort ¹¹ | Model | £ ^b | \$ ^c |
| Mortality due to AAA rupture | — | 482 | — | — |
| Mortality due to EVAR ^a | 140 ^f | — | — | — |
| Emergency repairs | — | 371 | £13 019 | \$37 068 |
| Elective EVAR repairs | 8744 | — | £13 019 | \$37 068 |
| Open re-interventions ^d | 166 | — | £ 5921 | \$ 21 485 |
| Endovascular re-interventions ^e | 1444 | — | £ 6510 | \$ 18 534 |
| Total costs (in millions) | £124.2 | £4.83 | | |
| | \$354.45 | \$13.75 | | |

^a Schermerhorn et al. 1.6% peri-operative EVAR mortality.¹¹

^b Brown et al. EVAR 1/2 trials.¹⁴

^c Lederle et al. OVER trial.¹⁵

^d Open re-intervention cost is estimated at 50% of elective open repair costs in OVER and EVAR trials.

^e Endovascular re-intervention cost is estimated at 50% of elective EVAR costs in OVER and EVAR trials.

^f A small difference (6) in cohort mortality exists due to percentages and rounding of life table numbers.

size estimates are larger than those measured by ultrasound.¹⁶ Although it has been pointed out that CT is more accurate in measuring AAA diameter,¹⁷ it is important to note that the 55 mm intervention threshold is based on ultrasound. As such, CT based size estimates should be normalised for ultrasound estimates.

Accelerated repair has been advocated as a means of further reducing AAA related mortality.¹⁸ Model outcomes show a modest effect of early repair on overall mortality but also that the accompanying costs of early EVAR far exceed the expected mortality benefit. Consequently, it has been pointed out that lowering the 55 mm intervention threshold in AAA treatment cannot be substantiated on basis of the existing evidence.¹⁹

Accelerated AAA repair may negatively impact EVAR cost effectiveness primarily through a mechanism referred to as competitive deaths. AAA disease is associated with high cardiovascular comorbidity and impaired life expectancy with a 2 year overall mortality rate which can be as high as 20%.^{11,20} As a consequence, postponing repair will reduce the need for AAA repair.

There appears to be great variation in AAA treatment between countries concerning type of intervention and diameter at time of repair. A report by Beck and colleagues²¹ presenting data of 11 international vascular registries showed that overall 28% of intact AAAs are repaired at diameters smaller than recommended by guidelines. In particular, EVAR seems to be associated with treating AAAs at lower diameters (31%).²¹ These observations are in line with the data from PHAST¹⁰ and the Vascular Quality Initiative.⁹

Possible explanations for this phenomenon are the lower procedural risk and impact of EVAR, pressure to meet volume requirements, and the presumption that earlier repair is associated with more favourable anatomy, making it more “difficult” to wait.

Premature decisions for repair will also prolong the in situ time of a graft by approximately 2 years and thus increase the likelihood of EVAR related complications and need for re-interventions.²² Data on the functional life span of

endografts are unavailable. Also, it cannot be stated for certain that all re-interventions in the Medicare cohort are due to graft failure, and as such this aspect could not be fully incorporated in the analysis. Nevertheless, observations in the Medicare population and EVAR 1 trial identify long-term stent graft function as a point of concern.^{11,23}

This study has some limitations. First, the consequences of early AAA repair are based on assumptions. A sensitivity analysis was performed with various annual rupture rates (0.7% and 1.3%) and the first 2 year population mortality rates (10% and 18%) to test for variation in model outcomes if some model assumptions or parameters were different. The results showed that EVAR cost effectiveness is mostly dependent on the effect on AAA related mortality as annual rupture risks below 1% drastically increase the cost of one prevented death by AAA rupture to 1.7 million USD. Yet, financial consequences are obviously influenced by procedural costs which may vary per device and country.

Second, the clinical data are derived from the Medicare database, which is subject to coding error.¹¹ A third limitation is the extreme variation in reported costs for EVAR related procedures and re-interventions. The costs for open repair and EVAR were estimated based on previously reported data.^{14,15} Costs for re-interventions (i.e., repair of false aneurysm, stent graft extension, embolisation) are not available. Those costs were therefore estimated at a conservative 50% of the costs of open repair and EVAR. Taking into account the striking differences in procedure related costs between the United States and Europe (UK), the costs for these countries were presented separately. Costs for other countries may differ from these estimates.

Finally, long-term data from the EVAR 1 trial report AAA ruptures after elective EVAR.²³ This aspect is not included in the analysis.

In conclusion, although the apparent real life practice of premature AAA repair moderately reduces AAA related mortality, it increases the number of EVARs and EVAR related re-interventions, thereby compromising EVAR cost effectiveness.

CONFLICT OF INTEREST

None.

FUNDING

None.

APPENDIX A. SUPPLEMENTARY DATA

Supplementary data related to this article can be found at <http://dx.doi.org/10.1016/j.ejvs.2017.03.025>.

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