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Case Study

Evaluating the decision to use fenestrated EVAR for the elective treatment of a complex AAA

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Introduction

An aneurysm is defined as a focal dilatation of all three walls of an artery wall. This can occur at any point in the arterial tree but most commonly presents as an abdominal aortic aneurysm (AAA), with a diameter of 50% greater than its normal size. The prevalence of AAAs is estimated to be between 1.2-7.6% in over 50 year olds in the UK, and it is sevenfold higher for men compared with women[1]. There is approximately a 1% mortality from ruptured AAAs, and as such current NHS guidelines recommend that all men over 65 are screened annually, a precedent supported by the Multicentre Aneurysm Screening Study (MASS)[2]. AAAs reaching 5.5cm in diameter require elective surgical repair, which can take the form of endovascular aneurysm repair (EVAR) or open surgical repair.

Case History

HQ is a 79 year old man (DOB 12/10/1939), who was admitted to the JR for elective surgery of his asymptomatic abdominal aortic aneurysm. It was discovered incidentally and had been ultrasound-monitored for several years, noted as being 5.6cm on 5/5/17. He received a CABG procedure on 15/12/2017 due to left circumflex and anterior descending coronary artery disease, at which point the aneurysm was 6.1cm in diameter. The CABG operation involved saphenous vein grafting and was perioperatively uneventful, with ITU admission after surgery for suspected sepsis (later excluded). An ECG prior to the operation also described aortic sclerosis and mild mitral and tricuspid regurgitation. Separately, he had a tibia operation involving bone grafting fifty years previously, and a lump removal from his left hip in the 1970s. His other previous significant medical history included benign prostate hyperplasia, hypertension, hypercholesterolaemia and COPD, plus gout. He is an ex-smoker, having smoked 20 cigarettes a day for 50 years before cessation four years ago. He is a retired jockey, with independent ADLs, an estimated METS of 7-8 and an exercise tolerance of less than one-mile walking and one flight of stairs.

Treatment options

A primary focus prior to both elective and ruptured AAA operations is the choice of EVAR versus open surgical repair. Open repair was the gold standard until the advent of EVAR from 1990, and involves a retroperitoneal or transperitoneal incision under general anaesthesia, cross-clamping of the aorta across the aneurysm before dissection and insertion of a graft. On the other hand, EVAR stents are inserted percutaneously through the femoral arteries and expand once positioned. EVAR has gained global support, partially due to its lower perioperative and 30-day post-operative mortality and morbidity relative to open repairs. The EVAR-1 and OVER RCTs additionally found that aneurysm-related mortality rate for EVAR versus open surgery is comparable in the mid- to long-term[3]. The higher 30-day post-mortality rate of open surgical repair is linked to such factors as aortic cross-clamping, which risks lower limb ischaemia, renal failure and mesenteric infarction. What is more, incisional hernias requiring reintervention occur in as many as 4.9% patients after open repairs. By contrast, EVAR operations are shorter, less invasive and have lower levels of blood loss. The repair itself is more amenable in patients with hostile abdomens, and the shorter recovery time with lower mechanical ventilation post-op means that patients can leave the hospital earlier, cutting costs and improving quality of life (QoL). Indeed, Reise et al (2010) delivered an information pack and questionnaire to men with asymptomatic aneurysms 4.5-5.1cm in diameter (n=167), and 46% participants declared a preference for an EVAR procedure versus 18% for open surgery[4].

However, emerging evidence from the longstanding EVAR1 and OVER trials amongst others has shown that in the longer term, EVARs have worse mortality outcomes than open repairs, with the total mortality benefit initially reported being lost after two to five years. For example, the 2017 DREAM trial update showed higher survival rates for open vs. EVAR (42.2% vs. 38.5%, respectively) and lower freedom from reintervation rates (78.9% (EVAR) vs. 62.2% (open))[5]. The risk of rupture is significantly higher for EVAR, found to be associated with the formation and rupture of a secondary sac.

Open repairs have better durability partly due to prolene suturing, as the aneurysm neck is sutured to the graft rather than being held in place by barbs or hooks. The latter can result in endoleaks and stent migration, generally via incomplete anchoring. Indeed, although EVAR stents are better designed than when the trials were first started, they still principally rely on a hook system. This in part explains another limitation to EVAR: the risk of endoleaks being higher requires regular surveillance of the graft, taking the form of CT scans at 1, 6 and 12 months after the operation and then annually. Secondary risk from high radiation exposure further complicates this monitoring system, and there is also high exposure to contrast medium during the procedure. As a result, in the elective setting EVAR is primarily reserved for older patients, with those under 80 being recommended for open repair if medically and anaesthetically possible.

In assessing HQ's suitability for open surgery, a standard cardiopulmonary exercise test (CPET) was issued. This involved exercising on a cycle ergometer with a progressively increasing workload whilst undergoing continuous ECG and expired gas analysis. Although similar results were yielded to a CPET performed before his CABG operation, the test was terminated due to dyspnoea, and his ECG additionally showed sinus rhythm with first degree heart block. These factors indicated a significantly higher than standard risk from open AAA repair, with the vascular anaesthetic team recommending EVAR instead. In the case of HQ, the aneurysm was juxtarenal, and thus classed as a complex aneurysm (cAAA). Here, fenestrated EVAR (FEVAR) is the alternative to open surgical repair.

What is FEVAR?

One further limitation of EVAR is in the anatomical requirements for eligibility: only 40-50% patients have permissive anatomy for the procedure. A significant barrier is in the 16% of aneurysms that have proximity to the origin of the renal arteries, termed pararenal (either juxta- or suprarenal) aortic aneurysms. In these cases, there is insufficient healthy aortic tissue above and/or below the aneurysm to facilitate EVAR stent graft attachment without causing damage to the renal ostia[6] (or blocking them altogether). Most EVAR devices state that the aortic neck must be straight for 10-15mm below the lowest renal artery; the proximal neck of a complex aneurysm is simply too short. However, a fenestrated system has been devised whereby holes, or fenestrations, in the EVAR graft align with these target vessels to retain renal perfusion and allow attachment of the stent at a more proximal juxtarenal zone[7]. These grafts can be further customised to enable perfusion of the superior mesenteric artery and coeliac arteries if required. The fenestrations are usually stented to prevent occlusion of the vessels, and as with EVAR, lifelong surveillance is required. Physician-modified endografts (PMEGS) use the same principal and are often included in FEVAR analyses.

However, FEVAR comes with its own limitations in addition to those discussed with EVAR. Firstly, perioperative time is prolonged due to the complexity of inserting the fenestrated graft and conduits for target vessel stenting, meaning the median length of operation time is longer than that of EVAR[8]. As such, there is higher risk of contrast-induced nephropathy and reperfusion injury, as well as blood loss. The requirement for larger sheaths can induce lower limb compartment syndrome[9]. Another caveat is the cost: customised stents as required in FEVAR to match the patient's anatomy can cost upwards of £20,000, excluding the cost of lifelong surveillance. The customisation element also negates their use in the emergency setting; FEVAR stents take 6-8 weeks to be manufactured and are restricted to larger specialised centres due to their complexity. Both open repairs and endovascular stenting can cause acute kidney injury - given the nature of FEVAR it is particularly important to assess renal function peri- and postoperatively. Endovascular approaches are desirable given the need to clamp above one or both renal arteries in open surgical repair.

Yet, as with EVAR, FEVAR has a high reintervention rate, with Dossabhoy et al (2017) finding that 26% of patients (n=123 over 25 months) who received fenestrated or branched EVAR required second operations, principally due to type III endoleaks and SMA or renal artery complications[10]. Indeed, this is only a mid-term follow up study, and further reinterventions may be required. Although most reinterventions are successful, they naturally increase morbidity and mortality risks, and underline the unique risks of FEVAR when stenting the renal, SMA and sometimes, coeliac, arteries. This also highlights a principal drawback of FEVAR research: the lack of long-term data to analyse due to the novelty of the technique. As such, FEVAR has no level 1 evidence and current techniques are somewhat a stab in the dark[11].

How does FEVAR compare?

Although open cAAA repair data is limited to high-level centres and small sample populations, studies have pooled results from different centres to review the 30-day mortality and 5-year survival[13]. This has demonstrated that although cAAAs are by nature more complex than infrarenal AAAs, open cAAA repairs have comparative morbidity and mortality outcomes to open infrarenal AAA repairs, reinforcing the idea of open repair as a gold standard[14,15]. It is difficult to directly compare open and FEVAR outcomes, partly due to the lack of a universal aneurysm classification system defining such terms as 'juxtarenal'. For example, within FEVAR more complex stents (3 or 4 branches) are

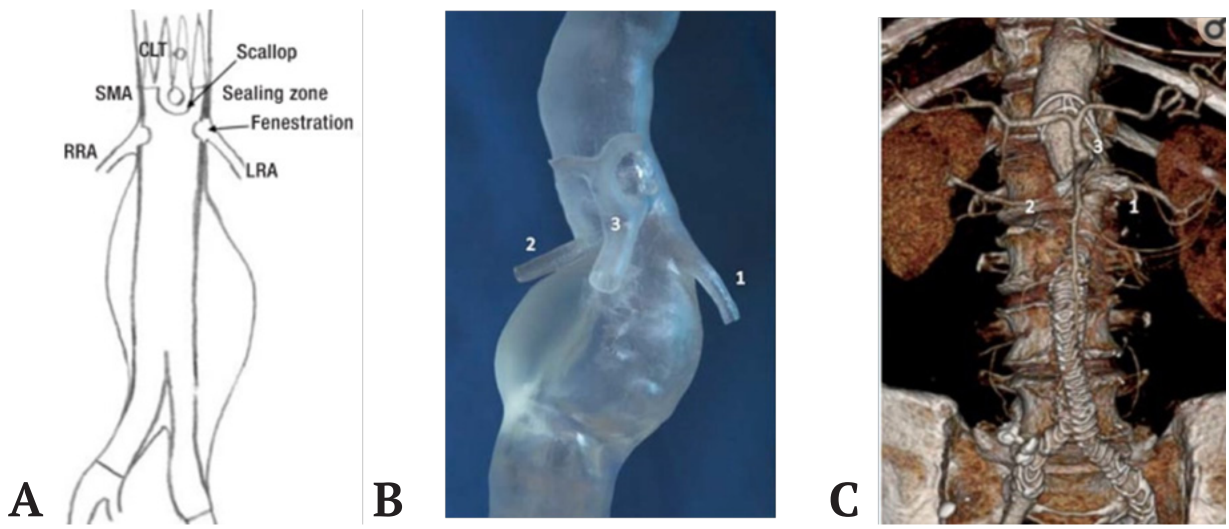

Figure1: A) Fenestrated stent graft with scallop; B) model of juxtarenal AAA; C) 3D reconstruction of graft in situ[12].

increasingly popular but have a higher hospital mortality; yet this could be a product of a more complex anatomy and the increased risk associated.

FEVAR appears to have a worse postoperative morbidity compared to EVAR, particularly with regards to renal and cardiac complications. Glebova et al (2015) found that FEVAR patients stayed longer (3.3 vs 2.8 days EVAR) and had higher post-op transfusion rates (15.3% vs. 6.1% even when extended operating time accounted for) and dialysis (1.5% vs. 0.8%)[8]. Overall complication rate was significantly higher (23.6% vs. 14.3%, p<0.001). On the other hand, there is a clear increase in the complexity of juxtarenal AAAs relative to infrarenal AAAs, and even given this, the mortality differences were non-significant (2.4% vs. 1.5%); this is however limited is by the small number of FEVAR patients relative to EVAR, and in a larger population more complications would be expected.

Nevertheless, in the short to mid-term, multiple studies have demonstrated similar or reduced mortality and morbidity for FEVAR when compared with open repairs in the unruptured cAAA setting[16,17]. Indeed, BSET-GLOBALSTAR, a nationwide registry of FEVAR operations from 2003-2009 continue to report good outcomes, with no aneurysm-related deaths over five years and most required reinterventions being performed successfully[18]. They do however record a 37.2% reintervention frequency over 5 years. Yet although visceral vessel occlusion risk and need for reintervention is higher for FEVAR, this is somewhat offset by the higher perioperative and worse 30-day outcomes of open surgery. Therefore, it could be said that FEVAR should be considered as the alternative to open surgery, particularly for elderly or high-risk patients[19].

However, this is now complicated by one of the most recent and largest reviews of FEVAR versus open repair for non-ruptured cAAAs, which was conducted on patients (n=3355) in the Vascular Quality Initiative between 2012 and 2018[20]. Importantly, they calculated propensity scores to overcome the bias arising from higher-risk patients undergoing FEVAR, as this group tended to be older, have larger aneurysms and harbour more comorbidities such as respiratory or cardiac complications. This is significant, since other research has also identified worse long-term outcomes for FEVAR operations, but attributed this to a potential selection bias for high-risk patients to FEVAR[21]. The Vascular Quality Initiative study revealed that propensity-weighted perioperative mortality was similar between the two procedures (4.7% open vs 3.3% FEVAR), and that open surgery had higher incidences of post-operative MI, AKI and new dialysis. Crucially though, longer-term data echoed that of the EVAR1 trial: higher mortality was seen after FEVAR, and in particular, PMEG, compared with open surgery (hazard ratio 1.7). This data is being continually collected, and as such 'long-term' is classified as 5 years, but it does weaken the advent of FEVAR as replacement of open repair.

The cost-analysis of FEVAR versus open repair is another aspect to evaluate, especially given the influence of NHS budgeting on NICE guidelines. Ciani et al (2018) used decision modelling to evaluate whether FEVAR investment was worthwhile, and estimated that the incremental cost of FEVAR was £74,580/ Quality of Life Year (QALY)[22]. Despite the improvement in QALY over patient lifetime, the cost of the device and predicted higher reintervention requirements (based on EVAR1 data) exceeds the NICE threshold range of £20,000 to £30,000 per QALY. The authors pointed to the current lack of RCTs and information around operative mortality as a limitation to the analysis. Draft NICE guidelines from May 2018 have aligned with this study, stating that cAAA repair of unruptured aneurysms should not be performed if the patient is unsuitable for open repair, regardless of age[23]. The draft cites the cost of FEVAR grafts, the fact that current grafts do not contain instructions for cAAA procedures, as well as the general lack of evidence for FEVAR efficacy. For EVAR, they state that the 'uncertain chance of a small net benefit' is overturned by the high cost of the operation, when taking into account the rupture risk against perioperative and long-term complications. This has been applied to FEVAR given the similarities between the two operations and their similar emerging long-term data. NICE do however advocate new RCTs comparing FEVAR with open repair, and thus recommend only conducting FEVARs in a trial-setting on patients who would also be suitable for open repairs. However, many specialist centres appear to be conducting FEVARs in a non-trial setting; given the breadth in stent design choice and technique, this further muddies the waters when trying to construct meaningful RCTs.

Following these draft NICE guidelines, HQ should not have been operated on, given his contraindication for open surgery. However, he did have a FEVAR procedure, and the guidelines were not mentioned by the surgical team or in MDTs. There appears to be a direct conflict between the NHS AAA recommendations, which are largely cost-driven, and UK centres, which continue to offer FEVAR to older, high-risk patients. And it appears many centres would argue that although FEVAR is increasingly being shown to have worse long-term outcomes relative to open repair of cAAAs, this is not such a great consideration for older patients with a shorter lifespan anyway; similar arguments to the use of EVAR. Then again, FEVAR showed higher mortality outcomes than open repair in only a five-year follow up, whereas the EVAR-1 trial reported the same over a longer period. This earlier FEVAR mortality dip may be explained by the relatively more complex anatomy of the patients, since open cAAA repairs have a slightly higher mortality rate than open AAA repairs. A separate aspect to consider is that patients tend to report a worse QoL post-(F) EVAR than open repair. Although the short-term recovery is far easier, both annual check-ups at the hospital and reintervention requirement appear to dampen the initial benefit.

When weighing up the various arguments, the decision to operate at all on HQ is incredibly complex. Screening programmes that can predict the growth and stability of an aneurysm would be invaluable, and the Oxford AAA study (OxAAA) is one such example. It aims to devise algorithms projecting timelines of individual aneurysm rupture, and has so far found an association between AAA and systemic inflammatory state, as well as the presence of certain novel biomarkers which may indicate AAA growth over time[24]. This would mean that elderly patients like HQ could avoid having any operation if their aneurysm was shown to be stable and slow-growing. The study is still in its early stages but may fundamentally change AAA vascular surgery protocol.

Conclusion

HQ was discussed over several months and in vascular MDT meetings. On the one hand, at time of operation he was less than 80 years old and relatively healthy, making open repair desirable compared to the relatively novel FEVAR technique. However, his CPET scores contraindicated open surgery, and did not improve post-CABG operation. Therefore, despite NICE draft guidelines counselling no operation, he underwent FEVAR, which was perioperatively uneventful. The operation involved bilateral groin percutaneous access and left axillary access. A type 3 endoleak was suspected but slowed following reballooning, and a four-branch graft was used. He was taken to ITU the same day due to lack of responsiveness, and although he recovered, there is some concern over longer-term cognitive impairment.

As discussed, FEVAR is an exciting and intricate minimally invasive procedure, with a similar success story to EVAR albeit on a smaller timeframe. However, as with EVAR, the fenestrated version of the technique shows promise over open repairs only in the short and mid-term, with worse mortality outcomes post-2 years. It is also marked by a higher reintervention rate, high cost, and the requirement for annual check-ups, not to mention a lack of RCTs. A better regulated system for monitoring both the aneurysm type and FEVAR graft/technique is needed to properly assess the viability of this procedure, as a lack of trial enforcement makes further study difficult. Newer alternatives to FEVAR are being trialled, including chimney (ChEVAR) grafts, Heli-FX endoanchors and endovascular aneurysm sealing (ChEVAS)[6]. These are used in conjunction with EVAR, and thus avoid the requirement for customised stents and more complex surgery. Yet they also have their drawbacks, and perhaps the question of 'which procedure' really stems back to the guidelines instructing elective operation at 5.5cm aneurysm dilation[25]. This is a somewhat arbitrary number, and if the rupture risk and growth rate could be accurately predicted, older patients could opt for neither FEVAR nor open repair, but a third, 'watching and waiting' policy to avoid the complications of either of the above.

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Consent
The patient has consented to the publication of this case study.

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