How Recent Guidelines will Change the Practical Indication of TAVR in the Coming Years?

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Grant/Research Support	Edwards Lifesciences, Abbott
Scientific Advisory Board	Medtronic
Executive Physician Council	Boston Scientific Corp

Guidelines TAVR vs SAVR

- 2017 ESC/EACTS Valvular Heart Disease
- 2014 ACC/AHA Valvular Heart Disease
- 2021 ESC/EACTS Valvular Heart Disease
- 2020 ACC/AHA Valvular Heart Disease

Guidelines TAVR vs SAVR

- 2017 ESC/EACTS Valvular Heart Disease
- 2014 ACC/AHA Valvular Heart Disease
- 2021 ESC/EACTS Valvular Heart Disease
- 2020 ACC/AHA Valvular Heart Disease
- What are the consensus and what are the differences?
- Current and near future practice change?

ESC
European Society of Cardiology

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STATE OF THE ART REVIEW
Valvular heart disease

ESC/EACTS vs. ACC/AHA guidelines for the management of severe aortic stenosis

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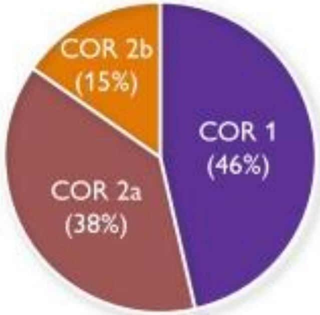
LOE A: 2
LOE B: 16
LOE C: 8



ACC/AHA Guidelines: distribution of class of recommendations (COR) as discussed for severe AS

Shared class of recommendations

General principles:

- Heart team approach

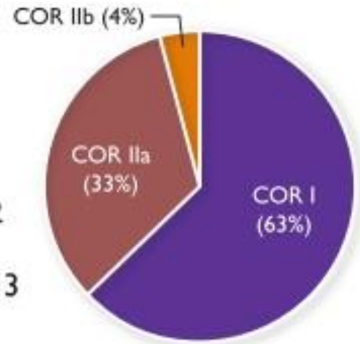
Timing for AVR:

- High gradient severe AS
- Low-flow low-gradient AS with reduced LVEF
- Asymptomatic AS with LVEF <50%

Mechanical vs. bioprosthetic:

- Patient factors and preferences

LOE A: 2
LOE B: 9
LOE C: 13



ESC

ESC/EACTS Guidelines: distribution of class of recommendations (COR) as discussed for severe AS

ACC/AHA Guidelines only

- Primary vs. comprehensive heart valve center
- Surgical risk scores
- Ross procedure
- Bicuspid aortic valve
- TAVI for asymptomatic AS
- Pre-TAVI PCI

One class of recommendations apart

Timing for AVR:

- Low-flow low-gradient severe AS with preserved LVEF
- Asymptomatic AS

TAVI vs. SAVR:

- SAVR and coronary artery bypass graft

ESC/EACTS Guidelines only

- AVR in low-flow low-gradient AS without contractile reserve
- Non-transfemoral TAVI

Key areas of differences

Asymptomatic AS: % LVEF threshold

Mechanical vs. bioprosthetic: Age threshold

TAVI vs. SAVR: Age threshold

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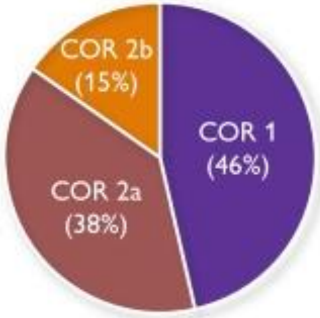
LOE B: 16
LOE C: 8



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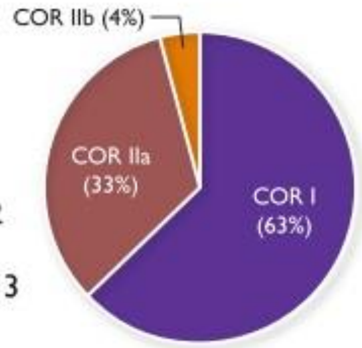

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Key areas of differences

Asymptomatic AS: % LVEF threshold	Mechanical vs. bioprosthetic: Age threshold	TAVI vs. SAVR: Age threshold

Table 1 Heart team management and risk scores

2020 ACC/AHA guideline[5]	2021 ESC/EACTS guideline[4]	Comparison of the evidence
Heart Team Management and Heart Valve Centre		
2.6. COR 1 LOE C-EO: patients with severe VHD should be evaluated by a Multidisciplinary Heart Valve Team when intervention is considered. **2.6.** COR 2a LOE C-LD: consultation with or referral to a Primary or Comprehensive Heart Valve Centre is reasonable when treatment options are being discussed for (i) asymptomatic patients with severe VHD, (ii) patients who may benefit from valve repair vs. valve replacement, or (iii) patients with multiple comorbidities for whom valve intervention is considered.	**5.2.3.** COR I LOE C: aortic valve interventions must be performed in Heart Valve Centres that declare their local expertise and outcomes data, have active interventional cardiology and cardiac surgical programmes on-site, and a structured collaborative Heart Team approach. **5.2.3.** COR I LOE C: the choice between surgical and transcatheter intervention must be based upon careful evaluation of clinical, anatomical, and procedural factors by the Heart Team, weighing the risks and benefits of each approach for an individual patient. The Heart Team recommendation should be discussed with the patient, who can then make an informed treatment choice.	Comparable recommendations. Shared Evidence: 2019 Association for Thoracic Surgery, American College of Cardiology, American Society of Echocardiography, Society for Cardiovascular Angiography and Interventions, and Society of Thoracic Surgeons expert consensus systems of care document: a proposal to optimize care for patients with valvular heart disease.[6]
Risk scores		
2.5. COR 1 LOE C-EO: for patients with VHD for whom intervention is contemplated, individual risks should be calculated for specific surgical and/or transcatheter procedures, using online tools when available, and discussed before the procedure as a part of a shared decision-making process.	No specific recommendations.	ACC/AHA Evidence: references the Society of Thoracic Surgeons Adult Cardiac Surgery Database for surgical morbidity and mortality risks.[7] References several TAVI risk prediction tools derived from observational cohort and registry studies.[8–12] Cited observational studies and one review to emphasize the importance of frailty assessments.[13–16]

ACC, American College of Cardiology; AHA, American Heart Association; COR, Class of Recommendation; EACTS, European Association for Cardio-Thoracic Surgery; EO, consensus opinion of experts based on clinical experience; ESC, European Society of Cardiology; LD, non-randomized observational studies with limitations in design or execution or meta-analysis of such studies, LOE, level of evidence; TAVI, transcatheter aortic valve implantation; VHD, valvular heart disease.

Table 1 Heart team management and risk scores

2020 ACC/AHA guideline[5]	2021 ESC/EACTS guideline[4]	Comparison of the evidence
Heart Team Management and Heart Valve Centre		
2.6. COR 1 LOE C-EO: patients with severe VHD should be ...	**5.2.3.** COR I LOE C: aortic valve interventions must be performed ...	Comparable recommendations. Shared Evidence: 2019 Association ...
Risk scores		
2.5. COR 1 L...		...

Heart Team:

Exact definition of a Heart Team?

All patients need a Heart Team? High risk and asymptomatic patients?

Mandatory in US due to Medicare and Medicaid

Risk Scores:

STS PROM as a reference, not decision point

TAVR vs SAVR based on life expectancy (life-time management) and prothesis durability

Frailty

Table 2 Symptomatic aortic stenosis

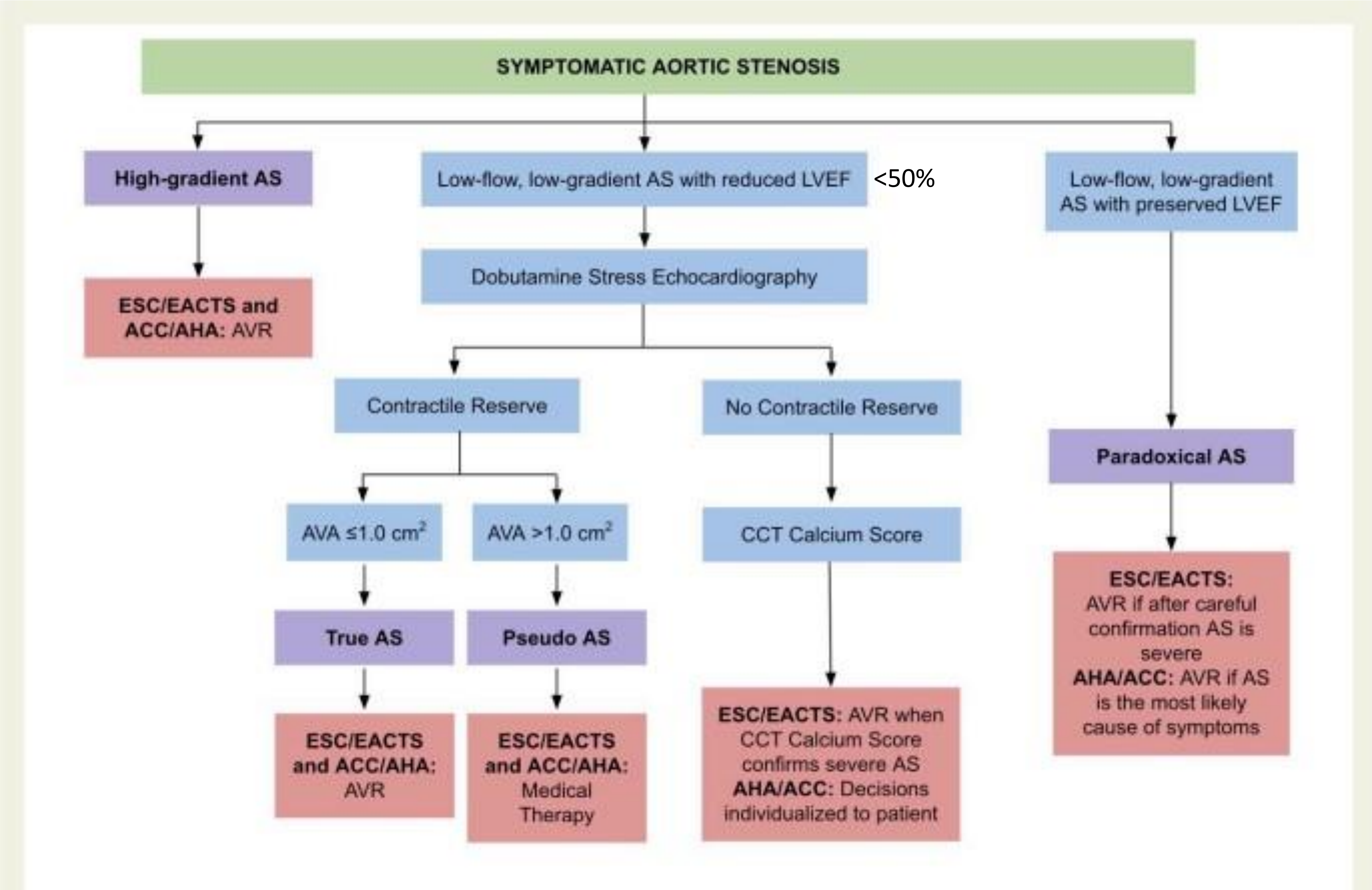
2020 ACC/AHA guideline[3]	2021 ESC/EACTS guideline[4]	Comparison of the evidence
High-gradient severe AS		
3.2.3. COR 1 LOE A: in adults with severe high-gradient AS and symptoms of exertional dyspnoea, HF, angina, syncope, or presyncope by history or on exercise testing, AVR is indicated.	**5.2.1.** COR I LOE B: intervention is recommended in symptomatic patients with severe, high-gradient AS.	Shared Evidence: natural history studies of symptomatic AS.[20,21] ACC/AHA Evidence: O'Brien et al. (2009): STS risk models for isolated valve surgery, including AVR.[22] Kvidal et al. (2000): observational study of 2359 patients which found excellent long-term survival after AVR.[23] PARTNER 1B Trial[24]
Low-flow low-gradient severe as with reduced LVEF		
3.2.3. COR 1 LOE B-NR: AVR is recommended in symptomatic patients with LFLG severe AS with reduced LVEF.	**5.2.1.** COR I LOE B: intervention is recommended in symptomatic patients with severe LFLG AS with reduced LVEF and evidence of flow (contractile) reserve. **5.2.1.** COR IIa LOE C: intervention should be considered in symptomatic patients with severe LFLG AS with reduced LVEF without flow (contractile) reserve, particularly when CCT calcium scoring confirms severe AS.	ESC/EACTS Evidence: Monin et al. (2003): prospective cohort study of 136 patients with low-gradient AS undergoing AVR. Found no contractile reserve to be a predictor of periprocedural mortality.[25] Tribouilloy et al. (2009): prospective cohort of 81 patients with LFLG AS found AVR to be associated with higher 5-year survival compared with medical therapy.[26] TOPAS-TAVI registry for possible role of TAVI.[27] ACC/AHA Evidence: no specific recommendations for low contractile reserve. The role of TAVI is unclear.
Low-flow low-gradient severe AS with preserved LVEF		
3.2.3. COR 1 LOE B-NR: in symptomatic patients with LFLG severe AS with normal LVEF, AVR is recommended if AS is the most likely cause of symptoms. E.g. a severely calcified aortic valve, an aortic velocity <4.0 m/s (mean pressure gradient <40 mmHg), and a valve area ≤1.0 cm^2 when stroke volume index is <35 mL/m^2. Requires additional testing e.g. aortic valve area index, Doppler and CCT calcium score.	**5.2.1.** COE IIa LOE C: intervention should be considered in symptomatic patients with LFLG (<40 mmHg) AS with normal ejection fraction after careful confirmation that the aortic stenosis is severe.	ESC/EACTS Evidence: four prospective studies performed before 2015.[28–31] Jander et al. (2011) Retrospective cohort study comparing patients with LFLG severe AS and preserved LVEF (*n* = 435) to patients with low-gradient moderate AS (*n* = 184) with preserved LVEF. Outcome: aortic valvular events: congestive heart failure due to AS, aortic valve replacement, cardiovascular mortality. Conclusion: patients with LFLG 'severe' AS and preserved LVEF have similar outcomes as 'moderate' AS. Clavel et al. (2012) Prospective cohort study comparing paradoxical LFLG severe AS with preserved LVEF (187 patients) to those with high-gradient severe AS with preserved LVEF (*n* = 187) and moderate AS (*n* = 187) Outcome: patients with LFLG severe AS had reduced overall 1-year survival. AVR in the LFLG severe AS group was associated with improved survival. Mehrotra et al. 2013 Retrospective cohort study comparing LFLG severe AS (*n* = 38) with preserved LVEF vs. normal-flow LG severe AS (*n* = 75) vs. moderate AS (*n* = 70). Outcome: all-cause mortality after 3 years Conclusions: 3-year survival significantly lower in LFLG severe AS compared with both other groups. Tribouilloy et al. (2015) Prospective study of 809 AS patients (57 patients had LFLG AS and preserved LVEF) undergoing real-world treatment Outcome: patients with LFLG AS with preserved LVEF had similar prognosis to moderate-severe AS ACC/AHA Evidence: 3 post-2015 prospective cohort studies.[32–34] Zheng et al. (2017): network meta-analysis comparing (a) LFLG severe AS vs. (b) low-flow high-gradient AS vs. (c) moderate AS vs. (d) normal-flow high-gradient AS

Continued

Table 2 *Continued*

2020 ACC/AHA guideline[5]	2021 ESC/EACTS guideline[4]	Comparison of the evidence
		vs. (e) normal-flow low-gradient AS in 15 studies and 9737 patients. Outcome: all-cause mortality. Conclusions: low-flow states of AS were associated with increased risk of mortality compared with moderate AS and normal-flow AS. Rusinaru et al. (2018): prospective cohort study comparing low-flow aortic stenosis ($n = 190$) vs. moderate ($n = 221$) and high-flow AS ($n = 1039$) in patients with preserved LVEF. Outcome: 5-year all-cause mortality. Conclusions: low-flow severe AS with preserved LVEF is associated with a higher mortality rate. Eleid et al. (2019): prospective cohort study evaluating TAVI for LFLG severe AS with LVEF. Outcome: increase in flow post-TAVI, indicating positive hemodynamic benefits.

Abbreviations as in *Table 1*. AS, aortic stenosis; AVR, aortic valve replacement; BNP, B-type natriuretic peptide; BP, blood pressure; CCT, cardiac computed tomography; LVEF, left ventricular ejection fraction; LFLG, low-flow, low-gradient; NR, non-randomized evidence.



SYMPTOMATIC AORTIC STENOSIS
High-gradient AS
ESC/EACTS and ACC/AHA: AVR
Low-flow, low-gradient AS with reduced LVEF
<50%
Dobutamine Stress Echocardiography
Contractile Reserve
No Contractile Reserve
AVA ≤1.0 cm²
AVA >1.0 cm²
True AS
Pseudo AS
ESC/EACTS and ACC/AHA: AVR
ESC/EACTS and ACC/AHA: Medical Therapy
CCT Calcium Score
ESC/EACTS: AVR when CCT Calcium Score confirms severe AS
AHA/ACC: Decisions individualized to patient
Low-flow, low-gradient AS with preserved LVEF
Paradoxical AS
ESC/EACTS: AVR if after careful confirmation AS is severe
AHA/ACC: AVR if AS is the most likely cause of symptoms

Table 3 Asymptomatic aortic stenosis

2020 ACC/AHA guideline[5]	2021 ESC/EACTS guideline[4]	Comparison of the evidence
3.2.3. COR 1 LOE B-NR: in asymptomatic patients with severe AS and LVEF < 50%, AVR may be considered. **3.2.3.** COR 2b LOE B-NR: in asymptomatic patients with severe high-gradient AS and a progressive decrease in LVEF on at least 3 serial imaging studies to <60%, AVR may be considered.	**5.2.2.** COR I LOE B: intervention is recommended in asymptomatic AS and systolic LV dysfunction (LVEF <50%) without another cause. **5.2.2.** COR IIa LOE B: intervention should be considered in asymptomatic AS and LV systolic dysfunction (LVEF <55%) without another cause.	Shared Evidence: Bohbot et al. (2019) and Lancellotti et al. (2018).[39,40] Bohbot et al. (2019): cohort study examining conservative vs. surgical management in patients with asymptomatic AS and various LVEFs: < 55% (n = 239), 55%–59% (n = 331) and ≥ 60% (n = 1108). Outcomes: 5-year mortality Conclusions: patients with LVEF <55% had higher mortality rates compared with both LVEF 55%–60% (P < 0.001) and LVEF >60% (P < 0.001). Patients with LVEF 55%–60% and >60% had a comparable prognosis. In patients with LVEF <55%, initial surgical management reduces all-cause mortality risk (P < 0.001). Lancellotti et al. (2018): registry cohort study of the natural history of 1375 patients with asymptomatic AS. Outcomes: patients with severe AS at baseline, Vmax >5 m/s and LVEF <60% were at increased risk of all-cause mortality. Anticipating trials on the suitability of TAVI for asymptomatic disease such as RECOVERY.[41]
Exercise testing		
3.2.3. COR 2a LOE B-NR: in apparently asymptomatic patients with severe AS and low surgical risk, AVR is reasonable when: (1) Exercise test demonstrates decreased exercise tolerance (normalized for age and sex) or a fall in SBP of ≥10 mm Hg from baseline to peak exercise. (2) Serum B-type natriuretic peptide (BNP) level is >3 times normal 3. At least 3 serial imaging studies shows an increase in aortic velocity ≥0.3 m/s per year. **3.2.3.** COR 2a LOE B-R: In asymptomatic patients with very severe AS (defined as an aortic velocity of ≥5 m/s) and low surgical risk, AVR is reasonable.	**5.2.2.** COR I LOE C: intervention is recommended in asymptomatic patients with demonstrable symptoms on exercise testing. **5.2.2.** COR IIa LOE B: intervention should be considered in asymptomatic patients with LVEF >55% and a normal exercise test if the procedural risk is low and one the following parameters is present: (1) very severe aortic stenosis (mean gradient ≥60 mmHg or Vmax >5 m/s). (2) Severe valve calcification (ideally assessed by CCT) and Vmax progression ≥ 0.3 m/s/year. (3) Markedly elevated BNP levels (>3 × age- and sex-corrected normal range) confirmed by repeated measurements and without other explanation. **5.2.2.** COR IIa LOE C: intervention should be considered in asymptomatic patients with a sustained fall in BP (>20 mmHg) during exercise testing.	ACC/AHA Evidence: prospective cohort studies and registry studies to support use of exercise testing and BNP levels.[42–46] Peak aortic Vmax supported by registry studies and the RECOVERY trial which set the inclusion criteria for early surgery as Vmax ≥4.5 m/s.[39,41,47] ESC/EACTS Evidence: recommendations surrounding peak aortic Vmax and mean gradient were supported by prospective cohort and retrospective database studies.[39,48] CCT scoring and progression of Vmax recommendations supported by a 2018 registry study[49] and historical studies from 2000 to 1997.[48,50,51] BNP recommendations supported by 2 large studies completed in 2014 (one registry study and one prospective cohort study).[52,53]
Concomitant cardiac surgery		
3.2.3. COR 1 LOE B-NR: in asymptomatic patients with severe AS who are undergoing cardiac surgery for other indications, AVR is indicated.	No specific recommendations.	ACC/AHA Evidence: prospective cohort studies examining the risk factors for asymptomatic AS are cited to suggest a lower risk associated with concomitant AVR than future reoperation.[39,41,54,55]

Abbreviations as in *Tables 1* and *2*. LV, left ventricular; SBP, systolic blood pressure.

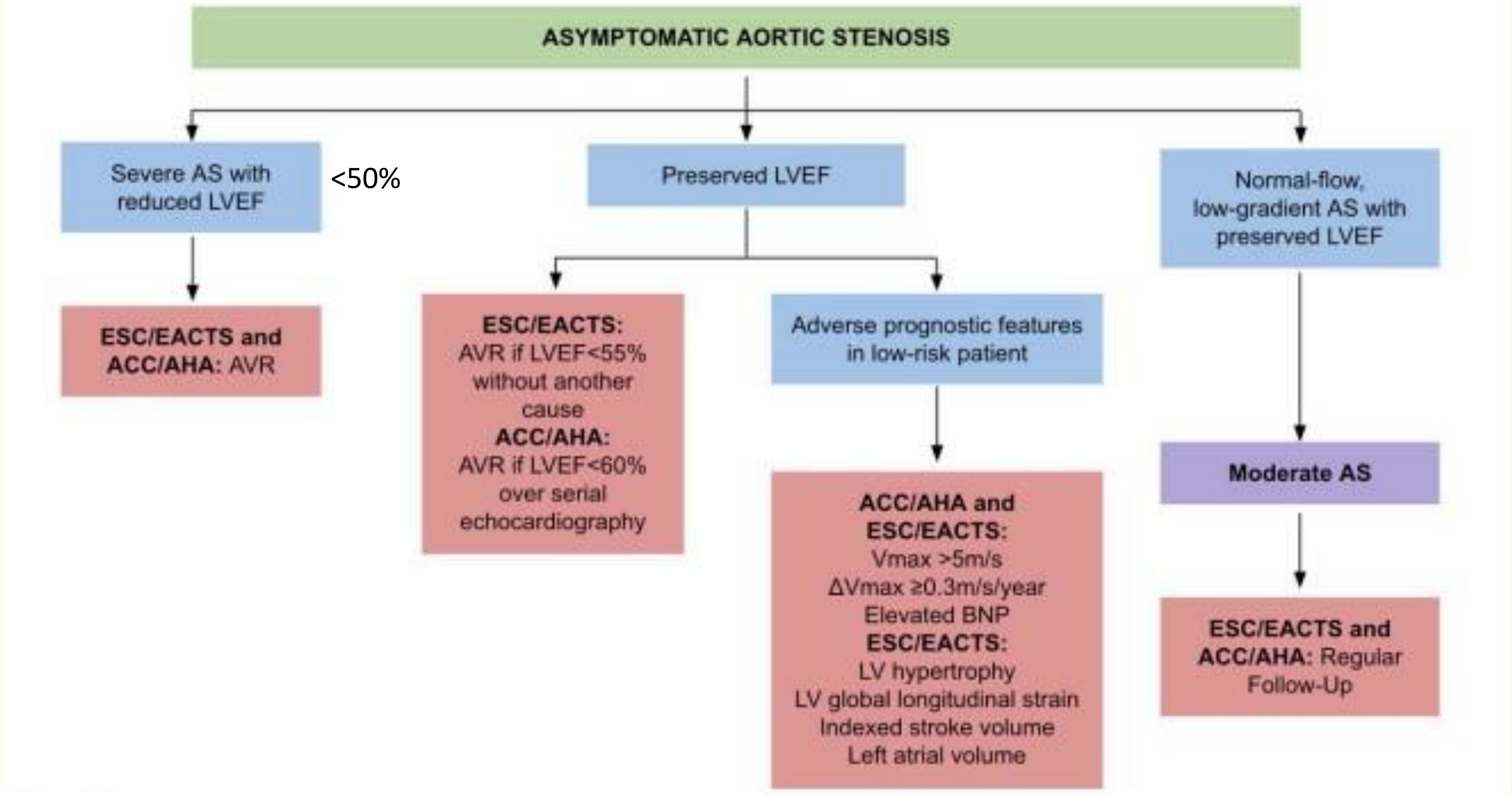


Figure 2 ESC/EACTS vs. ACC/AHA on timing of intervention. AS, aortic stenosis; BNP, blood natriuretic peptide; CCT, Cardiac CT; LVEF, left ventricular ejection fraction.

Preserved EF:

<50%, <55% or <60% (but with serial decline)

"Very Severe AS":

Vmax > 5m/s; mean gradient of > 60mmHg

Subtle definition of adverse prognosis features (low risk patients):

Elevated BNP, hypertrophy or strain

Left atrial volume

LFLG with preserved EF?

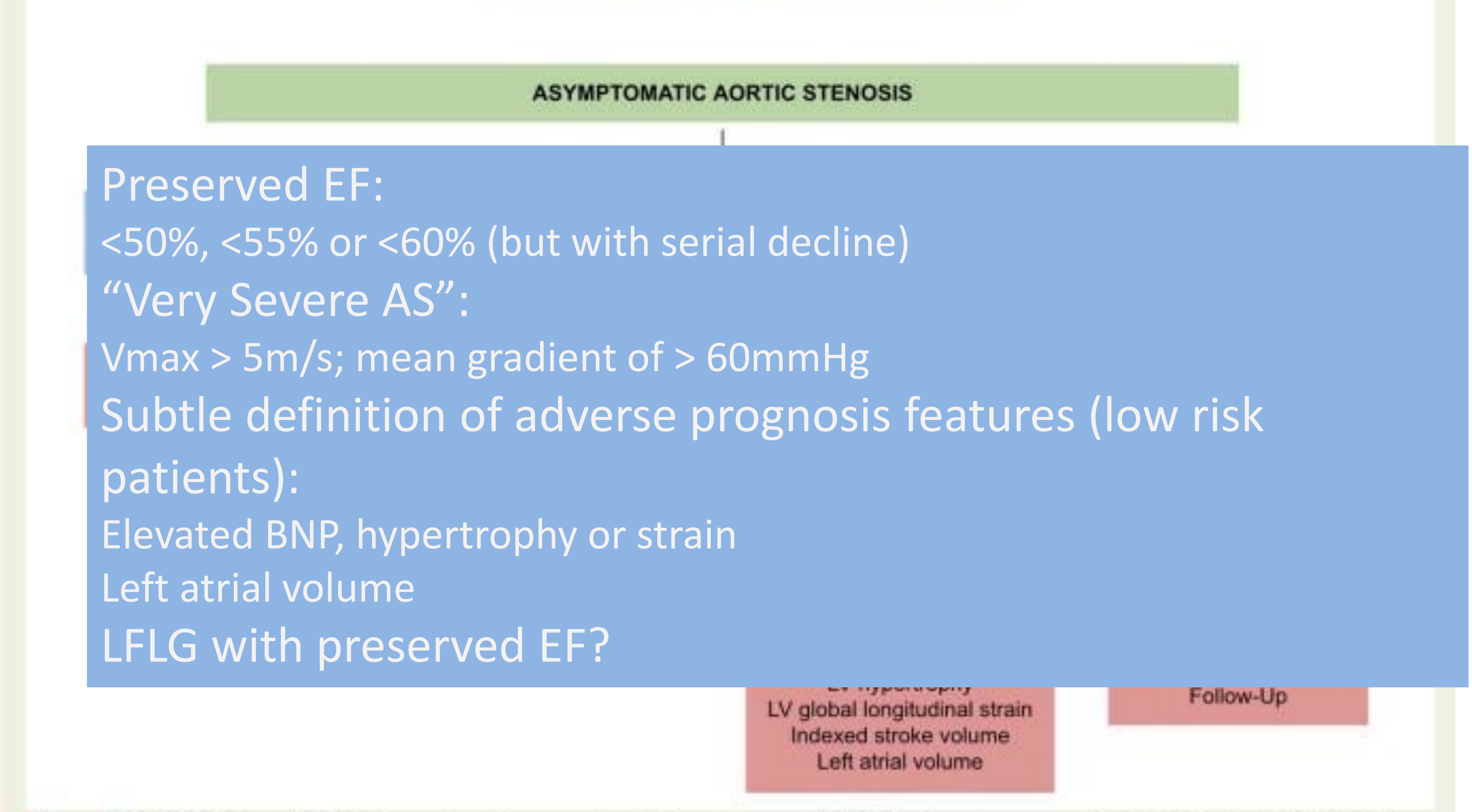


Figure 2 ESC/EACTS vs. ACC/AHA on timing of intervention. AS, aortic stenosis; BNP, blood natriuretic peptide; CCT, Cardiac CT; LVEF, left ventricular ejection fraction.

Table 5 **SAVR vs. TAVI**

2020 ACC/AHA guideline[5]	2021 ESC/EACTS guideline[4]	Comparison of the evidence
Age thresholds		
3.2.4.2. COR 1 LOE A: in symptomatic and asymptomatic patients with severe AS: (1) < 65 years of age or with a life expectancy >20 years, SAVR is recommended. (2) 65–80 years of age and with no anatomic contraindication to transfemoral TAVI, SAVR or transfemoral TAVI is recommended after shared decision-making about the balance between expected patient longevity and valve durability. Consider vascular access, cardiac and non-cardiac factors, function, mechanical vs. prosthetic. 1. > 80 years or for younger patients with a life expectancy <10 years and no anatomic contraindication to transfemoral TAVI, transfemoral TAVI is recommended in preference to SAVR. Consider patient anatomy for balloon-expandable or self-expanding valve.	**5.2.3.** COR I LOE B: SAVR is recommended in younger patients (<75 years) and who are low risk for surgery (STS-PROM/EuroSCORE II <4%) or in patients who are operable and unsuitable for transfemoral TAVI. **5.2.3.** COR I LOE A: TAVI is recommended in older patients (≥75 years), or in those who are high risk (STS-PROM/ EuroSCORE II >8%) or unsuitable for surgery. **5.2.3.** COR I LOE B: SAVR or TAVI are recommended for the remaining patients according to individual clinical, anatomical, and procedural characteristics.	ACC/AHA Evidence: PARTNER-3: randomized trial reporting 1-year TAVI superiority compared with SAVR.[78,79] Evolut Low Risk Trial: randomized trial supporting non-inferiority of TAVI at 2 years.[80] Siemieniuk et al. (2016): meta-analysis of 4 RCTs in comparing TAVI to SAVR.[81] Kumer et al. (2019): prospective cohort study ($n = 276$) finding higher rates of valve deterioration amongst young patients.[82] Siontis et al. (2019): meta-analysis of 7 major RCTs and 8020 patients finding that overall TAVI was associated with a reduction of 2-year all-cause mortality regardless of the STS risk score and method of TAVI.[83] ESC/EACTS Evidence: registry data for intermediate and high-risk patients, most of whom were elderly, indicate valve integrity up to 8 years. However, the data for the durability of TAVI for low-risk patients is only available for up to 2 years. Barbanti et al. (2018): REPLACE registry of bioprosthetic valves in 288 patients with a mean age of 80 years. At 8 years after TAVI, bioprosthetic valve failure and severe structural valve dysfunction occurred in 4.5% and 2.4% of patients, respectively.[84] Didier et al. (2018): FRANCE-2 Registry study showing that the rate of severe structural valve deterioration was 2.5% at 5 years and moderate deterioration was 13.3%.[85]
Bicuspid aortic valve		
5.1.2.2. COR 2b LOE B-NR: 2. In patients with BAV and symptomatic, severe AS, TAVI may be considered as an alternative to SAVR after consideration of patient-specific procedural risks, values, trade-offs, and preferences, and when the surgery is performed at a Comprehensive Valve Centre.	No specific recommendations.	ACC/AHA Evidence: Makkar et al. 2019: registry study of 2691 propensity-score matched patients undergoing TAVI for bicuspid vs. tricuspid AS.[86] Takagi et al. (2019): systematic review and meta-analysis of 12 TAVI studies comparing bicuspid vs. tricuspid aortic valves.[87] Kanjanahattakij et al. (2018): systematic review and meta-analysis of nine studies reporting TAVI outcomes in bicuspid vs. tricuspid AS.[88] ESC/EACTS Evidence: Forrest et al. (2020): STS/ACC Transcatheter Valve Therapy Registry study of 932 bicuspid valve patients vs. 26 154 tricuspid valve patients undergoing TAVI.[89] Halim et al. (2020): STS/ACC Transcatheter Valve Therapy Registry study of 5412 bicuspid valve patients tricuspid valve patients undergoing TAVI.[90] Yoon et al. (2017): observational study of 561 patients undergoing TAVI for bicuspid vs. tricuspid AS.[91]
TAVI for asymptomatic AS		
3.2.4.2. COR 1 LOE B-NR: in asymptomatic patients with severe AS and an LVEF <50% who are ≤80 years of age and have no anatomic contraindication to transfemoral TAVI, the decision between TAVI and SAVR should follow	No specific recommendations.	ACC/AHA Evidence: cites the same studies used to inform TAVI vs. SAVR decision-making in symptomatic AS.

Continued

Table 5 SAVR vs. TAVI

2020 ACC/AHA guideline[5]	2021 ESC/EACTS guideline[4]	Comparison of the evidence
Age thresholds		
3.2.4.2. COR 1 LOE A: in symptomatic and asymptomatic patients with severe AS: (1) < 65 years of age or with a life expectancy >20 years, SAVR is recommended. (2) 65–80 years of age and with no anatomic contraindication to transfemoral TAVI, SAVR or transfemoral TAVI is recommended after shared decision-making about the balance between expected patient longevity and valve durability. Consider vascular access, cardiac and non-cardiac factors, function, mechanical vs. prosthetic. 1. > 80 years or for younger patients with a life expectancy <10 years and no anatomic contraindication to transfemoral TAVI, transfemoral TAVI is recommended in preference to SAVR. Consider patient anatomy for balloon-expandable or self-expanding valve.	**5.2.3.** COR I LOE B: SAVR is recommended in younger patients (<75 years) and who are low risk for surgery (STS-PROM/EuroSCORE II <4%) or in patients who are operable and unsuitable for transfemoral TAVI. **5.2.3.** COR I LOE A: TAVI is recommended in older patients (≥75 years), or in those who are high risk (STS-PROM/EuroSCORE II >8%) or unsuitable for surgery. **5.2.3.** COR I LOE B: SAVR or TAVI are recommended for the remaining patients according to individual clinical, anatomical, and procedural characteristics.	ACC/AHA Evidence: PARTNER-3: randomized trial reporting 1-year TAVI superiority compared with SAVR.[78,79] Evolut Low Risk Trial: randomized trial supporting non-inferiority of TAVI at 2 years.[80] Siemieniuk et al. (2016): meta-analysis of 4 RCTs in comparing TAVI to SAVR.[81] Kumer et al. (2019): prospective cohort study ($n = 276$) finding higher rates of valve deterioration amongst young patients.[82] Siontis et al. (2019): meta-analysis of 7 major RCTs and 8020 patients finding that overall TAVI was associated with a reduction of 2-year all-cause mortality regardless of the STS risk score and method of TAVI.[83] ESC/EACTS Evidence: registry data for intermediate and high-risk patients, most of whom were elderly, indicate valve integrity up to 8 years. However, the data for the durability of TAVI for low-risk patients is only available for up to 2 years. Barbanti et al. (2018): REPLACE registry of bioprosthetic valves in 288 patients with a mean age of 80 years. At 8 years after TAVI, bioprosthetic valve failure and severe structural valve dysfunction occurred in 4.5% and 2.4% of patients, respectively.[84] Didier et al. (2018): FRANCE-2 Registry study showing that the rate of severe structural valve deterioration was 2.5% at 5 years and moderate deterioration was 13.3%.[85]
Bicuspid aortic valve		
5.1.2.2. COR 2b LOE B-NR: 2. In patients with BAV and symptomatic, severe AS, TAVI may be considered as an alternative to SAVR after consideration of patient-specific procedural risks, values, trade-offs, and preferences, and when the surgery is performed at a Comprehensive Valve Centre.	No specific recommendations.	ACC/AHA Evidence: Makkar et al. 2019: registry study of 2691 propensity-score matched patients undergoing TAVI for bicuspid vs. tricuspid AS.[86] Takagi et al. (2019): systematic review and meta-analysis of 12 TAVI studies comparing bicuspid vs. tricuspid aortic valves.[87] Kanjanahattakij et al. (2018): systematic review and meta-analysis of nine studies reporting TAVI outcomes in bicuspid vs. tricuspid AS.[88] ESC/EACTS Evidence: Forrest et al. (2020): STS/ACC Transcatheter Valve Therapy Registry study of 932 bicuspid valve patients vs. 26 154 tricuspid valve patients undergoing TAVI.[89] Halim et al. (2020): STS/ACC Transcatheter Valve Therapy Registry study of 5412 bicuspid valve patients tricuspid valve patients undergoing TAVI.[90] Yoon et al. (2017): observational study of 561 patients undergoing TAVI for bicuspid vs. tricuspid AS.[91]
TAVI for asymptomatic AS		
3.2.4.2. COR 1 LOE B-NR: in asymptomatic patients with severe AS and an LVEF <50% who are ≤80 years of age and have no anatomic contraindication to transfemoral TAVI, the decision between TAVI and SAVR should follow	No specific recommendations.	ACC/AHA Evidence: cites the same studies used to inform TAVI vs. SAVR decision-making in symptomatic AS.

Continued

Table 5 ***Continued***

2020 ACC/AHA guideline[5]	2021 ESC/EACTS guideline[4]	Comparison of the evidence
the same recommendations as for symptomatic patients. **3.2.4.2.** COR 1 LOE B-NR: for asymptomatic patients with severe AS and an abnormal exercise test, very severe AS, rapid progression, or an elevated BNP (COR 2a indications for AVR), SAVR is recommended in preference to TAVI.		
Non-transfemoral TAVI		
No specific recommendations.	**5.2.3.** COR IIb LOE C: non-transfemoral TAVI may be considered in patients who are inoperable and unsuitable for transfemoral TAVI.	ACC/AHA Evidence: PARTNER-1 substudy by Elmariah et al. in 2017 showed a disproportionately higher risk of cardiac mortality in patients with LV dysfunction who underwent transapical TAVI.[92]
Bystander coronary artery disease		
14.1.2. COR 2a LOE C-LD: in patients undergoing valve repair or replacement with significant proximal CAD, CABG is reasonable for selective patients. **14.1.1.** COR 2a LOE C-LD: in patients undergoing TAVI with significant left main or proximal CAD with or without angina, revascularization by PCI before TAVI is reasonable. **14.1.1.** COR 2a LOE C-LD: in patients with significant AS and significant CAD consisting of complex bifurcation left main and/or multivessel CAD with a SYNTAX score >33, SAVR and CABG are reasonable and preferred over TAVI and PCI.	**5.2.3.** COR I LOE C: SAVR is recommended in patients with severe aortic stenosis undergoing CABG or surgical intervention on the ascending aorta or another valve. **5.2.3.** COR IIa LOE C: SAVR should be considered in patients with moderate aortic stenosis undergoing CABG or surgical intervention on the ascending aorta or another valve after Heart Team discussion. 'PCI and TAVI may be undertaken as combined or staged procedures according to the clinical situation, pattern of CAD, and extent of myocardium at risk'	ACC/AHA Evidence: references a systematic review by Bajaj et al. (2017) and the TAVR-LM Registry by Chakravarty et al. (2016).[93,94] References an observational study by Thalji et al. that shows favourable results for those with concomitant coronary artery disease with CABG and SAVR over SAVR alone.[95] ESC/EACTS Evidence: does not address pre-TAVI PCI. Both guidelines await data from ACTIVATION and TAVR-PCI.

Abbreviations as in Tables 1–4. CAD, coronary artery disease; CABG, coronary artery bypass grafting; PCI, percutaneous coronary intervention; SAVR, surgical aortic valve replacement; STS-PROM, Society of Thoracic Surgeons' Predicted Risk of Mortality.

GL age criteria not robust ! NOTION, UK TAVI push equivalency to younger age!

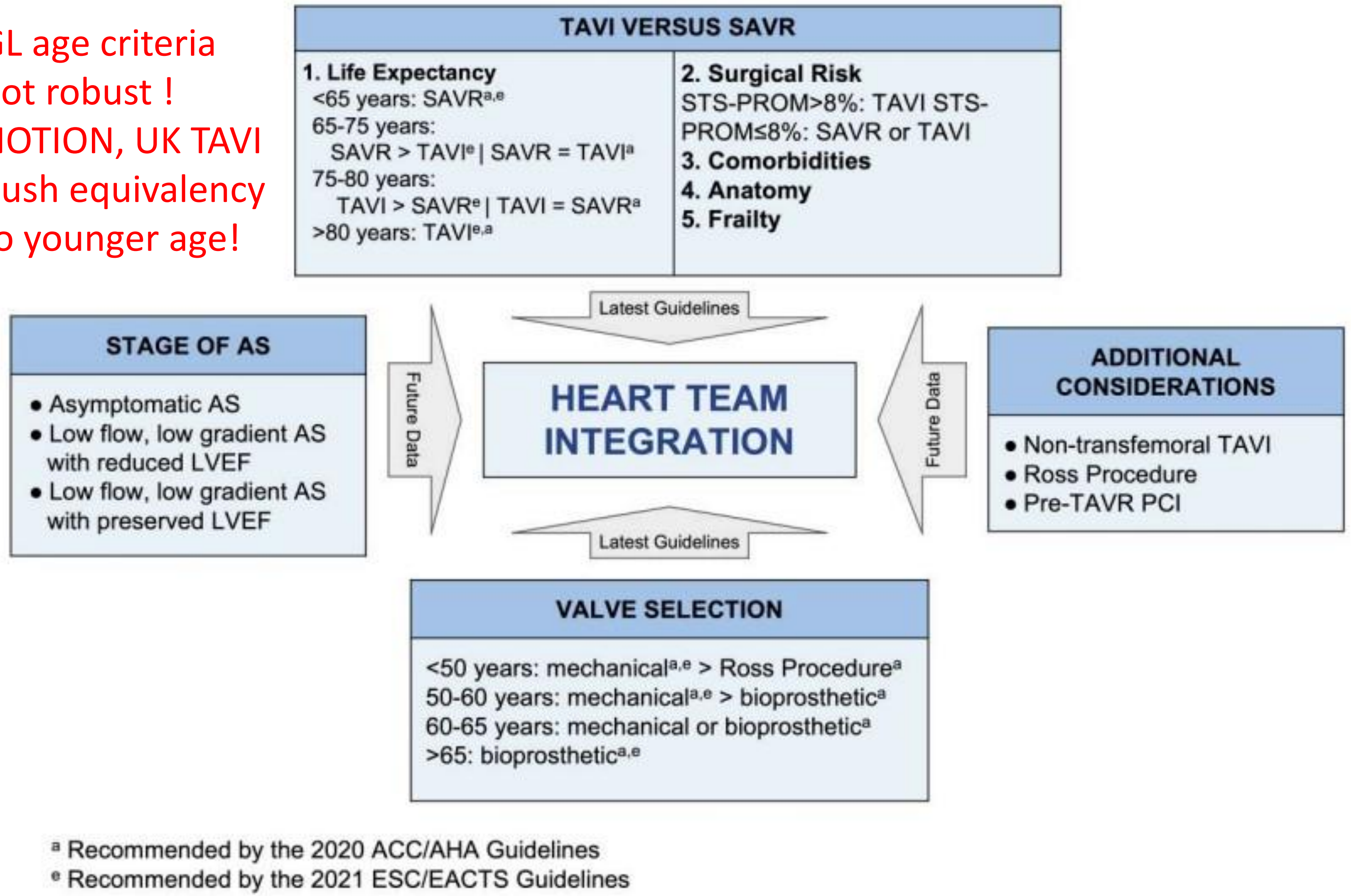


Figure 1 Factors influencing mode of intervention in aortic stenosis. AS, aortic stenosis; LVEF, left ventricular ejection fraction; PCI, percutaneous coronary intervention; SAVR, surgical aortic valve replacement; STS-PROM, Society of Thoracic Surgeons' Predicted Risk of Mortality; TAVI , transcatheter aortic valve implantation.

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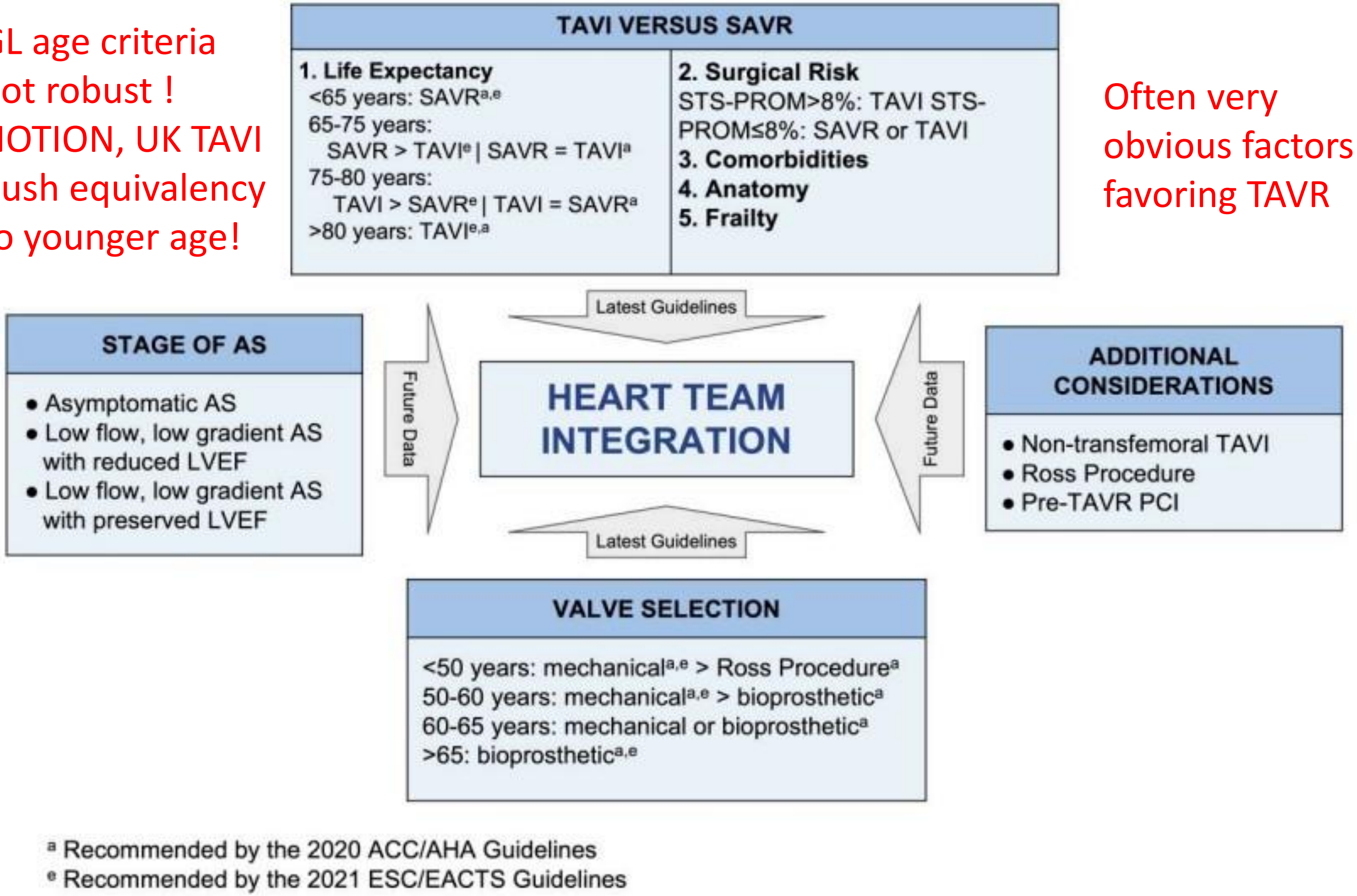

Figure 1 Factors influencing mode of intervention in aortic stenosis. AS, aortic stenosis; LVEF, left ventricular ejection fraction; PCI, percutaneous coronary intervention; SAVR, surgical aortic valve replacement; STS-PROM, Society of Thoracic Surgeons' Predicted Risk of Mortality; TAVI , transcatheter aortic valve implantation.

Often very obvious factors favoring TAVR

AS Severity Grading and Cardiac Staging

Grade or Stage	Stage 0 None	Stage 1 LV	Stage 2 LA-mitral	Stage 3 PA-tricuspid	Stage 4 RV
Grade 0 V_{max} <2m/s					
Grade 1 V_{max} 2-2.9m/s					
Grade 2 V_{max} 3-3.9m/s					
Grade 3 V_{max} ≥.4m/s					

AS Severity Grading and Cardiac Staging

Grade or Stage	Stage 0 None	Stage 1 LV	Stage 2 LA-mitral	Stage 3 PA-tricuspid	Stage 4 RV
Grade 0 V_{max} <2m/s					
Grade 1 V_{max} 2-2.9m/s					
Grade 2 V_{max} 3-3.9m/s					
Grade 3 V_{max} ≥.4m/s		AVR	AVR	AVR	AVR

AS Severity Grading and Cardiac Staging

Grade or Stage	Stage 0 None	Stage 1 LV	Stage 2 LA-mitral	Stage 3 PA-tricuspid	Stage 4 RV
Grade 0 V_{max} <2m/s					
Grade 1 V_{max} 2-2.9m/s					
Grade 2 V_{max} 3-3.9m/s	PROGRESS	PROGRESS	PROGRESS	PROGRESS	PROGRESS
Grade 3 V_{max} ≥.4m/s	EARLY TAVR				

AS Severity Grading and Cardiac Staging

Grade or Stage	Stage 0 None	Stage 1 LV	Stage 2 LA-mitral	Stage 3 PA-tricuspid	Stage 4 RV
Grade 0 V_{max} <2m/s					
Grade 1 V_{max} 2-2.9m/s					
Grade 2 V_{max} 3-3.9m/s	PROGRESS	PROGRESS	PROGRESS	PROGRESS	PROGRESS
Grade 3 V_{max} ≥.4m/s	EARLY TAVR	AVR	AVR	AVR	AVR

Multi-drug ‘precision’ medical Rx