

# Heartbeat: guidelines versus reality for patients with severe aortic stenosis

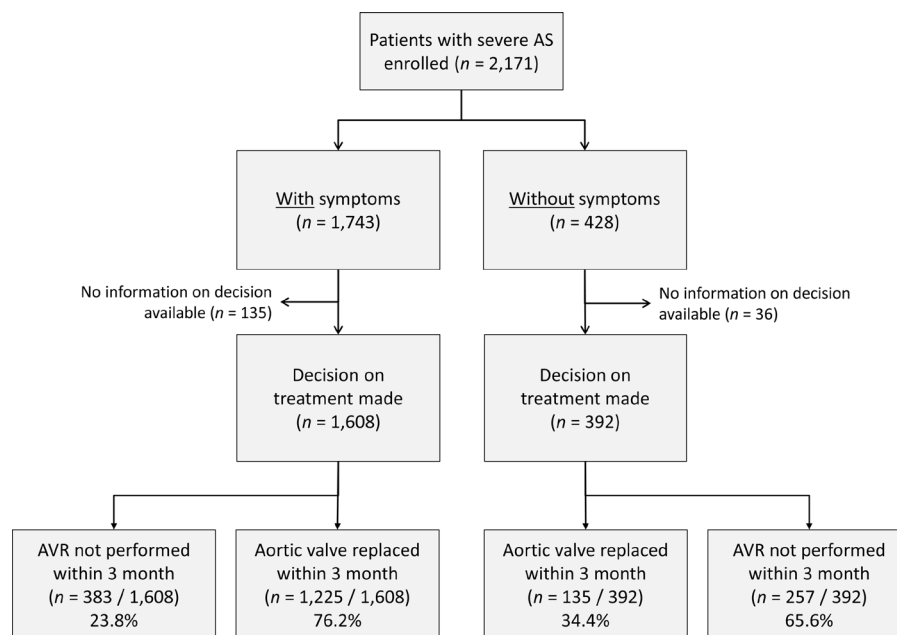
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The increasing prevalence of aortic stenosis (AS) in our ageing population and clinical trials demonstrating the benefits of transcatheter valve implantation for severe symptomatic AS have focused attention on this disease in recent years. Yet, despite clear recommendations from professional societies, it remains unclear whether all patients receive timely and appropriate treatment. To address this concern, Frey and colleagues<sup>1</sup> looked at data from the Study to Improve Outcomes in Aortic Stenosis (IMPULSE) registry which included 2171 adults with severe AS at 23 tertiary care hospitals in 9 European countries, including the UK. Patient mean age was 78 years, 48% were women and 27% had a left ventricular ejection fraction less than 50%. Over 80% of these patients were symptomatic, but only 76% of those with severe symptomatic AS were treated appropriately with aortic valve replacement (AVR), most often by the transcatheter approach (figure 1). Of even more concern, among asymptomatic patients with an indication for AVR, 42% (22/52) were not treated, whereas AVR was performed in 36% (123/339) of asymptomatic AS patients with no established indication.

In the accompanying editorial, Chambers<sup>2</sup> discusses the study design and comments that 'the IMPULSE registry is a useful 'snapshot' of current care and reminds us that the key to improving care for patients with valve disease is to develop a comprehensive valve service at three levels: 1. the detection of valve disease; 2. referral of patients with moderate or severe disease to a specialist valve clinic to plan management and follow-up until intervention is indicated and 3. intervention in a heart valve centre with recognised performance standards' (figure 2).

High-sensitivity cardiac troponin testing is integral for diagnosis of acute coronary syndromes (ACSs) but the potential value of troponin measurements months to years after the acute event has not been studied. In this issue of *Heart*, Adamson and colleagues<sup>3</sup> found that troponin

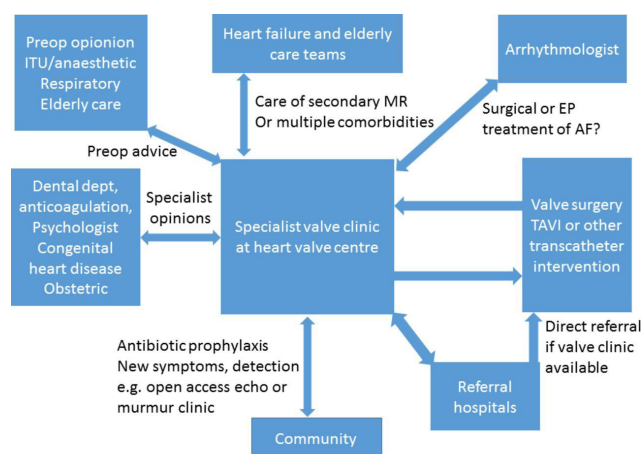


**Figure 1** Flowchart of the population and management according to functional status. AS, aortic stenosis; AVR, aortic valve replacement.

concentrations 4 months after an ACS were an independent predictor of cardiovascular death, with an HR of 1.4 (CI 1.3 to 1.5) per doubling of the serum level (figure 3). Risk was highest in patients who had increasing troponin levels at 12 months and in those with a 4-month level > 99th percentile compared those with a troponin  $\leq 5$  ng/L (29.5% (49/166) vs

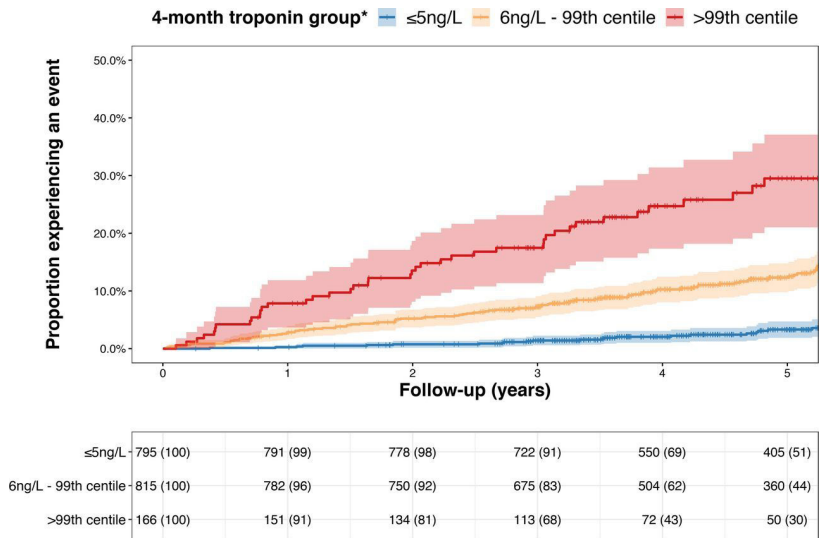
4.3% (34/795); adjusted HR 4.9, 95% CI 3.8 to 23.7).

In a provocative editorial, Kavask and Devereaux<sup>4</sup> commend the authors for 'undertaking and executing this study, laying the foundation for a possible testing protocol with high-sensitivity cardiac troponin following ACS.' However, in the context of varying definitions, methods



**Figure 2** The valve disease network. AF, atrial fibrillation; EP, electrophysiologic; ITU, intensive treatment unit; TAVI, transcatheter aortic valve implantation.

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**Figure 3** Cumulative incidence of cardiovascular death according to 4-month troponin concentration cumulative event curves for cardiovascular death according to troponin concentrations determined at the 4-month visit. Each cross-hair indicates when a subject is censored from further follow-up. The number at risk (% in group remaining) for each yearly interval is given for each troponin group. Follow-up begins from date of 4-month visit. \*For descriptive purposes, troponin concentrations have been rounded to nearest integer value. Therefore ≤5 ng/L includes all patients <5.5 ng/L.

and variability in high-sensitivity troponin testing, they point out that ‘a question lingers as to whether current laboratory practices can provide accurate and reproducible results around the thresholds of such a framework.’ Based on a simulation using their own quality control data

for troponin measurements, they suggest ‘that the percent change criterion as suggested by Adamson and colleagues<sup>3</sup> would be appropriate for concentrations near the 99th percentile but not at the lower concentration limit of 6 ng/L, where absolute changes (rather than percent) in

high-sensitivity cardiac troponin at this low concentration range have demonstrated clinical utility.’

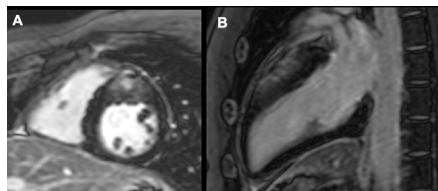
The importance of reporting and analysing sex difference in cardiovascular outcomes is discussed in detail in a review article and tutorial<sup>5</sup> by Woodward in this issue of *Heart*. Readers will find that this article provides a clear rationale for the optimal approaches to analysing sex differences with examples shown in figures and tables. Clinical researchers will find this article is a practical guide to study design and data analysis with a table (table 1) of specific recommendations for reporting study results.

Our *Education in Heart* article reviews clinical indications for cardiovascular magnetic resonance (CMR) imaging<sup>6</sup> with tables highlighting the strengths of different imaging techniques and detailing CMR findings that differentiate restrictive and hypertrophic cardiomyopathies (figure 4).

In our *Cochrane Corner* series, short summaries of recent Cochrane Reviews relevant to clinical cardiology, Stranges and colleagues<sup>7</sup> address the question ‘Does the Mediterranean-style diet help in the prevention of cardiovascular disease?’ They conclude: ‘At the present time, there is no definitive trial evidence regarding the effects of a Mediterranean-style diet on clinical endpoints for both the

Table 1 Recommendations for reporting sex differences in cardiovascular associations	
General	
G1	Consider whether the research is concerned with sex (biological) or gender (behavioural) differences, and report the results accordingly.*
G2	Routinely provide sex-disaggregated results when reporting research on cardiovascular associations. This includes prespecifying subgroup analyses by sex. When there are no important sex differences, still include sex-specific results, most likely in the appendix of a manuscript for publication.
G3	Even when a study is concerned with associations for a single sex, where possible compare results for the other sex, as a control.
G4	Adjust at least for age when comparing sex-specific cardiovascular associations.
G5	Consider analyses on both the relative and absolute scales. When it is only appropriate to present relative risks, provide (at least) the number of events and the number at risk across the sex by risk factor exposure cross-classes, to give context to the reader.
G6	Quantify the sex difference (with accompanying measure of uncertainty, such as a 95% CI), rather than merely test for a significant difference.
G7	When analysing raw (ie, individual participant) data, use the full interaction model (with all main effects and two-way interactions) to obtain the sex-specific results, as well as the sex comparison(s).
G8	Unless there is statistical or clinical significance in the sex difference (ie, the sex interaction), avoid sex-specific conclusions.
Specific to meta-analyses	
M1	Decide whether to use the fixed effect or random effects method before data are collected.
M2	Only include studies with results from both sexes.
M3	In the report, include a flow chart with reasons for exclusions. Clearly state the number of studies excluded for want of sex-disaggregated results.
M4	Use reliable, general, statistical software†, such as R or Stata.
M5	Include forest plots by sex and to compare the sexes‡. Show age-adjusted and multiple-adjusted analyses separately, where appropriate. This will typically require placing some forest plots in the appendix of a manuscript for publication.
M6	Following the meta-analysis, use meta-regression and bubble plots to explore sources of heterogeneity, to include overall risk and the difference between the sex-specific risks.
M7	Take care when pooling ORs together with relative risks or HRs. Stratify pooling by the metric used where risk (or, in cross-sectional studies, prevalence) is typically high.

\*In this manuscript no distinction is made, for simplicity of exposition.  
†These have the advantage of offering a wide range of other tools, so that the extra work of learning the basics of such a package (if necessary) will be worthwhile.  
‡For example, through the ratio of relative risks—see figure 2.



**Figure 4** Patient with hypertrophic cardiomyopathy with asymmetric anterior and anteroseptal hypertrophy and an associated non-ischaemic diffuse scar in the area of maximal hypertrophy (A, B).

primary and secondary prevention of major CVD. Overall, the available trial evidence is promising (though not conclusive) and generally supportive of favourable effects of the Mediterranean-style diet on individual cardiometabolic risk factors in primary prevention studies, and

potentially also on clinical endpoints such as stroke. Several ongoing trials, particularly those reporting clinical endpoints in secondary prevention, will add to the evidence base.’

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#### REFERENCES

- 1 Frey N, Steeds RP, Rudolph TK, *et al*. Symptoms, disease severity and treatment of adults with a new diagnosis of severe aortic stenosis. *Heart* 2019;**105**:1709–16.
- 2 Chambers JB. Aortic stenosis: service delivery before guidelines. *Heart* 2019;**105**:1686–7.
- 3 Adamson PD, McAllister D, Pilbrow A, *et al*. Convalescent troponin and cardiovascular death following acute coronary syndrome. *Heart* 2019;**105**:1717–24.
- 4 Kavsak P, Devereaux PJ. High-Sensitivity troponin testing months after an acute coronary syndrome: noise or notable results. *Heart* 2019;**105**:1688–90.
- 5 Woodward M. Rationale and tutorial for analysing and reporting sex differences in cardiovascular associations. *Heart* 2019;**105**:1701–8.
- 6 Nagel E. Clinical indications for cardiovascular magnetic resonance. *Heart* 2019;**105**:1755–62.
- 7 Stranges S, Takeda A, Martin N, *et al*. Cochrane corner: does the Mediterranean-style diet help in the prevention of cardiovascular disease? *Heart* 2019;**105**:1691–4.