15-Year Results of the EVAR 2 Trial
Comparing EVAR With Expectant
Treatment in Patients “Unfit” For Open
Repair: Improved Aneurysm-Related
Mortality Gives Us an Ethical Dilemma
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For the EVAR 2 trial investigators

Disclosure
Speaker name: Roger M Greenhalgh
✓ I have the following potential conflicts of interest to report:
  ✓ Receipt of grants/research support
  ✓ Receipt of honoraria and travel support
  ✓ Participation in a company sponsored speakers’ bureau
  ✓ Employment in industry
  ✓ Shareholder in a healthcare company
  ✓ Owner of a healthcare company RG
✓ I do not have any potential conflict of interest

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Randomisation between September 1999 and August 2004
404 patients randomised from 33 UK centres
- EVAR N=197
- No intervention N=207
Mean age 77 years
  86% male
  Mean AAA diameter 6.7 cm

EVAR-2: Patient eligibility
- Remains the sole randomised trial to identify whether EVAR reduces mortality rates in patients ineligible for open repair
- Traffic light system to determine patient fitness & eligibility

Optimise fitness - Neither EVAR-1 or EVAR-2. MI onset of angina, unstable angina at night or at rest within last 3 months
EVAR-2 eligibility: Past history of MI, revascularisation, angina, severe heart valve disease, arrhythmia, congestive cardiac failure OR FEV1 < 1.0 OR Creatinine > 200 μmol/L
EVAR-1 eligibility: None of the above

- Follow up the remaining 20% of patients
  - Physically fittest of all patients enrolled
  - May benefit most from EVAR
- Centres reminded to continue regular follow-up (protocol specified annual), including those with lapsed follow-up
- Complications and reinterventions recorded by trial centres
- Record-linkage until June 2015 for mortality records (NHS Digital)
  - Causes of death adjudicated by Trial Endpoint Committee
Summary of main results

- **High** 30-day operative mortality in the EVAR group: 9%
- **Half** the number of aneurysm-related deaths in EVAR group over full follow-up (14% vs. 29%)
- But... no overall survival benefit
  - Limited life expectancy (mean 4.2 years in both groups)
  - High comorbidities:
    - 17% died of CHD within 4 years
    - 9% died of cancer within 4 years
    - 8% respiratory deaths within 4 years
    (12% in EVAR group, 5% in no repair group)

Cross-overs (elective repairs)

- However...
  - 31% of no intervention group received an elective AAA repair during follow-up
  - 61% of those still alive at 4-years
  - 68% of those still alive at 8-years
- Patient fitness was better in those that underwent elective EVAR in the no intervention group (mean CPI* 5.97) vs. the EVAR group (mean 10.13), p=0.011
- CPI - Customised probability index (higher is worse fitness)

Randomisation-based causal estimate

- Results similar to intention-to-treat analyses

Predictors of long-term survival

- Those who survived more than 8 years...
  - were on average 3-years younger (p=0.013)
  - had higher mean BMI (27.8 vs. 26.2 Kg/m²; p=0.017)
  - had higher mean % predicted FEV₁ (70.1 vs. 63.6; p=0.0038)
  - had higher mean eGFR (63 vs. 57; p=0.0043)
- However, no evidence of an overall survival benefit from EVAR for any particular subgroup
  - e.g. patients with better lung function fared better no matter which group they were randomised to
Limitations

1. Many of the no intervention group crossed over.
2. The proportion of patients alive at >8 years is small.
3. Devices of today and epidural anaesthesia (not 47%) could give a different trial result.
4. Reinterventions of today could be better performed.
5. Loss to follow-up reduced reporting of:
   - Complications
   - Re-interventions
   - AAA related mortality.
6. Frailty may have prevented re-intervention.

Strengths

- Complete follow-up for total mortality
- Insight from supporting causal analysis
- EVAR 2 highlights high patient co-morbidities
- All-cause mortality is the driver

Summary for EVAR 2

- EVAR 2 is unique and never repeated
- EVAR did not increase overall life expectancy
- EVAR did reduce aneurysm-related mortality
- EVAR prevents aneurysm rupture