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CUSTOMISING YOUR PATIENT CARE

A CLINICAL & BUSINESS CASE FOR A-VIEW®™

A FLUID FILLED CATHETER FOR USE TO IMAGE THE DISTAL ASCENDING AORTA AND THE AORTIC ARCH PRIOR TO CABG AND TAVR.

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A- View™ Clinical & Business Case

Executive Summary

The use of Trans Esophageal (Oesophageal) Echocardiography (TEE) or (TOE) in screening patients for the presence of atherosclerosis who are undergoing Coronary Artery Bypass Grafting (CABG) or Trans Aortic Valve Replacement (TAVR) does not allow for a full visualization of the distal ascending aorta (DAA), the so called 'Blind Spot'. For the first time this area can be fully visualised real-time by TEE with the use of a fluid filled catheter called A-View® placed into the patients' trachea.
The use of A-View in a large observational study has demonstrated a > 30% mortality reduction in patients in which A-View was used [6].
34% of the global total healthcare expenditure is spent on treating stroke patients [12]. The routine use of A-View® prevents one in every 47 patients from developing a stroke[8] and this produces a saving of €3,030 per patient.[12]

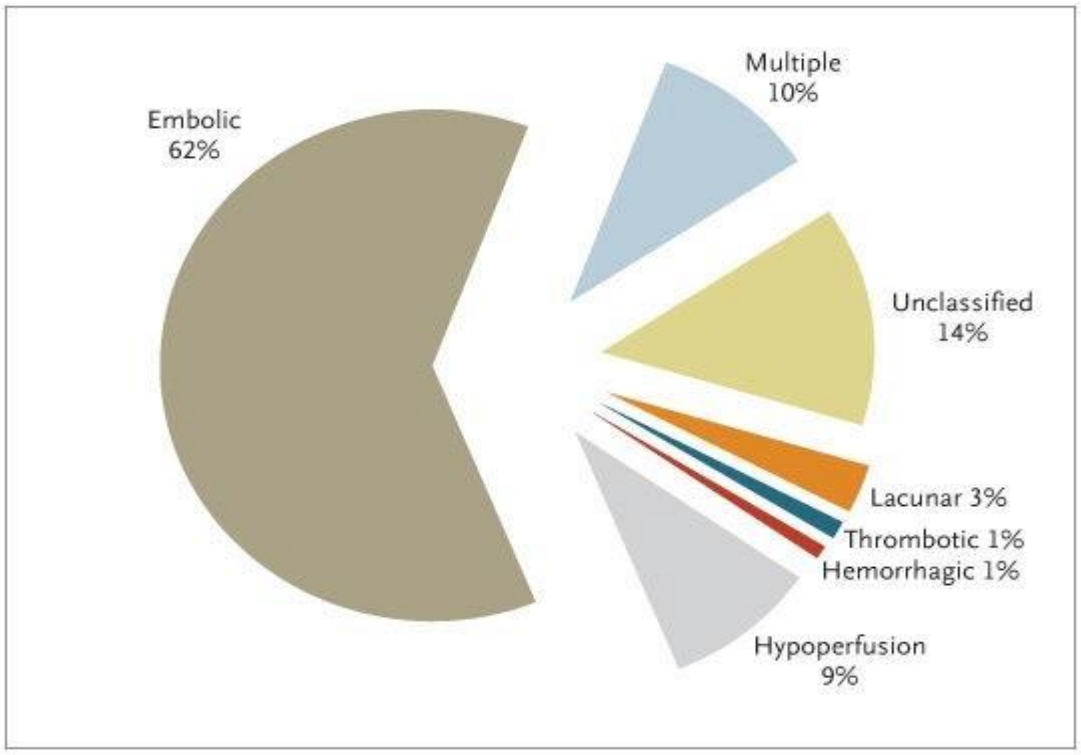
What is the problem?

The incidence of atherosclerosis in the general population has been reported as high as 42.1% and is more prevalent in older individuals and is predominantly found in the proximal left anterior descending artery [1]. Ageing is the dominant risk factor for clinically significant atherosclerotic lesion formation [7]. Symptomatic stroke occurs in 1.2 – 6% of patients after cardiac surgery and is higher in elderly patients. One of the risk factors for developing systemic atherosclerosis may be any degree of ICA stenosis [2].

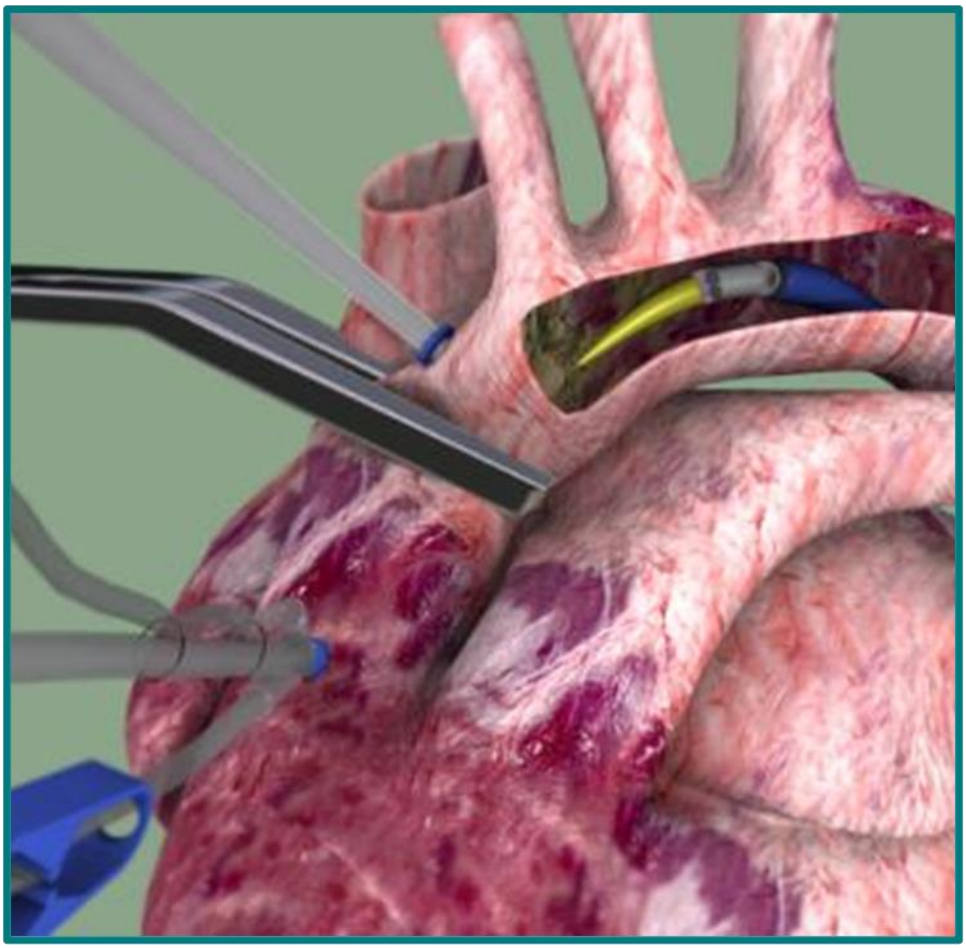
There are an estimated 2M cardiac surgeries performed annually and approximately 3-8% of these patients will have a post-operative stroke. Most of these post-operative strokes occur in older patients.
Neurocognitive impairment occurs in 15-66% of patients at discharge and up to 40% of patients after surgery [2].

The majority of perioperative strokes occur from emboli, and this can occur from aortic manipulation during cannulisation[4].

Fig 1. Mechanisms for Perioperative Stroke



Source: Selim M. *N Engl Med* 2007; 356:706-7013 [4]



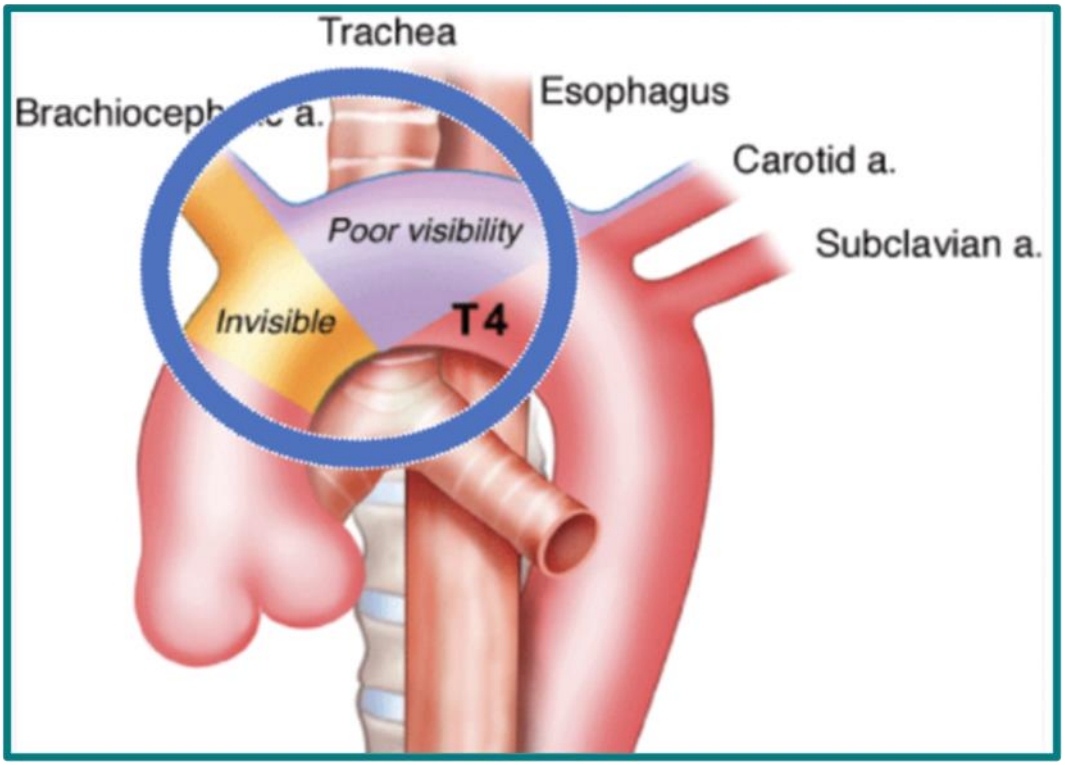
Source: Dr Arno Nierich, PowerPoint Presentation April 2022

The 'Blind Spot'

The Gold standard in working up patients who will undergo Coronary Artery Bypass Grafting (CABG) or Trans Aortic Valve Replacement (TAVR) is to carry out a detailed imaging of the proximal and distal ascending aorta for evidence of atherosclerosis plaques.

Trans Esophageal (Oesophageal) Echocardiography (TEE) or (TOE) is a technique that involves placing transducer into the oesophagus and giving its proximate location to the aorta it can provide some valuable image information with respect to the level of atherosclerosis in this area. One of the draw backs is that virtually all of the distal ascending aorta (DAA) and aortic arch is 'blind' to this method as result of the interposition of the air-filled trachea. This means that we have no real valuable information with respect to the level of atherosclerosis in this area.

The 'Blind Spot'



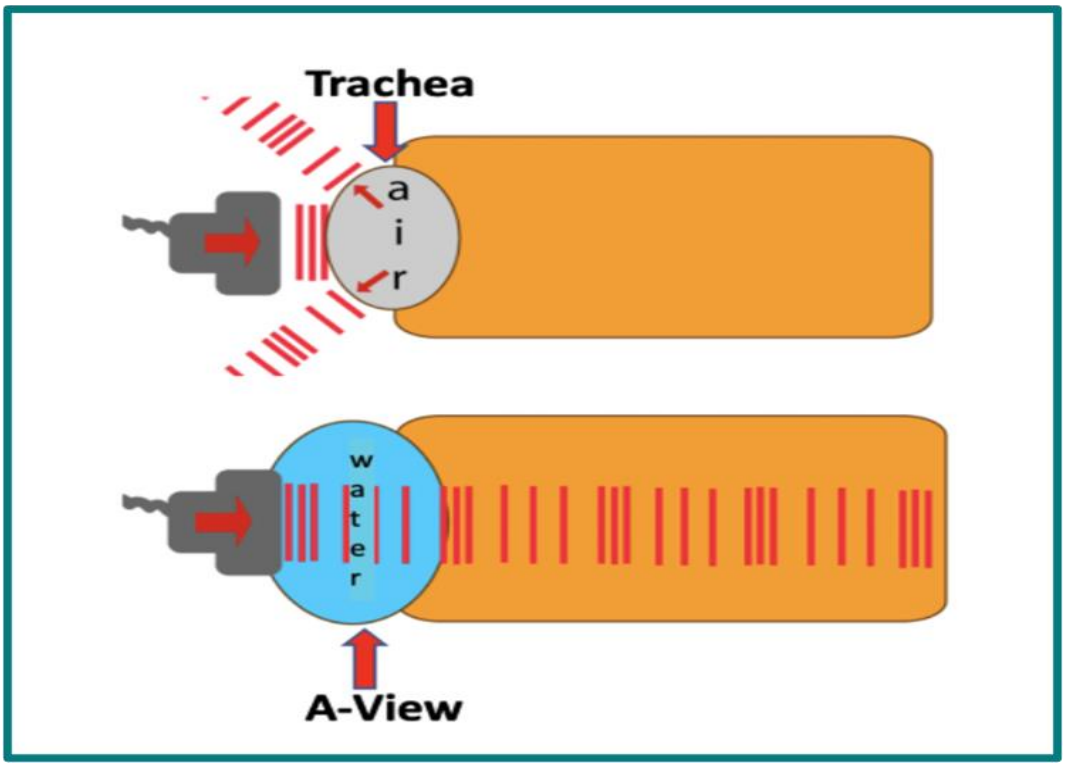
Source: Dr Arno Nierich, PowerPoint Presentation April 2022

It's all about Physics

Sound waves travel at different speeds through different materials. The denser the material the faster the sound wave will travel to the material and bounce back to the receiver. Visualization of the upper thoracic aorta is limited by the interposition of the air-filled trachea. Due to this so called 'blind-spot' the sensitivity of TEE for the diagnosis of atherosclerosis of the DAA is only 21% [15].

Material	Speed of Sound (m/s)
Air	343
Wood	3960
Water	1493

With the use of a saline filled balloon catheter inserted into the trachea allows for greater visualisation of the DAA.

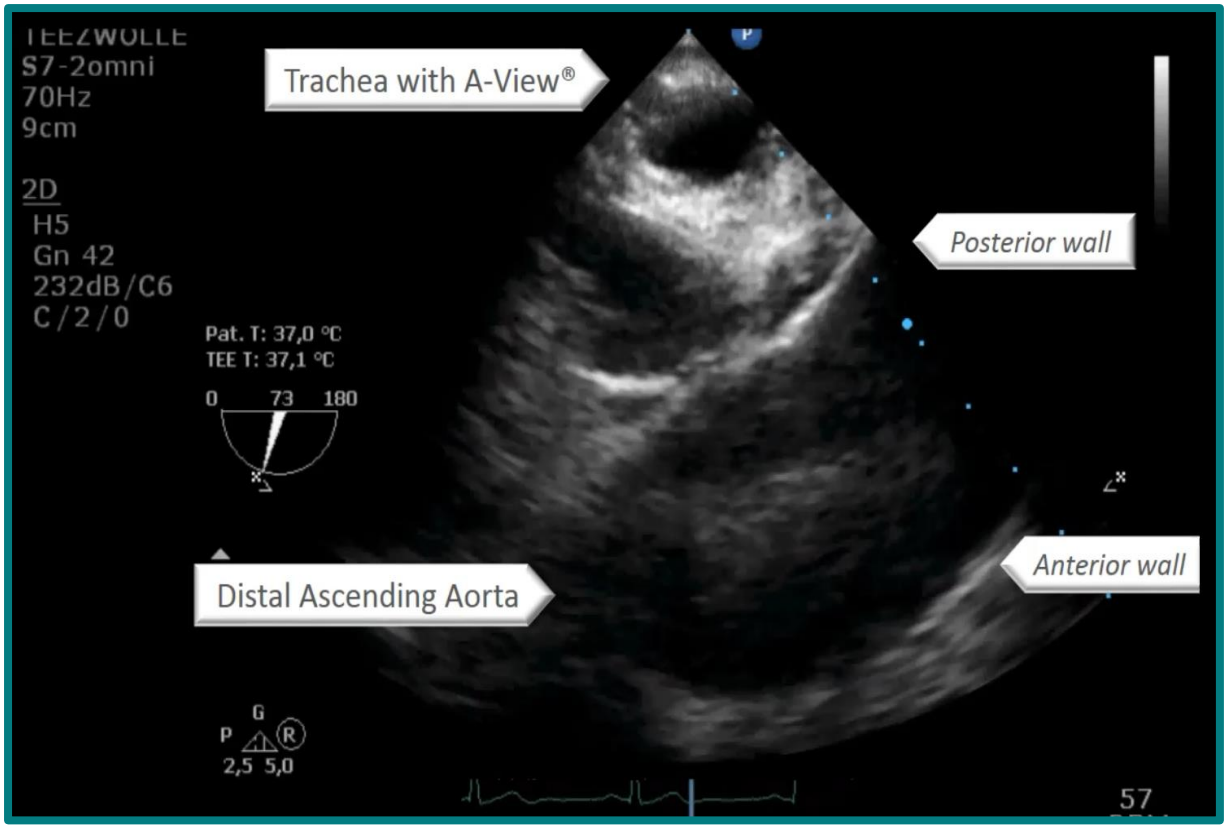


Source: Dr Arno Nierich, PowerPoint Presentation April 2022

Image of the 'Blind Spot' is needed

This allows for the following:

- Identify soft plaque
- Locate the risk spots for embolism
- Adjust Surgical Technique
- Improved outcomes



Source: Dr Arno Nierich, PowerPoint Presentation April 2022

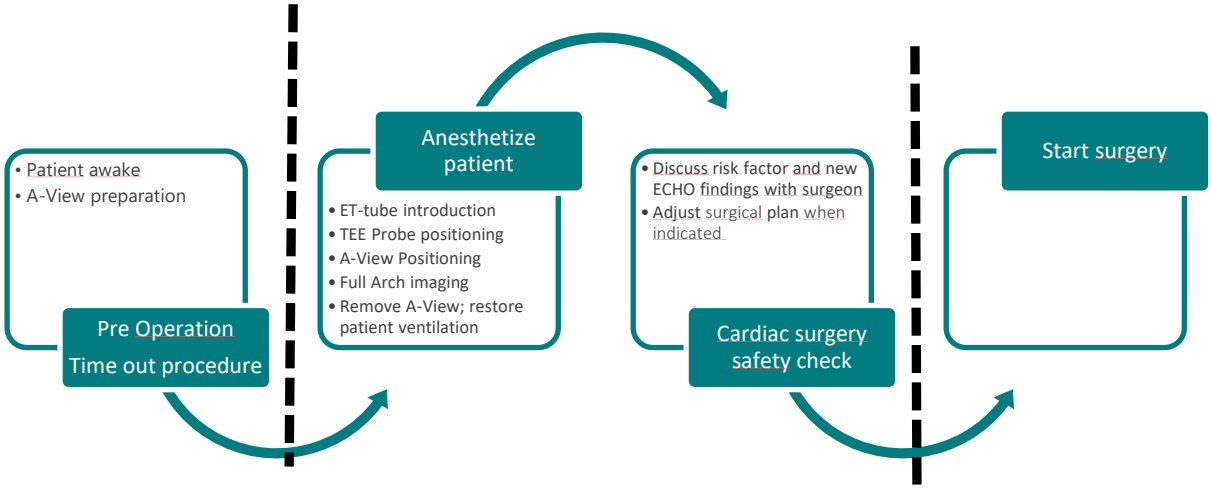
Patient Workflow with the use of A-View®

The following diagram outlines the patient flow when using A-View®. The patient is anaesthetised in the normal way. The patient is then placed on 100% oxygen for a couple of minutes before placing the saline filled catheter (A-View®) into the trachea to a depth of (24 cm maximum aligned with the ET 24 cm number), ventilation is stopped for 3 minutes and the DAA and arch are scanned by using the TEE probe.

This process takes a couple of minutes of time and provides critical information before the commencement of sternotomy. This information is shared with the surgical team, and it allows them to consider the best site for cannulation of the aorta.

The following diagram outlines the use of A-View® in a patient.

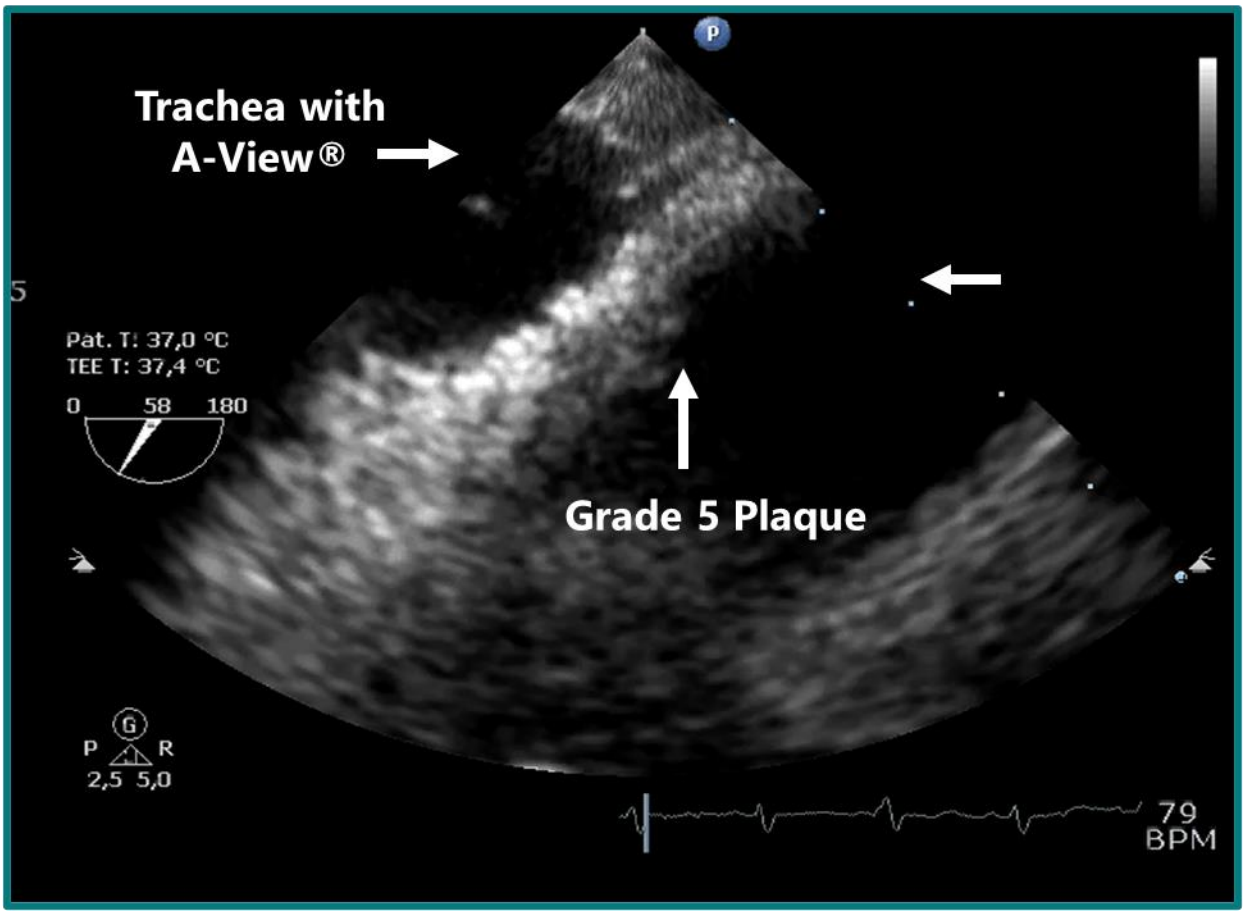
Patient workflow with A-View®



Source: Dr Arno Nierich, PowerPoint Presentation April 2022

A-View® In Diagnosis of Atherosclerosis

This is a typical image that we see with the use of A-View® on a patient with a Grade 5 Plaque in the DAA. Grade 5 means moving soft plaques in the real time image.



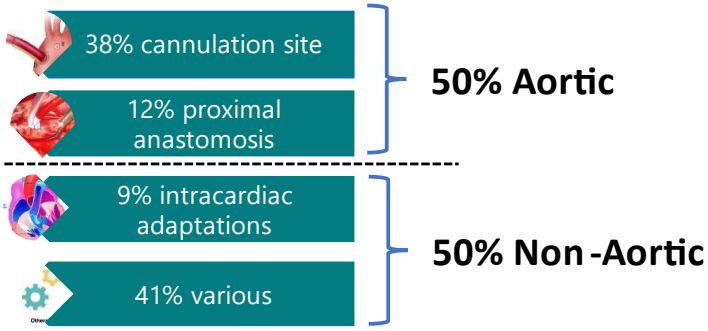
Source: Dr Arno Nierich, PowerPoint Presentation April 2022

Modification of Surgical Approach?

In a large observational study of 8,605 patients was carried out in the Isala Clinic, Zwolle, The Netherlands [6].

A-View® was used in 1,391 procedures. 12% of patients had to have their surgical approach modified following its use as outlined below.

12% adaptations per-operative



Impact of Modified TOE on Mortality and Stroke after Cardiac Surgery

Patients underwent TEE examination before sternotomy to screen for atherosclerosis of the proximal ascending aorta (PAA) and the descending aorta (DAA). Severity of atherosclerosis was graded following Katz classification. In general, if the TEE showed a grade 3 or above atherosclerosis, modified TEE (A-View®) was used to view the DAA and aortic arch. Modified TEE (A-View®) was carried out in 1,391 patients (16.2%).

Study Endpoints

All-cause 30-day mortality was the endpoint of primary interest
Secondary endpoint was in-hospital stroke, which was defined as a clinical suspicion of cerebral ischemia lasting longer than 24 hours. The diagnosis was confirmed by CT.

Statistical Analysis

First, the crude association of the use of modified TEE (intervention) as compared to not using this technique (control) was assessed for both outcomes using the relative risk (RR) and 95% CI.

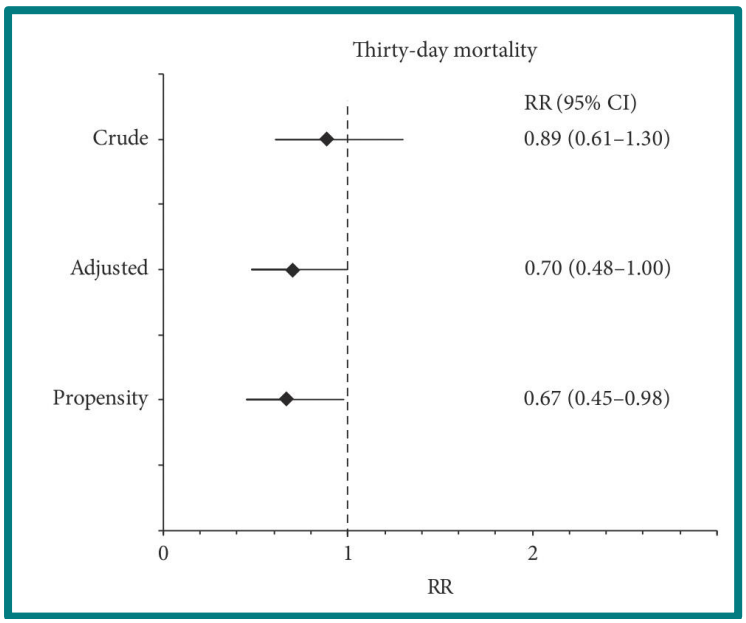
Secondly, the association regarding the use of modified TEE as compared to the control group was corrected for the above-mentioned confounders, again for both endpoints using a binominal regression analysis with a log-link to obtain RRs with a 95% CI, which are more easily interpretable than odds ratios and are synchronous with the crude association measure

Thirdly, it corrected for confounding with propensity-score (PS) analysis. Using logistic regression analysis, a PS was created, with modified TEE as the dependent variable and the confounders as covariates. After checking that the range of the PS was similar for the exposed and the unexposed and that the score was well balanced over quintiles of the PS, the individual propensity scores were added to a model with only modified TEE status as a covariate.

Results

30-Day Mortality

The EuroSCORE-predicted mortality was 5.9% in the intervention group and 4.0% in the control group ($p < 0.001$). The observed 30-day mortality was 2.2% and 2.5% in both groups, respectively (RR: 0.89; 95% CI: 0.61–1.30, $p = 0.55$. Perioperative screening for aortic atherosclerosis was associated with a significant lower mortality after both multivariate adjustment (RR 0.70, 95% CI: 0.48–1.00, $p = 0.050$) and propensity-score adjustment (RR 0.67, 95% CI: 0.45–0.98, $p = 0.040$).



In- Hospital Stroke

The predicted incidence of stroke was 4.1% (1.2%–4.8%) in patients with modified TEE and 2.8% (0.9%–3.4%) in the control group. The observed in-hospital stroke rate was 2.9% and 2.1%, respectively (RR 1.37; 95% CI: 0.98–1.93, $p = 0.067$. The multivariable- and propensity-score adjusted RRs for in-hospital stroke were 1.03 (0.73–1.45) and 1.01 (0.71–1.43), indicating that stroke risk is similar in patients with and without modified TEE screening.

Both the expected and the observed incidence of stroke were higher in the modified TEE group; after correction for confounding, the stroke incidence was similar in both groups. This contrasted our expectation that modified TEE would be associated with a reduced incidence of stroke. Several explanations can be hypothesized for this finding. First, although we consider the large cohort a strength of this study, potentially we were still underpowered to show statistical significance of a difference in stroke incidence. Second, it is possible that there is still residual confounding because of unmeasured covariates. Third is the fact that in observational clinical outcome registries, stroke rates are generally underreported. Taking into account also that 30% of stroke patients decease

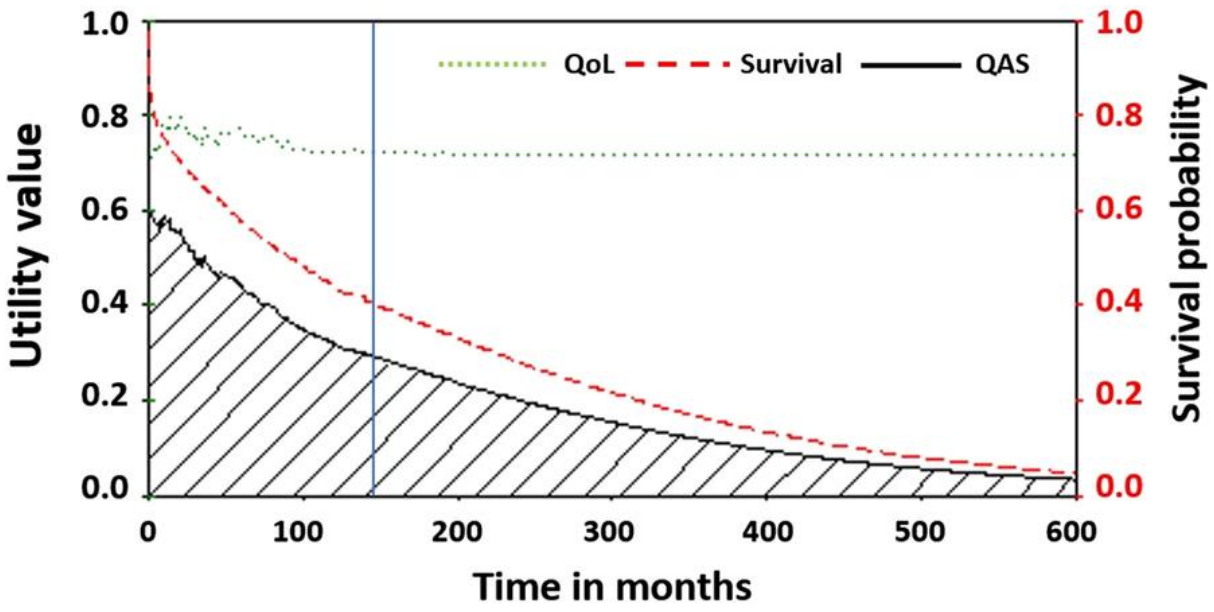
after major stroke, mortality remains an important and undisputable outcome [17] . To conclude that use of modified TEE indeed reduces the risk of stroke, with similar incidences and a power of 0.80, would require an RCT with inclusion of 3825 patients per group [18] .

The Health Economic Benefits of A-View®

Cardiovascular disease (CVD) is a non-communicable disease and the world's main cause of death resulting in 17.9 million deaths annually [8]. The cost of treating stroke patients is placing increasing financial burden on healthcare providers. As of now, approximately 34% of the global total healthcare expenditure is spent on stroke. The average healthcare cost of stroke per person, including in patient care, rehabilitation, follow-up care, is estimated at USD 140,048 in the United States [12].
The largest cost component of stroke was direct medical costs and indirect medical costs, accounting for 86.2% and 1.8% of the total cost respectively [13].

Stroke patients who survive have a reduced Quality of Life (QoL). One way of examining the trade-offs between survival time and QoL is to combine them in a single measure of quality- adjusted life years (QALY) [14].

Figure 1 demonstrates the estimated survival average QoL score and the quality-adjusted survival (QAS) function for patients with stroke over 144 months then extrapolating to 600 months. QoL was lower in the initial months following a stroke and slowly increased to a sable level.
QAS probability throughout the patient's lifetime was estimated by multiplying lifetime survival function and QoL[10].



Is there a financial benefit to using modified TEE (A-View®)?

In Busting *et al* (2022)[10] they found that on average a patient would lose 10.27 QALY's due to stroke.

Routine use of A-View® on patients reduces the economic health burden by €800 per patient. For every 47 patients screened using A-View ® prevents 1 stroke[8].

With a typical cost of A-View® of €300 per device and a €800 reduction in healthcare burden per patient, there is net benefit €500 per patient for the health authority. There are no changes to surgical time as the screening of patients with A-View® takes place prior to sternotomy. We also need to consider the savings made in preventing a stroke in one in every 47 patients with the use of Modified TEE (A-View®)

Input Costs €uros	Output Costs	Overall Patient savings
€300	Stroke prevention Cost for treating a stroke patient $140,048. Equivalent to €133,045. **One in every 47 patients has a stroke prevented with the use of A-View** **133,045/47= €2,830.76**	€500.00 €2,830.76 ========= €3,330.76

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