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STATE-OF-THE-ART REVIEW

Aortic Stenosis Management in Patients With Acute Hip Fracture

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ABSTRACT

The treatment of severe aortic stenosis (SAS) has evolved rapidly with the advent of minimally invasive structural heart interventions. Transcatheter aortic valve replacement has allowed patients to undergo definitive SAS treatment achieving faster recovery rates compared to valve surgery. Not infrequently, patients are admitted/diagnosed with SAS after a fall associated with a hip fracture (HFx). While urgent orthopedic surgery is key to reduce disability and mortality, untreated SAS increases the perioperative risk and precludes physical recovery. There is no consensus on what the best strategy is either hip correction under hemodynamic monitoring followed by valve replacement or preoperative balloon aortic valvuloplasty to allow HFx surgery followed by valve replacement. However, preoperative minimalist transcatheter aortic valve replacement may represent an attractive strategy for selected patients. We provide a management pathway that emphasizes an early multidisciplinary approach to optimize time for hip surgery to improve orthopedic and cardiovascular outcomes in patients presenting with HFx-SAS. (JACC Adv 2024;3:100912) © 2024 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

Despite the introduction of systematic osteoporosis treatment in the United States, the incidence of hip fractures (HFx) will rise in the next decades due to the aging of the population.[1] The mean age of patients suffering from HFx is 80 years, 75% of whom are women.[2] HFx represents a substantial economic burden, being among the top 20 most expensive diagnoses. The consequences of HFx are devastating, particularly if not timely addressed. Unfortunately, due to the frequent coexistence of severe comorbidities, up to 10% of patients with HFx are deemed inoperable leading to irreversible long-term disability and increased mortality.[3] While 5% of patients die during the first month, 25% die in the first year after the index event.[2,4] Advanced age, frailty, prior cardiovascular disease, and time to surgery (TTS) are among the strongest predictors of early mortality after HFx.[4]

Aortic stenosis (AS), due to age-related valve degeneration and calcification, is 1 of the most common and significant valvular heart diseases in the older population.[5] Although there are scarce reports

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ABBREVIATIONS AND ACRONYMS

AS = aortic stenosis

AVR = aortic valve replacement

BAV = balloon aortic valvuloplasty

HFx = hip fracture

HOS = hip orthopedic surgery

LOS = length of stay

MACE = major adverse cardiac events

NCS = noncardiac surgery

QOL = quality of life

SAS = severe aortic stenosis

SAVR = surgical aortic valve replacement

STS = Society of Thoracic Surgeons

TAVR = transcatheter aortic valve replacement

TEE = transesophageal echocardiogram

TTE = transthoracic echocardiogram

TTS = time to surgery

analyzing the concomitance of AS and HFx, about 3 to 8% of hospitalized patients with HFx have moderate or severe AS (SAS) (Table 1).[6-9] This is not surprising, since the incidence of SAS is ~5% in patients >75 years.[5] SAS places the patient at risk for perioperative cardiac complications,[10,11] having 3 to 4-fold increased 30-day mortality compared to patients with HFx without SAS,[6,8,12] Furthermore, 1-year mortality in this group reaches ~50%.[6,8] However, delaying hip orthopedic surgery (HOS) for cardiovascular risk management may increase TTS, with an impact on functional recovery and mortality.[13,14]

The best management strategy for patients with HFx and SAS remains unclear. Currently, there are no specific guidelines for what the best strategy is, namely HFx correction under general anesthesia (GA) with strict hemodynamic monitoring followed by aortic valve replacement (AVR) if indicated, preoperative balloon aortic valvuloplasty (BAV) to allow HOS before definitive AVR, or conservative management for either of these conditions. Since 2002, the story of transcatheter aortic valve replacement (TAVR) has been characterized by rapid technological advancements and procedural refinements, leading to expanded utilization in different groups of patients. The aim of this review is to provide a comprehensive analysis of the potential advantages and drawbacks of different management strategies of SAS in the setting of acute HFx, introducing a streamlined protocol for treating these patients.

DIAGNOSING SEVERE AORTIC STENOSIS IN PATIENTS WITH HIP FRACTURES: A SIMPLE BYSTANDER?

Clinical characteristics of patients with calcific AS with or without HFx are not significantly different (Figure 1).[6] Interestingly, valvular calcifications exhibit features of bone formation, and ectopic calcification is frequently accompanied by decreased mineral density or disturbed bone turnover.[9] Moreover, osteoporosis (ie, severe decrease in bone mineral density accompanied by increased fracture risk) has been proposed as an etiologic factor contributing to the calcific changes in the aortic valve as well as in other cardiac structures, a phenomenon called "calcification paradox".[15,16] Regardless of the etiological link,[16,17] patients with SAS can suffer a fall and develop an HFx. Whether the SAS itself increases the risk of HFx after falling (eg, orthostatic hypotension, syncope, deconditioning, and heart failure) has not been directly evaluated. However, patients who experience syncope, which is usually accompanied by falling, have an increased risk of HFx.[18]

Studies revealed that a single cause for falls is evident in a minority of cases; rather, a multitude of factors, such as environmental triggers, frailty, comorbidities (including SAS), and medications influence the risk of falling.[18] Importantly, a syndrome of geriatric falls and fractures as a consequence of a cycle of weakness, immobility, instability, and falls has been described.[19] SAS may also contribute to the overall risk of falling, considering that older patients frequently reduce their physical activity due to symptoms associated with SAS. In this scenario, SAS may be diagnosed incidentally after the HFx during medical/cardiac surgical risk assessment (Figure 2).[6] Importantly, the detection of a SAS may lead to changing the anesthetic strategy (spinal to GA), adoption of close hemodynamic monitoring, or may warrant a specific cardiac intervention, all of which aim to limit perioperative complications.[10,11]

HIGHLIGHTS

- Delayed HFx surgery is associated with an increased risk of permanent disability and mortality.
- The presence of uncorrected SAS increases the perioperative risk and impairs functional rehabilitation.
- Timely diagnosis of AS in the setting of HFx is key to a preoperative strategy.
- A streamlined multidisciplinary approach for AS and HFx management may reduce time to hip surgery and improve outcomes.
- Preoperative minimalist TAVR may represent the state-of-the-art treatment for selected patients.

MANAGEMENT OF SEVERE AORTIC STENOSIS IN PATIENTS WITH ACUTE HIP FRACTURE

Patients with SAS are at risk of hemodynamic deterioration during the noncardiac surgery (NCS) (Figure 3). According to the American College of Cardiology/American Heart Association and the European Society of Cardiology guidelines[10,11] patients with symptomatic SAS should undergo surgical aortic valve replacement [SAVR] or TAVR prior to elective

NCS. Recommendations for asymptomatic patients with SAS may vary according to the NCS risk. If intermediate- or high-risk NCS is planned in asymptomatic SAS patients, elective surgery should be performed only if strictly necessary and using invasive monitoring.[10,11] However, patients suffering from HFx require urgent HOS to reduce irreversible impairment and mortality.[13,14] **Figure 4** provides a general management pathway according to whether patients have high-risk features and if they are candidates for TAVR, SAVR, or preoperative/palliative BAV (Group 0-4).

"LAISSEZ-FAIRE AS" BEFORE ORTHOPEDIC HIP SURGERY. Tashiro et al[20] challenged the concept of SAS as an unequivocal risk factor for mortality in the setting of NCS. By comparing patients with SAS and matched controls undergoing intermediate-/high-risk NCS (~30% HOS), the authors observed no differences in 30-day mortality between groups.[20] However, major adverse cardiac events (MACEs) were higher in the SAS group, mainly explained by higher rates of heart failure. Outcomes in the symptomatic group were significantly worse than in the asymptomatic group. In these patients, MACE at 30 days was higher compared with their controls, although the difference in mortality did not reach statistical significance. Conversely, the asymptomatic group had very similar outcomes when matched to their controls.

The presence of symptoms in patients with SAS is a strong predictor of mortality and a robust indication for AVR.[10,11] However, the assessment of symptoms in patients with SAS and HFx is not always accurate[21,22] and the realization of a stress test in the setting of HFx is obviously not possible. Studies undertaken specifically in geriatric patients with SAS and HFx undergoing urgent HOS demonstrated an excess risk of MACE, 30-day, and 1-year mortality compared to patients without AS, regardless of the presence of symptoms.[6,8,12] The CURRENT-AS registry compared the clinical outcomes of patients with uncorrected SAS vs patients with corrected SAS (SAVR/TAVR, including prophylactic AVR) after NCS (~30% HOS).[23] Prophylactic AVR was defined as AVR that was performed just prior to NCS in patients with no formal indication of AVR to get through NCS and avoid related complications. At 30 days, 4.3% died in the untreated SAS group (50% HOS), whereas no patients died in the AVR group. Of note, of 29 patients with untreated SAS undergoing hip surgery, 4 died (2 symptomatic and 2 asymptomatic) within 30 days of surgery (ie, 14% of subgroup mortality), representing 50% of total deaths in the registry.[23] Although bias is expected due to the retrospective nature of the study, the fact that these patients were "protected a priori" and associated with better outcomes (regardless of symptoms) supports valve intervention prior to surgery. Interestingly, the RECOVERY trial reported that the incidence of cardiovascular death in asymptomatic patients with SAS (V_{max} >4.5 m/s, ΔP_{mean} >50 mm Hg, aortic valve area ≤0.75 cm^2) was significantly lower in patients who underwent early SAVR vs those managed conservatively.[24] Thus, it seems reasonable to treat SAS before hip surgery, especially when the assessment of symptoms may be inaccurate or in the presence of extreme valvular severity. In the absence of these criteria, patients should undergo HOS with no delays (Group 0) (**Figure 4**).

PREOPERATIVE BALLOON AORTIC VALVULOPLASTY. BAV was originally proposed as an alternative to SAVR for definitive valve treatment.[25] However, due to restenosis rates up to 80% and lower survival at follow-up compared to SAVR, this technique was strongly criticized.[25,26] Granulation tissue, fibrosis, and ossification are commonly observed in restenosed valves after BAV.[27] The inability to obtain long-lasting results would be particularly detrimental for postoperative HFx patients, as achieving recovery after surgery depends on the ability to engage in physical rehabilitation. BAV is also associated with a variable risk (~7%-15%) of acute complications.[27,28] Although uncommon (~2%),[25] iatrogenic acute severe aortic regurgitation after BAV can lead to flash pulmonary edema and hemodynamic collapse. This complication can now be managed with emergent TAVR.

In parallel with the enhanced global experience with TAVR, BAV was reinforced as a bridging therapy, so the number of BAV procedures increased again leading to several procedural refinements.[29] New balloons allow now to perform this procedure with 8-9-F sheaths, reducing the risk of vascular access-related complications. Moreover, some centers have published their initial experience with single or biradial BAV.[30] However, despite the incorporation of additional safety measures (eg, careful balloon size selection), contemporary reports confirmed only its brief temporizing nature with no long-term survival benefits (>3-6 months).[29]

Currently, BAV is still considered in SAS patients as a bridge to destination therapies (SAVR/TAVR) in those requiring clinical optimization before urgent NCS (Groups 2-3), or as a palliative procedure in patients who are not suitable for AVR (Group 4) (**Figure 4**).[10,11,22,31,32] In fact, preoperative BAV is a common practice in different institutions among patients with HFx and symptomatic SAS in the absence of contraindications (eg, significant AR).

TABLE 1 Summary of Studies That Analyzed the Clinical Significance of AS in the Setting of HOS

First Author (Year)	Study Population	Female	Comparator	Female	Mean Age (y)	Incidence of AS in HFx	Symptoms	Valve Intervention
Rostagno et al (2019)	Severe AS	32 (NR)	Age and sex matched non-AS patients with HFx	283 (NR)	87 ± 6 vs 83 ± 8, P = NS	3.5%[a]	NR	None
Keswani et al (2016)	Moderate + severe AS	65 (72%)	Non-AS patients with HFx	129 (69%)	89 ± 7 vs 83 ± 10, $P < 0.001$	8%[b]	Unable to assess	None
Adunsky et al (2008)	Mild + moderate + severe AS	62 (90%)	Age, sex, ethnicity, and date of sample collection matched non-AS patients with HFx	100 (74%)	85.9 ± 7.4 vs 83.2 ± 6.7, $P = 0.09$	NR	20%	None
Leibowitz et al (2009)	Severe AS	32 (84%)	Non-AS patients with HFx	88 (76%)	84.5 vs 86, $P = 0.69$	NR	Unable to assess	None
McBrien et al (2009)	Severe AS	30 (93%)	Non-AS patients with HFx	3,481 (75%)	86.1 ± 9.0 vs 78.4 ± 12.0, $P < 0.001$	1%[e]	Unable to assess	None
Chen et al (2020)	Moderate + severe AS	20 (NR)	Non-AS patients	334 (NR)	~82	5.6%	NR	None
Ferre et al (2021)	Severe AS without preoperative BAV	30 (77%)	Severe AS with preoperative BAV	29 (76%)	~89	NR	Unable to assess	Preoperative BAV

TABLE 1 Continued

			Postoperative Complications at 30 Days		Postoperative Mortality		
First Author (Year)	TTS (d)	LOS (d)	Delirium	Major Adverse Cardiac Events[d]	In-Hospital	30 Days	1 Year
Rostagno et al (2019)	3.2 ± 4.4 vs 2.6 ± 1.6, $P < 0.001$	15.7 ± 7.6 vs 14.6 ± 5.6, P = NS	28.1% vs 19.8%, $P = 0.02$	MI: 15.6% vs 1.1%, $P < 0.001$, heart failure: 15.6% vs 0.7%, $P < 0.001$	NR	12.5% vs 3.1%, $P = 0.06$	46%[b] vs 18%, $P < 0.001$
Keswani et al (2016)	3.3 ± 3.7 vs 1.9 ± 3.4, $P = 0.01$	8.4 ± 7.0 vs 7.9 ± 6.7, P = NS	20.0% vs 1.9%, $P < 0.001$	17.0% vs 8.4%, P = NS	NR	14.7% vs 4.2%, $P < 0.001$	46.8% vs 14.1%, $P < 0.001$
Adunsky et al (2008)	3.8 ± 2.9 vs 3.1 ± 2.4, $P = 0.04$	33.2 ± 18.5 vs 32.7 ± 11.5[c], P = NS	NR	8% vs 3.6%, $P = 0.02$ (in-hospital)	6.5% vs 3.3%, $P = 0.01$	NR	17.7% vs 16.1%, P = NS
Leibowitz et al (2009)	2.48 ± 1.5 vs 1.78 ± 1.5, P = NS	NR	NR	18.7% vs 11.8%, P = NS	NR	6.2% vs 6.8%, $P = 0.10$	NR
McBrien et al (2009)	5.5 vs 5.0, P = NS	NR	NR	NR	NR	10%[f] vs 7.4%, P = NS	36.7% vs 22.2%, P = NS
Chen et al (2020)	NR	NR	NR	30% vs 6.3%, $P = 0.001$	NR	20% vs 1.8%, $P < 0.05$	NR
Ferre et al (2021)	1 vs 3, $P < 0.001$	9 vs 13, $P = 0.02$	27% vs 31%, P = NS	MI: 7% vs 0%, P = NS, heart failure: 9% vs 0%, $P < 0.001$	NR	9% vs 2%, $P < 0.05$	NR

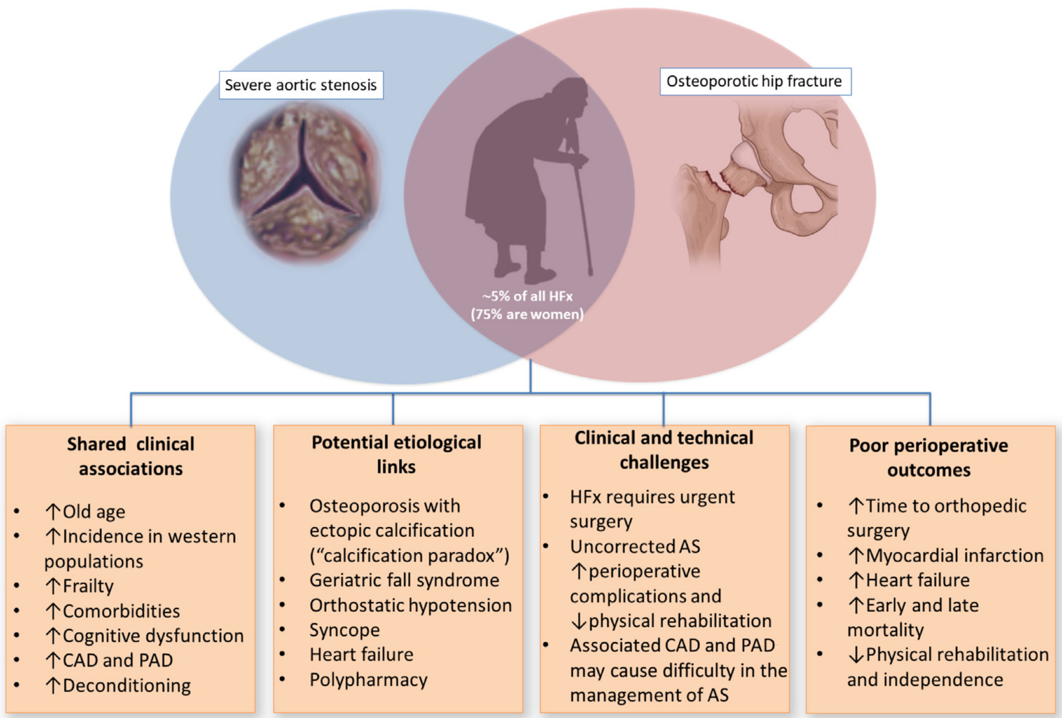
[a]Based on author's clarification. [b]Includes moderate and severe AS. [c]Includes postacute care rehabilitation. [d]Postoperative cardiac events may include MI, significant arrhythmias, and heart failure. [e]Per the authors, the true incidence of AS in this population is underestimated since some patients with known AS were excluded and no systematic TTE was performed to diagnose AS (only guided by auscultation findings). [f]6 patients with severe AS were excluded, 2 of whom died in the 30-day period, which would have resulted in a 30-day mortality close to 14% in the severe AS group.

AS = aortic stenosis; BAV = balloon aortic valvuloplasty; HFx = hip fracture; LOS = length of stay; MI = myocardial infarction; N/A = not applicable; NR = not reported; NS = not significant; TTE = transthoracic echocardiogram; TTS = time to surgery.

However, the efficacy and safety of preoperative BAV have only been evaluated in small contemporary case series or nonrandomized studies.[22,32] These studies showed a potential decrease in 1-month mortality in the BAV group compared to a non-BAV control group, despite an increase in TTS of 48 hours.[22,32]

SURGICAL AORTIC VALVE REPLACEMENT IN THE SETTING OF HIP FRACTURE. It has been widely recognized that the prognosis of patients with surgically corrected SAS is comparable to their peers with similar comorbidities without SAS, whereas medical management of symptomatic SAS is associated with a median survival of ~2 years.[10,11,33] Intuitively, the correction of symptomatic SAS before NCS could eventually decrease mortality in the perioperative setting and in the long-term. However, performing "preoperative SAVR" in the setting of HFx would be unrealistic unless the subsequent HOS is delayed, which entails a significant risk of mortality and permanent disability.[3,13] Preoperative SAVR would also imply a heavy physical burden on a patient that requires HOS and soon begin physical rehabilitation. For such patients, a less invasive treatment is

FIGURE 1 Inter-Relationship Between Severe Aortic Stenosis and Hip Fracture



SAS and HFx share common pathological mechanisms, comorbidities and often coexist leading to worse clinical outcomes. AS = aortic stenosis; CAD = coronary artery disease; HFx = hip fracture; PAD = peripheral artery disease; SAS = severe aortic stenosis.

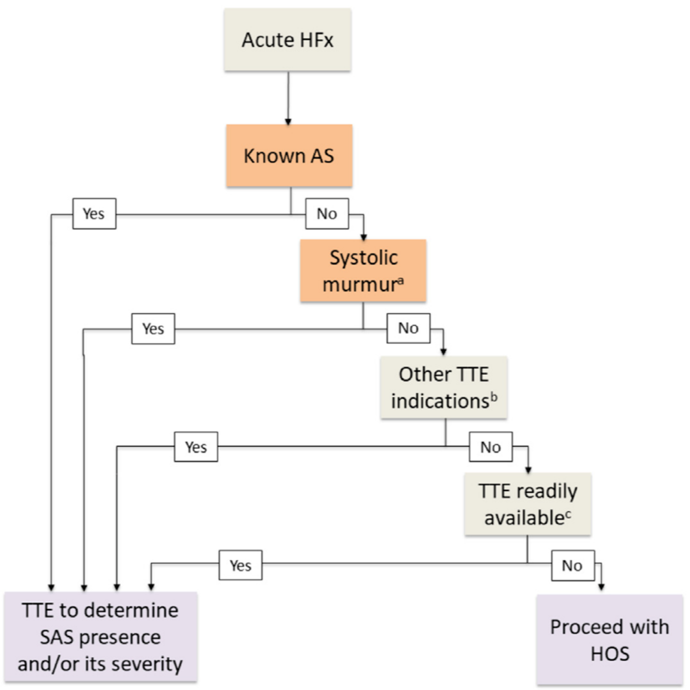
desirable. In certain patients who may not be suitable candidates for TAVR (Table 2), bridge BAV to HOS followed by SAVR might be the most reasonable approach (Group 3) (Figure 4).

PREOPERATIVE TRANSCATHETER AORTIC VALVE REPLACEMENT. The evolution and current safety of TAVR have prompted to lower the threshold and move forward with this treatment in patients otherwise considered for palliative or "bridge BAV".[34] This could be the case for those with symptomatic SAS requiring NCS. In fact, despite the lack of data on the efficacy or safety of preoperative TAVR for patients with SAS who undergo NCS, both the AHA/ACC and European Society of Cardiology guidelines have released a potential role for preoperative TAVR in this group of patients to prevent perioperative events and possibly decrease mortality.[10,11] Therefore, TAVR would be a reasonable option to avoid delays and reduce complications of elective/urgent NCS (Group 1) (Figure 4). Another advantage of TAVR over BAV is the ability to treat mixed AS/AR disease, in which preoperative BAV is discouraged.

CLINICAL EVIDENCE SUPPORTING TRANSCATHETER AORTIC VALVE REPLACEMENT IN PATIENTS WITH SEVERE AORTIC STENOSIS. Principal findings. The clinical benefit of different TAVR technologies and manufactured valves has been extensively demonstrated in different groups of patients with SAS (including those with prohibitive surgical risk) in the PARTNER and CoreValve US Pivotal Series of Trials with sustained benefits at 5 years.[35-39] On the other hand, only small registries have analyzed the role of introducing TAVR in the setting of NCS.[23,40-43] However, after introducing TAVR in the therapeutic toolbox, more geriatric and high-risk patients became candidates for 2-staged operations, where HOS became the most common NCS.[42]

Hospital length of stay and symptomatic treatment. It is particularly relevant for older patients with SAS and HFx to achieve a rapid recovery after the SAS correction so they can undergo the HOS timely and safely. Among others, changes in hospital length of stay (LOS), symptoms, and quality of life (QOL) could reflect the ability of TAVR in preparing these patients for a subsequent surgery.

FIGURE 2 Use of Transthoracic Echocardiography in the Setting of Acute Hip Fracture



The detection of a SAS in the perioperative setting has important clinical implications. [a]The use of POCUS may help clinicians to expedite the diagnosis of SAS. [b]Known or suspected heart failure, ischemic heart disease or abnormal ECG. [c]TTE may be still obtained if readily available, as about ~10% of patients with SAS and HFx will remain undiagnosed. AS = aortic stenosis; ECG = electrocardiogram; HFx = hip fracture; HOS = hip orthopedic surgery; POCUS = point-of-care ultrasound; SAS = severe aortic stenosis; TTE = transthoracic echocardiogram.

Over the last decade, the hospital LOS after TAVR has steadily decreased in association with increasing experience in post-TAVR management.[44] While patients in the TAVR group of the PARTNER 1 Cohort-A trial had a LOS of 8 days, the use of SAPIEN 3 system (designed with lower delivery profile and an external sealing skirt to reduce paravalvular regurgitation) had a median LOS of 3 days.[38] Although shorter LOS are also associated with lower surgical risk, different retrospective[45,46] and validation cohort studies[47,48] have demonstrated that the adoption of the transfemoral (TF) minimalist TAVR approach (conscious sedation, low-profile TAVR devices, transthoracic echocardiogram guidance, and well-standardized TAVR-specific clinical care pathways) facilitates recovery and allows a safe early (<72 hours)[47] or a next-day discharge in about 80% of high-risk patients.[48] TAVR also resulted in a faster improvement of symptoms and QOL (eg, ADLs) at 30 days compared to SAVR,[36,38,39,48-50] as assessed with the use of the Kansas City Cardiomyopathy Questionnaire-12, the NYHA functional classification, or the 6-minute walk test. These benefits were further enhanced with the minimalist approach observing very early changes in QOL,[50] a valuable advantage for patients planning for NCS and physical rehabilitation.

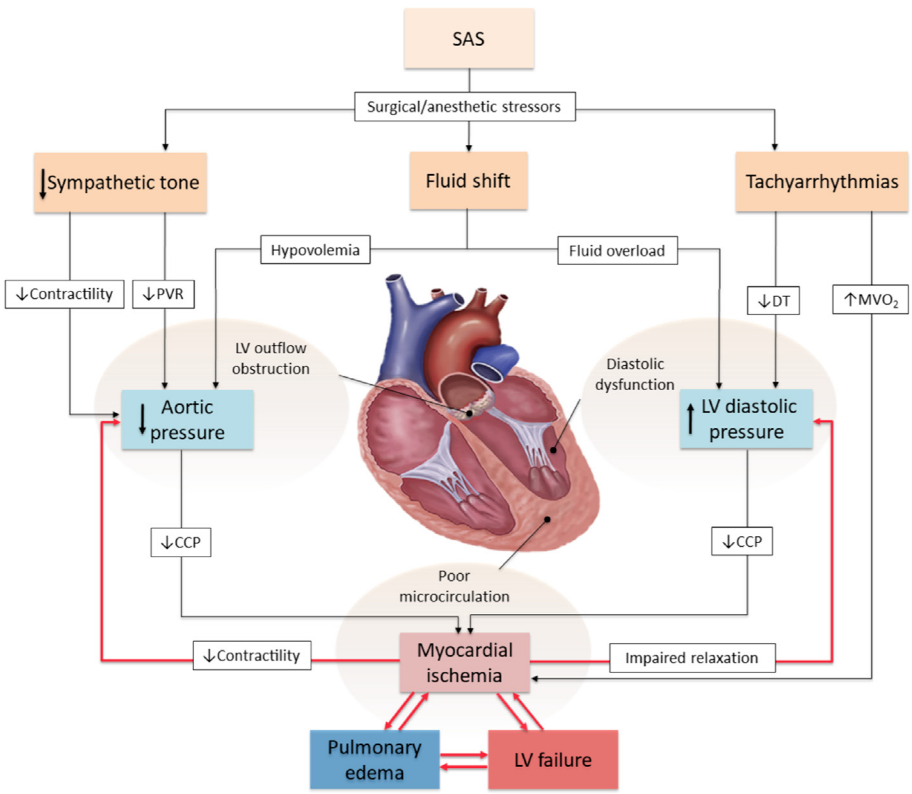
SPECIAL CONSIDERATIONS FOR PREOPERATIVE TRANSCATHETER AORTIC VALVE REPLACEMENT IN THE SETTING OF SUBSEQUENT ORTHOPEDIC HIP SURGERY. Special considerations of preoperative TAVR warrant further analysis (Table 2).

General anesthesia vs conscious sedation plus local anesthesia. TAVR used to be performed by default under GA and strict transesophageal echocardiogram guidance.[35-37] Although this strategy has its own advantages, some older patients can experience prolonged postoperative delirium with problematic recovery.[51] The incidence of in-hospital delirium in patients undergoing TAVR was more common with increasing age, GA, non-TF approach, and prolonged procedural time, among others.[52,53] While the HFx itself entails a major stressor and significant contributor to delirium, the presence of uncorrected SAS is associated with a higher use of GA and delirium after HOS.[6] A key element of the TF minimalist TAVR approach is the use of conscious sedation and local anesthesia, which was demonstrated by randomized evidence to be safe in TAVR.[54] By facilitating a rapid recovery, minimalist TAVR can play a key role in allowing a subsequent semiurgent HOS to be safely performed at the same index hospitalization (Table 2).

Vascular access. Major vascular complications (eg, pseudoaneurysms, hematomas) remain an important drawback of TAVR.[55,56] A larger sheath-to-femoral artery ratio represents 1 of their strongest predictors.[56] In the PARTNER 1 trials, patients undergoing TAVR with SAPIEN 23 to 26 mm through a 22-24-F sheath resulted in 11 to 16% major vascular complications at 30 days.[35,36] As expected, this outcome was coupled with a challenging anatomic substrate, characteristic of older patients with frequent calcified peripheral artery disease.[56] A better understanding of their predictors,[57,58] together with the development of lower-profile devices (14-F with newer valve generations), wider use of computed tomography planning, peripheral artery disease treatment (intravascular lithotripsy), and safer percutaneous closure procedures have markedly reduced the risk of vascular complications.[39,48,56,59,60] As TF TAVR is associated with earlier recovery and better outcomes, minimalist TF TAVR has become the approach of choice.[10,11]

The use of transradial access as the secondary access represents another major step forward in the

FIGURE 3 Pathophysiology of Severe Aortic Stenosis in the Setting of Noncardiac Surgery

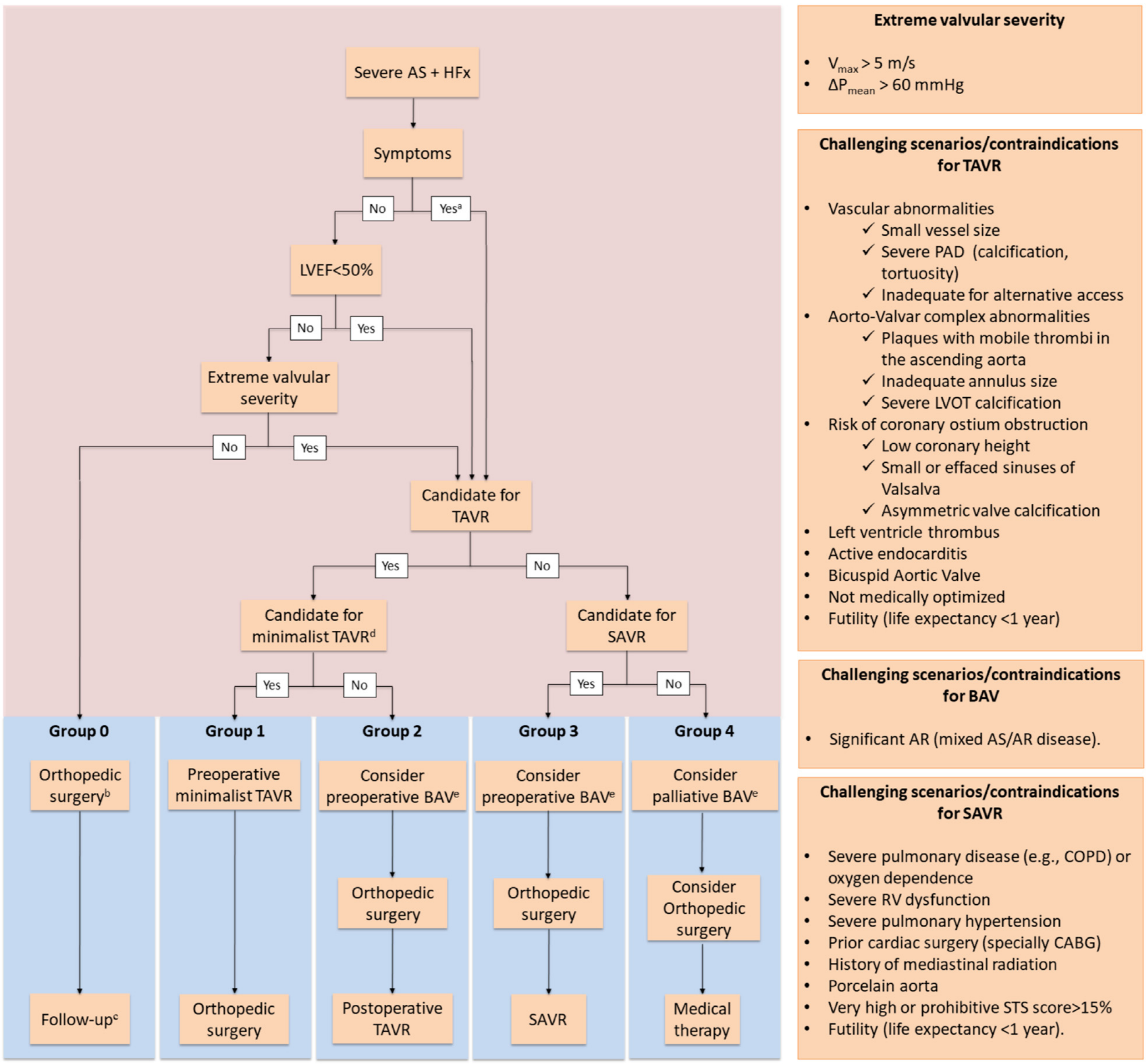


Patients with severe LV outflow obstruction due to SAS are particularly susceptible to sudden hypotension during the anesthetic period, rapid fluid shifts and tachyarrhythmias precipitating a vicious circle of reduced coronary perfusion, myocardial ischemia, impaired ventricular function, and worsening hypotension that may fail to respond to vasopressor treatment. CCP = coronary perfusion pressure; DT = diastolic time; LV = left ventricular; MVO_2 = myocardial oxygen consumption; PVR = peripheral vascular resistance; SAS = severe aortic stenosis.

safety of TAVR.[55] In a retrospective analysis (n = 4,949, age ~81 years), the use of transradial approach as secondary access, as compared to TF secondary access, was associated with a significant reduction in vascular and bleeding complications.[55] Certainly, the incorporation of alternative approaches for both primary and secondary accesses in TAVR could be of benefit for HFx patients, as most of them are women with characteristically smaller iliofemoral arteries and a higher risk of vascular complications. In cases where the TF approach or SAVR are not possible, a non-TF TAVR approach could be considered after a risk-benefit discussion is held, as no evidence to date has proven noninferiority vs TF approach.

Antithrombotic therapy. The use of antithrombotic therapy in TAVR and the periprocedural prophylactic anticoagulation required after hip surgery to prevent the occurrence of venous thromboembolic disease have both direct implications on the "TAVR-HOS combo," adding to the overall bleeding risk of both invasive procedures. Similar to coronary stenting,[61] the use of antithrombotic therapy in TAVR has experienced a significant evolution during the last few years. While concerns about ischemic stroke, valve thrombosis, and long-term durability suggest the need for a stronger antithrombotic regimen, the high bleeding risk of older patients with SAS and the current lack of strong evidence in favor of a more aggressive antithrombotic strategy require caution. Among patients without an indication for anticoagulation, recent RCTs suggested that antiplatelet therapy would be as effective and safer in TAVR than anticoagulation-based regimens. Recently, the incidence of the composite of bleeding and thromboembolic events at 1 year were significantly less frequent with aspirin than with dual antiplatelet therapy administered for 3 months.[62] The use of preoperative minimalist TAVR under procedural heparin (followed by reversal) and single

FIGURE 4 Triage and Management Pathways for Patients With Severe Aortic Stenosis and Hip Fracture



[a]Due to the high prevalence of cognitive dysfunction, comorbidities and low functional capacity, the assessment of symptoms of SAS is not always accurate. [b]Patients undergoing HOS with an uncorrected SAS should have invasive monitoring (eg, A-line, Swan-Ganz catheter). [c]Patients need close follow-up to verify if criteria for AVR are met. [d]A collaborative structure for fast track preoperative minimalist TAVR-HOS protocol (Group 1) needs to be readily available. [e]BAV is generally discouraged in the presence of moderate or severe AR. AR = aortic regurgitation; AS = aortic stenosis; BAV = balloon aortic valvuloplasty; CABG = coronary artery bypass graft; COPD = chronic obstructive pulmonary disease; HFx = hip fracture; HOS = hip orthopedic surgery; LVEF = left ventricular ejection fraction; LVOT = left ventricular outflow tract; PAD = peripheral artery disease; SAS = severe aortic stenosis; SAVR = surgical aortic valve replacement; STS = Society of Thoracic Surgeons; TAVR = transcatheter aortic valve replacement.

antiplatelet therapy can be instrumental by allowing a safer use of spinal anesthesia (with less risk of delirium) for the subsequent HOS.[51] Indeed, spinal anesthesia is usually not preferred in patients with critical SAS due to the risk of both refractory hypotension and epidural/vertebral canal hematomas when under dual antiplatelet therapy or anticoagulation.[11,63]

Infective endocarditis. Despite timely and aggressive management, TAVR-associated prosthetic valve infective endocarditis (IE) is associated with a very high mortality.[64] There is a theoretical concern that

TABLE 2 Role of Preoperative Minimalist TAVR in Patients With SAS in the Setting of HFx

Setting	Clinical/Technical Challenges	Potential Benefits	Potential Risks
Preoperative minimalist TAVR	• Requires femoral (primary) access in the contralateral groin (or other alternative vascular accesses if not suitable) • Small iliofemoral arteries (ie, women) and PAD • Challenging aortic anatomy for TAVR (eg, aortic tortuosity, effaced sinuses of Valsalva, low coronary height). • Requires a dedicated specialize platform for expedite TAVR	• Consistent hemodynamic improvement • Immediate cardiovascular risk reduction for surgery • Interventional resource for valve-in-valve if needed	• Potential increase in TTS/LOS • Vascular/access site complications • Coronary obstruction and annular rupture • Stroke • Conduction disturbances requiring transient transvenous pacer or definitive PPM implantation • ↑Risk of DVT while not on prophylactic AC • Use of antithrombotic therapy may induce/ worsen eventual HFx-related bleeding. • Other bleeding complications.
Hip orthopedic surgery	• Labile hemodynamics post-TAVR (ie, uncontrolled hypertension or "suicide LV" after sudden afterload reduction)	• Spinal anesthesia can be safely used • ↓Myocardial infarction • ↓Heart failure • ↓Postoperative delirium • ↓Short-term mortality	• Patients may not recover quickly (ie, <4 d) • Bradyarrhythmia and high degree AV block. • Bleeding complications (access, HFx related, acquired vWF deficiency)
Postoperative/ long-term	• Physical rehabilitation[a]	• Definitive treatment of SAS • ↓Symptoms • ↑Discharge home rate/SAR • ↑Physical rehabilitation and independence • ↑Quality of life • ↓Long-term mortality • Cost-effective strategy	• Risk of endocarditis • Risk of PPM pocket/lead infection if pre-operative PPM implanted. • ↑Mortality (associated with HFx) and disability if surgical repair is delayed • ↑Overall medical expenses on index hospitalization

[a]Although the correction of the SAS by preoperative TAVR may provide an adequate "substrate" for physical rehabilitation, ie, by resolving or preventing the occurrence of symptoms related with the SAS resulting in impaired functional capacity, both the contralateral femoral access and the ipsilateral groin surgery can both induce bilateral groin discomfort that can ultimately limit immediate physical rehabilitation.

CAD = coronary artery disease; DVT = deep venous thrombosis: HFx = hip fracture; LOS = length of stay; LV = left ventricular; PAD = peripheral artery disease; PPM = permanent pacemaker; SAR = subacute rehabilitation; SAS = severe aortic stenosis; TAVR = transcatheter aortic valve replacement; TTS = time to surgery; vWF = von Willebrand factor.

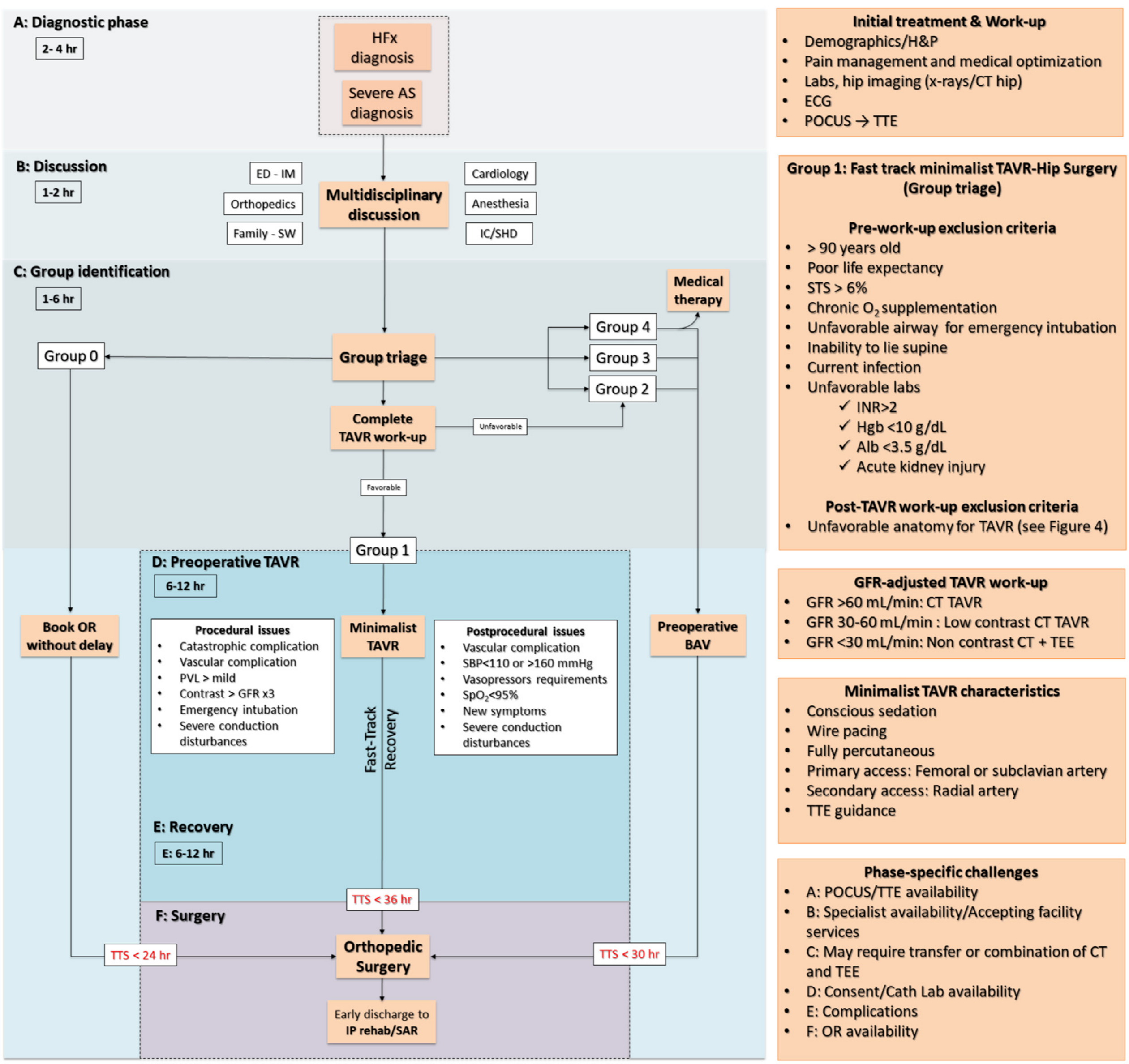
preoperative TAVR may carry an increased risk of IE as the subsequent NCS might induce bacteremia and seeding of the newly implanted bioprosthetic valve.[11] While the risk of IE of TAVR is similar[65,66] or even lower[67] than SAVR at 5-year follow-up (~1%), it is likely that performing TAVR before a hip surgical repair of a closed traumatic fracture may not carry a significant IE risk. In fact, the insertion of a new pacemaker during the index TAVR admission was not associated with a subsequent increased risk of IE at follow-up.[68] The risk of IE could be more relevant in NCS associated with significant bacteremia (eg, dental, urgent digestive surgery, or septic orthopedic surgery) and not after femoral neck fracture surgery, which has a very low risk of bacteriemia, even in patients with postoperative fever.[69]

The need for a dedicated platform and clinical pathway for expediting hip fracture treatment in patients with severe aortic stenosis. Patients with symptomatic SAS admitted to the hospital due to HFx usually spend multiple days undergoing work-ups, consultations (eg, surgery, anesthesiology, heart team meetings), and ultimately are considered for preoperative BAV.[22] The time spent before surgery during the admission or the fact that they spend several days in bed before surgery promotes deconditioning and several complications (skin lesions/ ulcers, delirium) leading to an overall increased mortality risk.[8,12] Geriatric HFx patients with at least 1 comorbidity such as SAS will experience a 2.5-fold risk of 30-day mortality if HOS is delayed >4 days.[14] Preoperative minimalist TAVR could represent the state-of-the-art treatment for these patients. However, a dedicated platform with an on-site computer tomography scanning facility and a cath lab need to be readily available (**Central Illustration**).[32] Based on prior studies,[48,70] we propose a protocol for all comers aimed to decrease TTS by analyzing potential institution-specific barriers (**Figure 5**). A special focus on proceeding with TAVR only in selected patients with AS/AR mixed disease could be considered in institutions with higher post-TAVR morbimortality, where preoperative BAV would be discouraged.

EFFECT OF SEVERE AORTIC STENOSIS ON FUNCTIONAL RECOVERY AFTER HIP FRACTURE SURGERY

Older patients recovering from HFx are at high risk for muscle weakness, immobility, recurrent fractures, and dependence that last for months after surgery.[16,19] About 50% of patients after HFx do not recover their prefracture level of function; up to 50% of patients will never be able to ambulate without

FIGURE 5 Proposed Time-Sensitive Protocol for Patients With Hip Fracture and Severe Aortic Stenosis

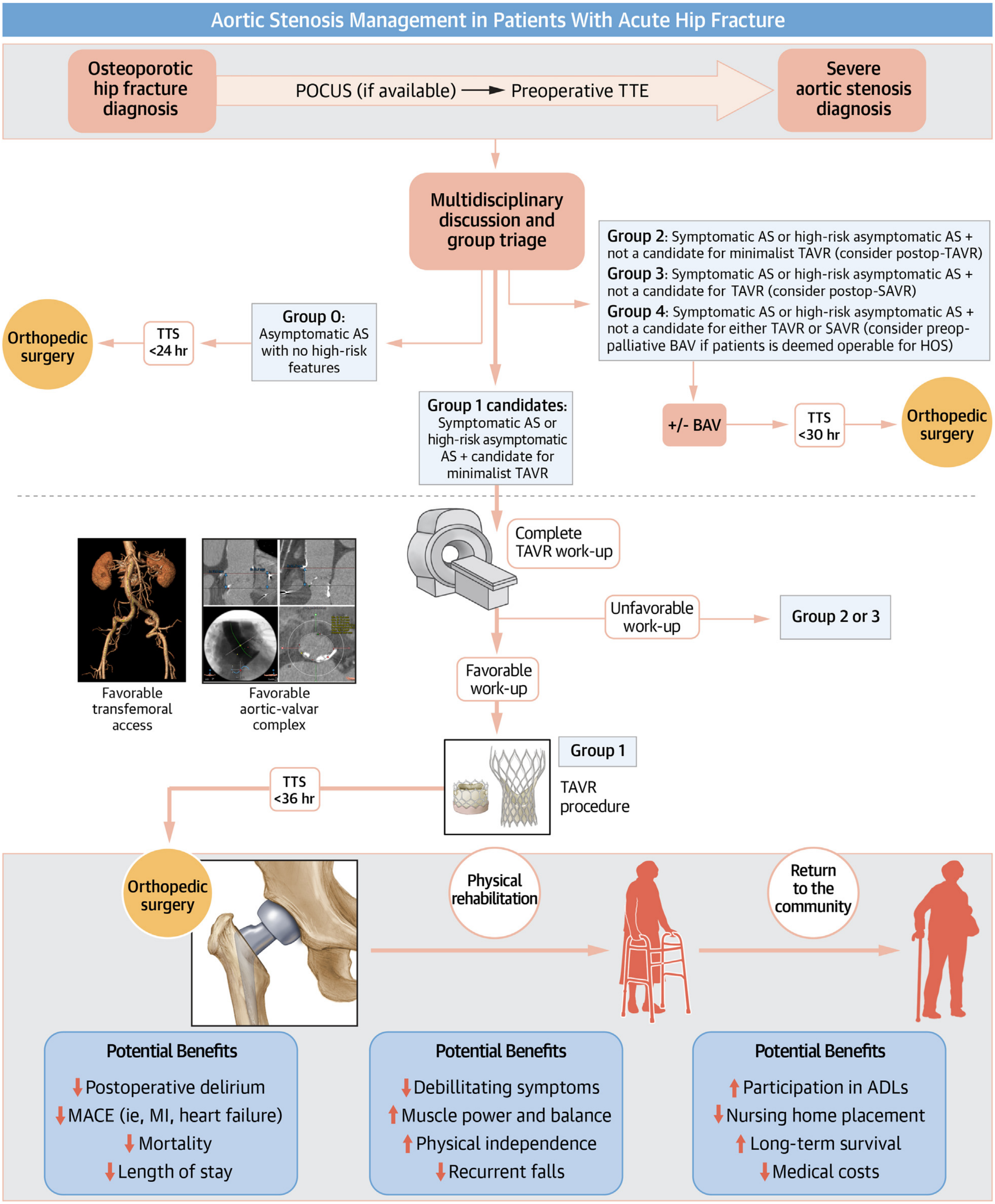


Depending on resource availability, patients may need to be transferred to complete TAVR work-up at the TAVR-capable facility. We adapted[48,70] and identified pre-, intra- and post-procedural issues that may exclude a patient from either entering a fast track minimalist TAVR-HOS protocol or completing it on time. These issues can be treated and favor an expedited surgery (eg, active fixation TVP for new conduction disturbances). BAV = balloon aortic valvuloplasty; CT = computed tomography; ED = emergency department; GFR = glomerular filtration rate; HOS = hip orthopedic surgery; IC = interventional cardiologist; IM = internal medicine; SHD = structural heart disease specialist; STS = Society of Thoracic Surgeons; SW = social worker; TAVR = transcatheter aortic valve replacement; TEE = transesophageal echocardiogram; TTE = transthoracic echocardiogram; TVP = transvenous pacing.

assistance, and 25% will require long-term care.[71] However, a large body of evidence has indicated that physical rehabilitation programs (ie, progressive resistance training) implemented soon and for an extended period of time after the HFx surgery (>6 months) lead to a substantial improvement in physical functioning, balance, muscle power, performance of basic activities of the daily living (ADLs), and possibly survival.[72]

Certain factors, such as cardiovascular comorbidities, GA, prolonged TTS, or longer operative time may hamper the chance of patients to receive immediate physical therapy following HOS.[73,74] The presence of SAS not only increases the risk of all these factors

CENTRAL ILLUSTRATION Severe Aortic Stenosis Management Options in the Setting of Acute Hip Fracture



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A dedicated time-sensitive protocol and a TAVR collaborative multidisciplinary structure is key for the management of these patients. This structure needs to be mounted in advance to rapidly detect inclusion/exclusion criteria, so the risks of delaying HOS can be minimized, and the potential benefits of the intervention enhanced. ADLs = activities of the daily living; AS = aortic stenosis; BAV = balloon aortic valvuloplasty; HOS = hip orthopedic surgery; MACE = major adverse cardiac events; MI = myocardial infarction; SAVR = surgical aortic valve replacement; TAVR = transcatheter aortic valve replacement; TTE = transthoracic echocardiogram; TTS = time to surgery.

individually,[6,8,75] but the presence of symptoms related to the uncorrected SAS will also limit the participation in a postoperative physical program. Moreover, progressive physical training or exercise loading is discouraged in patients with symptomatic SAS due to risk of subsequent falling, syncope, and sudden cardiac death.[10] Anemia is extremely common in patients with SAS (~40%)[76] and a significant contributor of fatigue, recurrent falls, and increased mortality in patients with uncorrected SAS.[76] The acquired von Willebrand factor deficiency seen in Heyde's syndrome is postulated to reverse following AVR, as the shear stress is minimized. Anemia and HFx repair can both contribute to a high cardiac output state, the latter by inducing inflammation and pain. This can maximize the detrimental effects of SAS on hemodynamics with negative impact on rehabilitation. Considering the transient hemodynamic results of BAV, pushing toward an early "minimalist TAVR-HOS combo strategy" in appropriate candidates (Group 1) or, in defect, an early postoperative TAVR (Group 2) may increase the chances of physical rehabilitation by allowing safer participation in physical therapy programs.[77] If an early AVR is not feasible, patients should undergo a close clinical and echocardiographic follow-up after BAV-HOS to determine the need for definitive SAS correction.

CONCLUSIONS

The adverse hemodynamic effects of anesthesia/surgery may be poorly tolerated in patients with SAS. Preoperative BAV is oftentimes performed to reduce the cardiovascular risk before HOS, although its unpredictable hemodynamic effect and risk of complications make this approach unattractive. TAVR represents the best strategy to achieve a rapid and consistent hemodynamic improvement, with a potential role in decreasing morbimortality during and after HOS. Considering the accelerating procedural refinements and improved outcomes, minimalist TAVR may become the standard of care for carefully selected patients with SAS who require urgent NCS, such as HFx. We proposed a time-sensitive clinical pathway to triage all comers that allows reductions in time to hip surgery, aimed to improve clinical outcomes and quality metrics.

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