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ORIGINAL RESEARCH

STRUCTURAL

Hypoattenuated Leaflet Thickening and Reduced Leaflet Motion After Transcatheter Tricuspid Valve Replacement

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ABSTRACT

BACKGROUND Reduced leaflet motion (RLM) induced by hypoattenuated leaflet thickening (HALT) is a known complication after bioprosthetic aortic valve replacement, associated with adverse outcomes. A similar phenomenon has been observed after transcatheter tricuspid valve replacement (TTVR) but remains unclassified.

OBJECTIVES The aim of this study was to introduce a grading system for valve thrombosis and dysfunction after TTVR and describe its clinical and echocardiographic associations.

METHODS Thirty-day follow-up computed tomographic (CT) scans from all patients undergoing orthotopic TTVR were analyzed. Grading systems for RLM_{CT} severity (none, mild to moderate, and severe) and HALT (0°-4°) were developed. These were correlated with clinical and echocardiographic parameters at 30 days and up to 3 years.

RESULTS Among 53 patients, 45 had 30-day CT data. Moderate to severe HALT was present in 12 cases (27%). RLM_{CT} severity was none in 15 (33%), mild to moderate in 21 (74%), and severe in 9 (20%). HALT was correlated with RLM_{CT} severity ($P < 0.001$), and both were associated with increased transvalvular gradient ($P = 0.032$ and $P < 0.0001$) and reduced NYHA functional class improvement at 30 days ($P = 0.002$ and $P = 0.003$). RLM_{CT} was correlated with echocardiographic RLM ($P < 0.0001$), but RLM_{echo} was less sensitive, detecting just 6 of 9 severe cases of RLM. Similarly, severe HALT was detected on echocardiography in just 3 of 7 cases. There was no association between HALT or RLM_{CT} and anticoagulation strategy.

CONCLUSIONS HALT and RLM_{CT} are common after TTVR and are associated with elevated gradients and reduced symptomatic alleviation. Transthoracic echocardiography is insensitive for detecting HALT and RLM, and routine CT imaging may aid early diagnosis, but the long-term impact of low-grade HALT and RLM_{CT} remains unclear.

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ABBREVIATIONS AND ACRONYMS

CRP = C-reactive protein

CT = computed tomographic

DOAC = direct oral anticoagulant agent

HALT = hypoattenuated leaflet thickening

INR = international normalized ratio

RLM = reduced leaflet motion

RVEF = right ventricular ejection fraction

RVFAC = right ventricular fractional area change

TAPSE = tricuspid annular plane systolic excursion

TAVR = transcatheter aortic valve replacement

TTE = transthoracic echocardiography

TTVR = transcatheter tricuspid valve replacement

VKA = vitamin K antagonist

Reduced leaflet motion (RLM) and hypoattenuated leaflet thickening (HALT) are well-recognized phenomena following both transcatheter and surgical bioprosthetic aortic valve replacement, with the reported prevalence of HALT ranging from 12.3% to 38.1%.[1-6] However, HALT and RLM involving bioprosthetic tricuspid valves have thus far been limited to isolated case reports and series.[7] Surgical studies have, however, shown higher rates of thrombosis on the tricuspid, compared with left-sided valves, likely because of lower pressure gradients and flow conditions as well as greater surface areas.[8]

With the advent and commercial availability of dedicated transcatheter tricuspid valve replacement (TTVR),[9] and given the potential prognostic implications, consideration of systematic evaluation of leaflet thrombosis and early impairment of leaflet motion in this setting is warranted. In transcatheter aortic valve replacement (TAVR), HALT is classified semiquantitatively using 4-dimensional computed tomographic (CT) imaging, on the basis of the extent of hypoattenuation from the leaflet base in quartiles.[5] CT RLM (RLM_{CT}) is defined by the degree of opening in systole, described as none, partially restricted, and severe or immobile.[5]

In this study, we propose a novel, adjusted classification system for HALT and RLM_{CT} in TTVR and report the prevalence of HALT and RLM_{CT} in a consecutive cohort in which CT was performed routinely after tricuspid valve replacement. We report the association of RLM_{CT} and HALT with anticoagulation strategy, including changes in anticoagulation strategy, as well as the diagnostic value of CT compared with echocardiography to detect clinically relevant RLM_{CT} and HALT. This is correlated with clinical and echocardiographic outcomes in this initial patient cohort.

METHODS

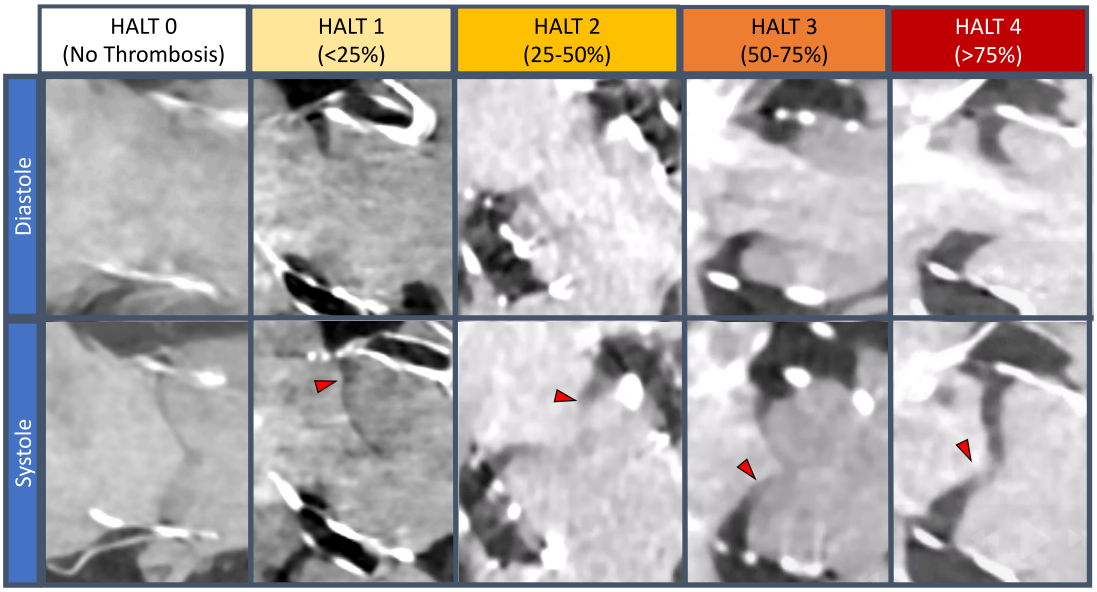
STUDY COHORT AND VARIABLES. Data were collected for all patients undergoing orthotopic TTVR between December 2019 and April 2025 at a high-volume heart valve center. The study protocol was approved by the Institutional Review Board, and all participants provided informed consent prior to inclusion. Baseline right heart catheterization, echocardiographic, clinical, and laboratory data were recorded, including NYHA functional class and anticoagulation strategy.

Echocardiography was performed immediately after valve implantation, as well as at 30 days, 6 months, 12 months, and then annually, and included assessments of right ventricular size and function and tricuspid valve gradient. Patients were reviewed clinically at each of these time points, including for functional status (assessed by NYHA functional class) and changes to anticoagulation therapy. Patients were scheduled for postprocedural 4-dimensional CT at 30 days and were included in this analysis if there was at least 1 4-dimensional cardiac CT examination after TTVR. When significant HALT was detected on the initial CT scan, or there was clinical concern for valve thrombosis or dysfunction, subsequent CT scans were performed, including at 1-year follow-up. These results are reported, in conjunction with changes in anticoagulation strategy.

CT AND ECHOCARDIOGRAPHIC ANALYSIS. CT scans were acquired using a third-generation dual-source SOMATOM Force CT scanner (Siemens Healthineers) with retrospective electrocardiographic gating. Contrast was administered intravenously (typically 60-80 mL iodinated contrast) using bolus tracking in the ascending aorta. Image reconstruction was performed over the entire cardiac cycle (in 5% or 10% increments of the R-R interval or 50-ms increments after the R wave) with a temporal resolution of about 66 ms. Images were reconstructed with a slice thickness of 1.0 mm, matrix size of 512 × 512, and iterative reconstruction algorithms. Overall imaging quality was generally good, allowing adequate assessment of HALT and RLM.

CT images of the valve prostheses were independently analyzed by 2 investigators blinded to concurrent echocardiographic findings and categorized according to the severity of HALT (interobserver correlation coefficient = 0.91; 95% CI: 0.84-0.95), as well as the presence or absence of RLM_{CT} (intraclass correlation coefficient = 0.88; 95% CI: 0.74-0.96) (Figure 1). On the basis of the experience in TAVR,[5] the severity of HALT was semiqualitatively classified according to the extent of leaflet thrombosis, from the leaflet base, as no apparent thrombosis (grade 0), thrombosis <25% of the leaflet length (grade 1), thrombosis 26% to 50% of the leaflet length (grade 2), thrombosis 51% to 75% of the leaflet length (grade 3), and thrombosis >75% (grade 4). RLM_{CT} was classified as grade A, B, or C according to the absence of RLM_{CT}, mild or

FIGURE 1 **Classification of HALT Severity**



The severity of hypoattenuated leaflet thickening (HALT) was semiqualitatively classified according to the extent of leaflet thrombosis, from the leaflet base, as no apparent thrombosis (grade 0), thrombosis <25% of the leaflet length (grade 1), thrombosis 26% to 50% of the leaflet length (grade 2), thrombosis 51% to 75% of the leaflet length (grade 3) and thrombosis >75% (grade 4). Severity was based on the appearance of the most severely affected leaflet.

moderate RLM_{CT}, or leaflet immobility in diastole, respectively.

When asymmetry was present, grading was completed on the basis of the most severe degree of HALT or RLM_{CT} on any given leaflet. The CT appearances of the valve were compared with concurrent echocardiographic images for HALT and RLM_{echo}, which was scored as normal, reduced, or immobile by 2 independent investigators, blinded to CT findings. Mean echocardiographic transvalvular gradient was also reported at each follow-up time point. Right ventricular function was also assessed, using 3-dimensional echocardiography, right ventricular fractional area change (RVFAC), and tricuspid annular plane systolic excursion (TAPSE).

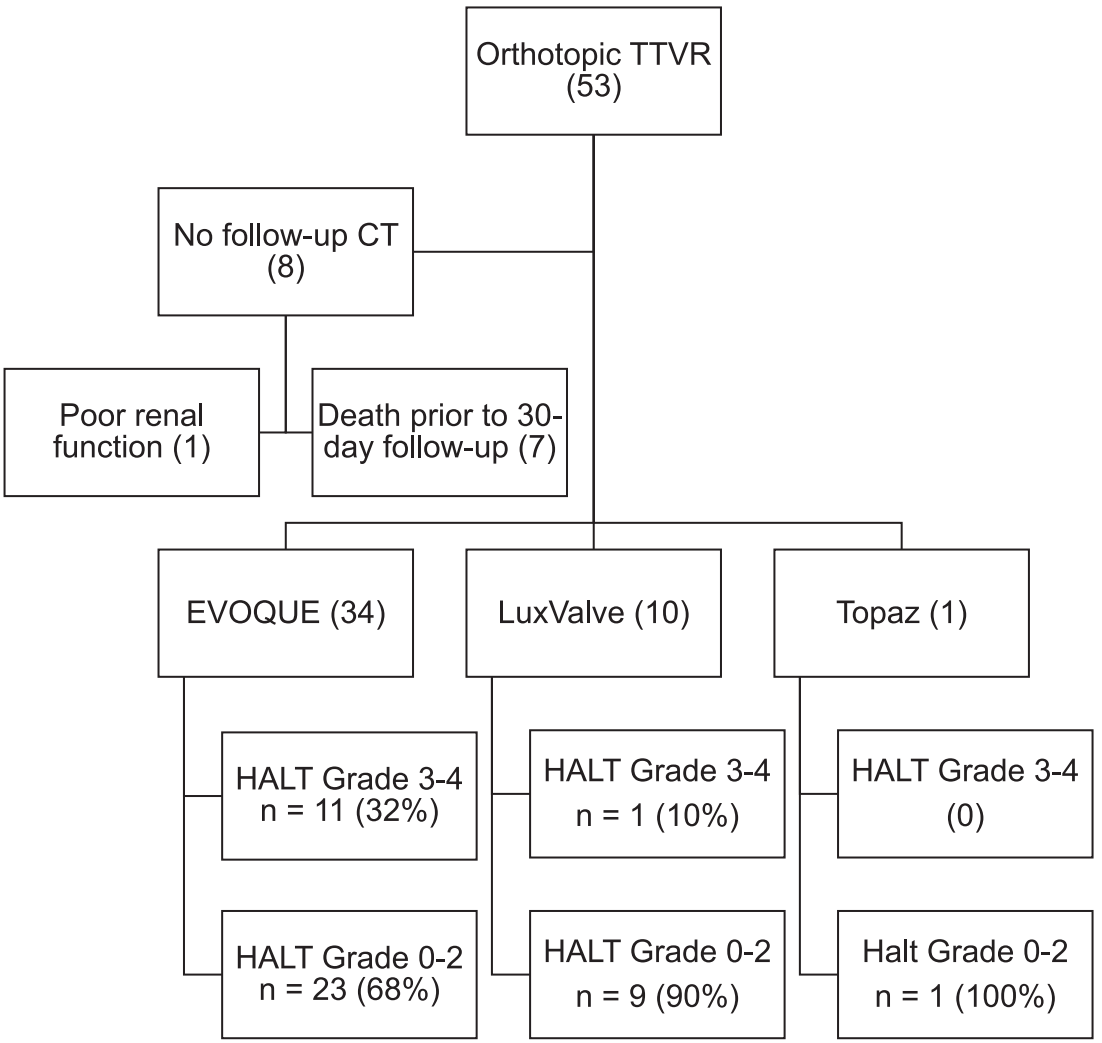
STATISTICAL ANALYSIS. Baseline characteristics are expressed as mean ± SD and percentages for continuous and categorical variables, respectively. Analyses were completed to establish any significant correlation between HALT and RLM_{CT} or RLM_{echo} and tricuspid valve gradient, mortality, anticoagulation regime (direct oral anticoagulant agent [DOAC] or vitamin K antagonist [VKA]), and improvement in NYHA functional class by at least 1 grade, as a binary outcome. Spearman rank correlation was used to examine correlations between ordinal variables.

Associations between ordinal variables (HALT and RLM grades) and continuous variables were assessed using the Jonckheere-Terpstra test. Because HALT and RLM grades involve ties by definition, *P* values were obtained from 10,000-permutation resampling to provide robust estimates rather than relying on the normal approximation. Analyses between HALT grade and RLM_{CT} or RLM_{echo} and binary outcomes were completed using a Cochran-Armitage test. Continuous variables (eg, between group differences in renal function) were compared using unpaired Student's *t* tests. A significance level of 0.05 was used for all analyses. Analysis was completed using RStudio version 4.4.1 (Posit).

RESULTS

Fifty-three patients underwent orthotopic TTVR between December 2019 and May 2025. This included 38 EVOQUE (Edwards Lifesciences), 11 LuX-Valve Plus (Jenscare Scientific), 2 Topaz (TRiCares), and 2 VDyne valves (Supplemental Table 1). Of these, postprocedural CT scans were available for analysis in 45 patients (**Figure 2**). Among the 8 patients without follow-up CT scans, 7 died before 30-day follow-up and 1 (LuX-Valve Plus) did not undergo a

FIGURE 2 TTVR Case Exclusions, Valve Type, and HALT Severity



CT = computed tomography; HALT = hypoattenuated leaflet thickening; TTVR = transcatheter tricuspid valve replacement.

CT scan during follow-up, because of severely impaired renal function. Of these, 2 died of hemodynamic complications after surgical conversion. Another died in the weeks following the procedure of an ischemic stroke complicated by hemorrhagic transformation, 3 of non-procedure-related infections, and 1 of complications of malignancy. The early mortality rate (13%) reflects both the multimorbidity of this population, as well as the advanced stage of valvular heart disease at the time of referral for intervention.

BASELINE CHARACTERISTICS. The baseline demographic and clinical characteristics are presented in Table 1. Patients had a median age of 80.0 ± 6.3years, 33 (73%) were women, and the median TRISCORE was 5 (range: 4-9). Fifteen patients (33%) had massive tricuspid regurgitation, and 30 (67%) had torrential tricuspid regurgitation. The majority of the cohort (41 patients [91%]) had pre-existing atrial fibrillation, and 42 patients (93%) were taking anticoagulation prior to the procedure. The majority of patients had diminished renal function (mean estimated glomerular filtration rate 44 ± 16 mL/min/1.73 m^2), and 8 (18%) had estimated glomerular filtration rates <30 mL/min/1.73 m^2. Similarly, liver function was not significantly impaired in the majority of the cohort, and only 9 (20%) had elevated bilirubin (>1.2 mg/dL) prior to the procedure. The average baseline C-reactive protein (CRP)

TABLE 1 Baseline Demographic and Clinical Characteristics (N = 45)

Age, y	80.0 ± 6.3
Female	33 (73)
BMI, kg/m^2	23.0 ± 4.5
Valve type	
EVOQUE	34 (76)
LuX-Valve	10 (22)
Topaz	1 (2)
Baseline NYHA functional class	
III	38 (84)
IV	7 (16)
TRISCORE	5; 4-9
STS (tricuspid valve) score, %	8.9 ± 6.2
LVEF <50%	9 (20)
RVEF <45%	12 (27)
Massive TR	15 (33)
Torrential TR	30 (67)
RAP, mm Hg	13 ± 5
mPAP, mm Hg	23 ± 8
PCWP, mm Hg	15 ± 6
PVR, WU	2.0 ± 1.2
Previous CTS	8 (18)
Other valve interventions	
TAVR	4 (9)
M-TEER	4 (9)
T-TEER	4 (9)
Atrial fibrillation	41 (91)
PPM	15 (33)
ICD	3 (7)
Hematocrit, %	37.9 ± 5.7
Platelets, ×10^9/L	193 ± 71
eGFR <30 mL/min/1.73 m^2	8 (18)
eGFR, mL/min/1.73 m^2	45 ± 17
Elevated bilirubin (>1.2 mg/dL)	9 (20)
AST, U/L	35 ± 14
ALT, U/L	25 ± 13
Bilirubin, mg/dL	1.0 ± 0.5
Albumin, g/dL	4.1 ± 0.6
BNP, ng/L	2968 ± 2520
CRP, mg/L	0.6 ± 0.4
APTT, s	30 ± 8.2
INR	1.3 ± 0.3
Anticoagulation	
None	3 (7)
DOAC	36 (80)
VKA	6 (13)
Antiplatelet agents	
Aspirin	2 (4)
Clopidogrel	5 (11)
Baseline furosemide dose,[a] mg	113 ± 103

Values are mean ± SD or n (%). [a]Loop diuretic doses normalized to furosemide, torsemide multiplied by 4.

ALT = alanine aminotransferase; APTT = activated partial thromboplastin time; AST = aspartate aminotransferase; BMI = body mass index; BNP = brain natriuretic peptide; CRP = C-reactive protein; CTS = cardiothoracic surgery; DOAC = direct oral anticoagulant agent; eGFR = estimated glomerular filtration rate; ICD = implantable cardioverter-defibrillator; INR = international normalized ratio; LVEF = left ventricular ejection fraction; mPAP = mean pulmonary arterial pressure; M-TEER = mitral transcatheter edge-to-edge repair; PCWP = pulmonary capillary wedge pressure; PPM = permanent pacemaker; PVR = pulmonary vascular resistance; RAP = right atrial pressure; RVEF = right ventricular ejection fraction; STS = Society of Thoracic Surgeons; TAVR = transcatheter aortic valve replacement; T-TEER = tricuspid transcatheter edge-to-edge repair; TR = tricuspid regurgitation; VKA = vitamin K antagonist; WU = Wood units.

Continued in the next column

concentration was not significantly elevated (0.6 ± 0.4 mg/L).

All patients underwent preprocedural right heart catheterization. The average mean pulmonary arterial systolic pressure was 23 ± 8 mm Hg, and mean pulmonary vascular resistance was 2.0 ± 1.2 Wood units. On baseline echocardiography, the left ventricular ejection fraction was normal (≥55%) in 36 patients (80%) (mean 56% ± 8.5%). Twelve patients (27%) had right ventricular dysfunction at baseline, defined by 3-dimensional right ventricular ejection fraction (RVEF) < 45%. The average RVEF was 47.0% ± 6.5% at baseline, mean RVFAC was 39.1% ± 5.5% and mean TAPSE was 15.0 ± 4.5 mm (**Table 2**; Supplemental Table 2).

CT RESULTS. The median time from procedure to first follow-up CT examination was 43 days (Q1-Q3: 37-55 days). Eighteen patients underwent repeat CT studies (median 370 days; Q1-Q3: 167-677 days), either for follow-up of significant HALT on the initial CT study (n = 10) or because of a change in clinical status or echocardiographic findings raising concern for valve dysfunction and possible HALT (n = 8). Of these, 4 patients underwent a third follow-up CT study (median 782 days; Q1-Q3: 575-962 days), 3 of whom showed HALT grade 2 and 1 grade 1 HALT.

Seven of the initial CT scans (16%) demonstrated severe (grade 4) HALT. Grade 3 HALT was present in 5 cases (11%), grade 2 in 3 cases (7%), and grade 1 in 17 cases (38%), and 13 (29%) had no evidence of HALT. Accordingly, grade 3 or 4 HALT was diagnosed in 12 patients (27%). Patients with grade 1 or 2 HALT on the initial follow-up CT examination did not undergo additional CT imaging unless there was clinical or echocardiographic suspicion of progression, which did not occur in this cohort. Consequently, it cannot be excluded that some patients may have developed subclinical HALT beyond 30 days.

Nine patients (20%) had severe RLM_{CT}, 21 patients (47%) had mild to moderate RLM_{CT}, and 15 patients (33%) had normal leaflet motion. All 7 patients with

TABLE 2 Summary of Clinical, Computed Tomographic, and Echocardiographic Results

	P Value
HALT grade and RLM_{CT}	<0.001
HALT grade and TV gradient	0.111
RLM_{CT} and TV gradient	0.015
Clinical endpoints	
HALT and mortality	0.267
RLM_{CT} and mortality	0.330
HALT and NYHA functional class improvement	0.002
RLM_{CT} and NYHA functional class improvement	0.003
RLM_{echo} and NYHA functional class improvement	0.024
TV gradient and NYHA functional class improvement	<0.001
HALT and loop diuretic dose reduction	0.071
RLM_{CT} and loop diuretic dose reduction	0.205
Echocardiographic endpoints	
RVFAC and HALT	0.611
RVFAC and RLM_{CT}	0.979
HALT and RLM_{echo}	0.001
RLM_{CT} and RLM_{echo}	<0.001
Anticoagulation	
HALT grade and DOAC vs VKA	0.276
RLM_{CT} and DOAC vs VKA	0.052
HALT and antiplatelet therapy	0.371
30-d TV gradient analyses	
HALT and 30-d TV gradient	0.032
RLM_{CT} and 30-d TV gradient	<0.001
RLM_{echo} and 30-d TV gradient	0.068

CT = computed tomography; RLM = reduced leaflet motion; RVFAC = right ventricular fractional area change; TV = tricuspid valve; other abbreviations as in Table 1.

severe HALT had severe RLM_{CT}. In 2 patients with severe HALT, there was asymmetrical leaflet thrombosis, in which HALT severity was graded from the most severely affected leaflet, while the remaining leaflets had only grade 1 or 2 HALT. HALT severity was correlated with RLM_{CT} ($P < 0.0001$).

There was no significant association between HALT grade and echocardiographic tricuspid valve gradient at discharge ($P = 0.111$). However, RLM_{CT} was significantly associated with valve gradient ($P = 0.015$), and at 30-day follow-up, there was a significant association between valve gradient and both HALT and RLM_{CT} ($P = 0.032$ and $P < 0.0001$, respectively) but not RLM_{echo} ($P = 0.068$). These results are summarized in Table 2.

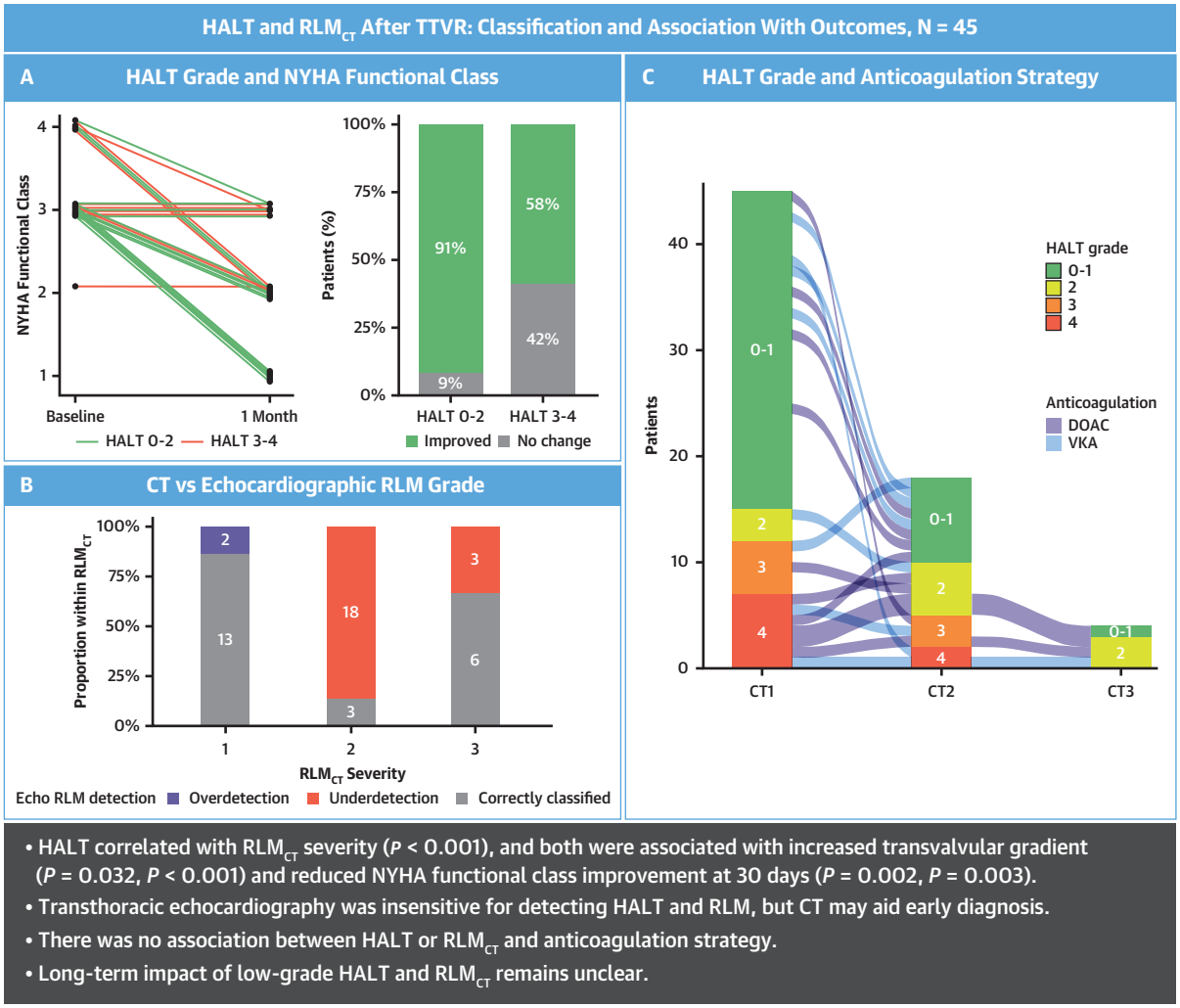
CLINICAL OUTCOMES. Five patients died subsequent to the first CT scan, of a combination of chronic cardiac failure, renal impairment, and malignancy (median 187 days; range: 165-371 days). There was no significant association between HALT or RLM_{CT} and mortality ($P = 0.267$ and $P = 0.330$, respectively). In terms of bleeding events, there were 3 minor and no major periprocedural bleeding events, with no additional events to 30 days or 12 months.

At baseline, NYHA functional class was III in 38 patients (84%) and IV in the other 7 (16%). At 30-day follow-up, NYHA functional class was <III in 36 patients (80%) and III in 9 (20%). Patients with more severe HALT were less likely to see improvement in 30-day NYHA functional class than patients without HALT ($P = 0.002$). Similarly, patients with RLM_{CT} were less likely to see improvement in NYHA functional class ($P = 0.003$), and this was also related to higher 30-day mean valve gradient ($P < 0.001$) (Central Illustration). RLM_{echo} was also related to less clinical improvement defined by NYHA functional class ($P = 0.024$). There was no significant association between the change in postprocedural diuretic dose and either HALT grade ($P = 0.071$) or RLM_{CT} ($P = 0.205$). Postprocedure, CRP was significantly elevated compared with baseline (3.6 ± 3.3 mg/L; $P < 0.0001$), but patients with grade 3 or 4 HALT were not more likely to have elevated CRP (2.9 ± 2.0 mg/L; $P = 0.79$). Similarly, renal function was not significantly more impaired in this cohort (46 ± 17 mL/min/1.73 m^2; $P = 0.67$).

ECHOCARDIOGRAPHIC RESULTS. Forty-two of 45 patients underwent transthoracic echocardiography (TTE) within 3 days of the initial CT scan. One patient was referred directly for transesophageal echocardiography, and 2 patients underwent TTE within 1 month of follow-up CT imaging. Right ventricular function, by RVEF, RVFAC, and TAPSE, declined immediately after the intervention and subsequently improved at follow-up (Table 3). There was no correlation between RV function (RVFAC) and HALT or RLM_{CT} ($P = 0.611$ and $P = 0.979$, respectively). The mean tricuspid valve gradient was not clinically significantly elevated immediately postprocedure (2.0 ± 0.8 mm Hg), or at 30 days (3.0 ± 1.2 mm Hg) (Table 3). Thirty-six patients (80%) presented with normal leaflet motion, and 9 (20%) demonstrated mild to moderate RLM_{echo}. There was a significant association between echocardiographic HALT grade and RLM_{echo} ($P = 0.001$) and RLM_{CT} ($P < 0.001$). However, echocardiography detected HALT in just 3 of the 7 patients with grade 4 HALT, and severe RLM_{echo} was detected in 6 of the 9 patients with severe RLM_{CT} (Central Illustration).

ANTICOAGULATION AND SUBSEQUENT CT SCANS. Post-TTVR, 3 of the 12 patients who developed grade 3 or 4 HALT were prescribed VKAs at discharge, and 9 were prescribed DOACs. There was no association between HALT or RLM_{CT} and postprocedural anticoagulation strategy (DOAC or VKA) ($P = 0.276$ and $P = 0.052$, respectively). Postprocedural antiplatelet medication had no influence on HALT or leaflet

CENTRAL ILLUSTRATION **Assessing Leaflet Thickening and Reduced Motion After TTVR**



- HALT correlated with RLM$_{CT}$ severity ($P < 0.001$), and both were associated with increased transvalvular gradient ($P = 0.032$, $P < 0.001$) and reduced NYHA functional class improvement at 30 days ($P = 0.002$, $P = 0.003$).
- Transthoracic echocardiography was insensitive for detecting HALT and RLM, but CT may aid early diagnosis.
- There was no association between HALT or RLM$_{CT}$ and anticoagulation strategy.
- Long-term impact of low-grade HALT and RLM$_{CT}$ remains unclear.

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(A) Change in NYHA functional class on the basis of hypoattenuated leaflet thickening (HALT) and reduced leaflet motion on computed tomography (RLM$_{CT}$) before transcatheter tricuspid valve replacement (TTVR) and at 30-day follow-up. (B) RLM$_{CT}$ compared with RLM$_{echo}$ at 30-day follow-up. (C) Alluvial plot depicting the evolution of HALT grade among the 12 patients who presented with grade 3 or 4 HALT on the initial computed tomographic (CT) scan. The plot illustrates how HALT severity changed on subsequent CT examinations, alongside the corresponding anticoagulation regimen at each time point. DOAC = direct oral anticoagulant agent; VKA = vitamin K antagonist.

restriction ($P = 0.371$ and $P = 0.165$, respectively). Preprocedurally, just 3 patients were not anticoagulated, with all others anticoagulated with either a DOAC (n = 36 [80%]) or a VKA (n = 6 [13%]). Postprocedure, patients were anticoagulated with either a DOAC (n = 33 [73%]), most commonly apixaban (n = 25 [76%]), or a VKA (n = 11 [24%]). Just 1 patient was not immediately anticoagulated, because of a history of myelodysplastic syndrome, and was maintained on aspirin until 1 month after the procedure, at which time a DOAC was commenced. This patient had no HALT and no RLM$_{CT}$ at 30-day follow-up. Including this patient, 11 patients (24%) received postoperative antiplatelet agents, 7 (16%) aspirin, and 4 (9%) clopidogrel. In 1 patient, the indication was percutaneous coronary intervention 3 months prior to TTVR. For the other 10 patients, the antiplatelet medication was commenced post-procedure, in conjunction with anticoagulation for HALT prophylaxis.

TABLE 3 Echocardiogram Results to 12 Months

	Pre-TTVR (n = 45)	Post-TTVR (n = 45)	30 Days (n = 45)	6 Months (n = 27)	12 Months (n = 25)
RVEF, %	47.0 ± 7	35.0 ± 6.1	38 ± 7	40 ± 6	42 ± 6
TAPSE, mm	15.5 ± 4.5	9.0 ± 4.0	11.0 ± 4.2	8.6 ± 3.6	9.9 ± 3.5
RVFAC, %	39.1 ± 5.5	27.0 ± 7.5	29.0 ± 7.0	30.5 ± 4.8	32.3 ± 6.8
TV gradient, mm Hg	–	2.0 ± 0.8	3.0 ± 1.2	2.3 ± 1.0	2.0 ± 0.9

Values are mean ± SD.
TAPSE = tricuspid annular plane systolic excursion; TTVR = transcatheter tricuspid valve replacement; other abbreviations as in Tables 1 and 2.

Eighteen patients underwent repeat follow-up CT scans after the procedure. The indication was either grade 3 or 4 HALT on initial CT imaging (n = 12) or clinical or echocardiographic concern for HALT (n = 6). The **Central Illustration** shows the difference between CT and echocardiographic detection of HALT, as well as the anticoagulation strategies and subsequent HALT scores. Of the 12 patients with grade 3 or 4 HALT on initial CT imaging, just 2 were changed from DOACs to VKAs, 7 were maintained on DOACs, and 3 remained on VKAs, with intensification of therapy to a target international normalized ratio (INR) level of 2.5 to 3.5. Regardless of anticoagulation strategy, HALT grade improved for all patients. **Figure 3** shows an example of a significant improvement in HALT, from grade 4 to grade 1, for a patient who was maintained on a DOAC throughout the follow-up period.

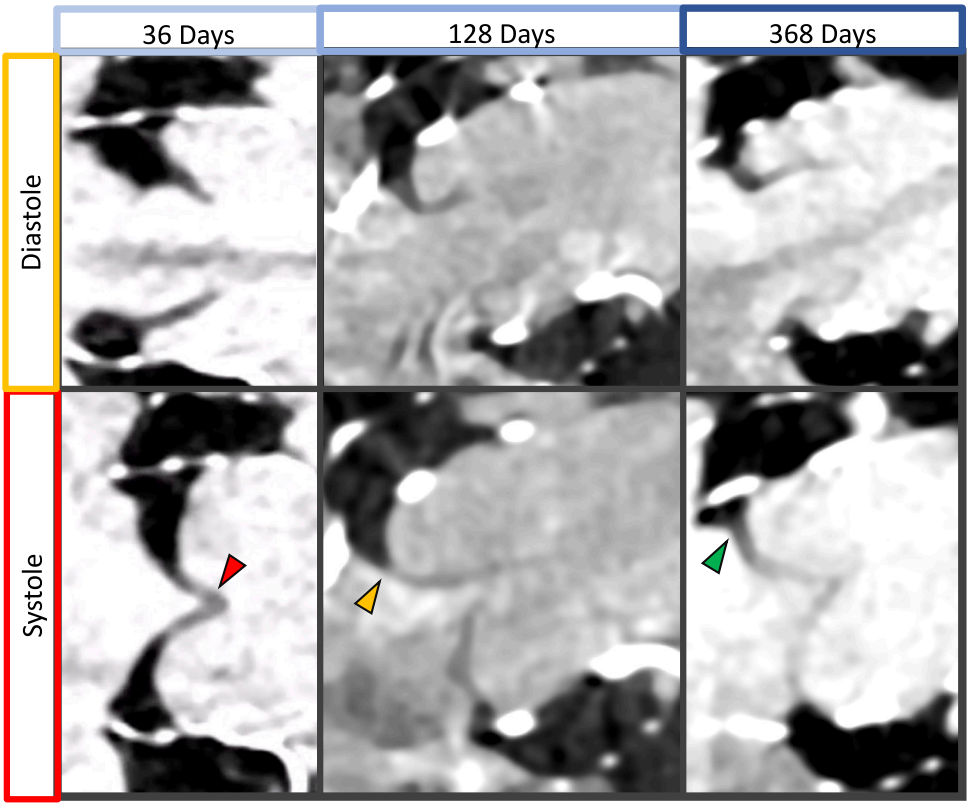
During follow-up, 2 patients had VKAs changed to DOACs because of persistently subtherapeutic INRs. One had no HALT, and the other grade 2 HALT. All other patients who changed to or remained on VKAs maintained INRs >2.0 at subsequent follow-up. After the initial CT examination, DOAC dose was changed in 1 patient with grade 4 HALT, with a dose increase of apixaban from 2.5 to 5 mg, despite older age and lower body weight. The HALT grade was subsequently 1 on the second CT scan. All other patients remained either on the full dose or the renally adjusted DOAC dose that was commenced postprocedurally.

DISCUSSION

Considering the high rate of tricuspid valve thrombosis in surgical cohorts, as well as of the association with poor outcomes after bioprosthetic aortic valve replacement, HALT and RLM could be expected to contribute significantly to clinical outcomes after TTVR.[3,8] This study presents an adjusted classification of HALT for TTVR and reported moderate to severe HALT in 12 (27%) of cases within 30 days of valve implantation. Leaflet thrombosis has been associated with increased mortality after aortic valve replacement,[3] but HALT is often subclinical and can occur at any time after valve implantation.[1] Analysis of this cohort showed that patients with HALT reported a greater burden of right heart failure symptoms including dyspnea, edema, and reduced exercise tolerance. This is supported by the observation that these patients are less likely to see improvement in NYHA functional class. This makes HALT difficult to detect clinically, as these symptoms are the same as those before TTVR, necessitating imaging to exclude HALT at follow-up.

Although anticoagulation after valve replacement has been shown to be protective in some aortic cohorts, it does not completely ameliorate the risk for HALT, nor do changes in anticoagulation necessarily result in regression of thrombosis.[1,10] HALT regression is also influenced by other factors, including anticoagulation, platelet and renal function, hemodynamic status, inflammation, and prosthesis type. Therapeutic strategies for HALT are therefore diverse and depend on the severity of HALT, clinical symptoms, hemodynamic function, and bleeding risk. In this cohort, there was no association between HALT or RLM_{CT} and anticoagulation strategy. However, moderate or severe HALT regressed in all cases, regardless of anticoagulation or antiplatelet strategy, although VKA therapy was intensified for patients taking VKAs. Patients with significant HALT on VKA therapy were not reported to have subtherapeutic INRs. All patients had clear recommendations for tight INR control and were informed about potential consequences of subtherapeutic INRs at the time of discharge; however, these data are limited to the results at follow-up, and unrecognized subtherapeutic INR levels between visits may have contributed to the development of HALT. Furthermore, compared with those with grade 0 to 2 HALT, patients with grade 3 or 4 HALT were not more likely to have renal impairment, or significantly elevated CRP levels at discharge, as a marker of pre- and postprocedural inflammation.

FIGURE 3 Series of CT Images Demonstrating Change in HALT Severity Over 3 Follow-Up CT Scans



The initial scan shows grade 4 hypoattenuated leaflet thickening (HALT), with thickening extending to the leaflet tip (red arrow); apixaban 2.5 mg twice daily was intensified to 5 mg. At 4 months, HALT had improved to grade 2, with regression of the leaflet thickening approximately to the midleaflet (yellow arrow). At 1 year, further improvement to grade 1 was observed, with regression of leaflet thickening to the leaflet base (green arrow).

Although there was no association between HALT severity and mean valve gradient, there was a significant association between RLM_{CT} and mean valve gradient, suggesting that RLM_{CT}, which is strongly associated with HALT severity, may be the link between valve thrombosis and clinical outcomes. HALT, RLM_{CT} or RLM_{echo}, and valve gradient were also each associated with the lack of improvement in NYHA functional class, as a marker of functional recovery. Patients with HALT reported ongoing poor exercise tolerance, peripheral edema and dyspnea at follow-up, compared with those without significant HALT. This suggests that the valve function, rather than the HALT burden, is the clinically significant element of valve thrombosis, but larger clinical studies will be required to more clearly define these associations, as well as the natural history of HALT.

With regard to the echocardiographic findings, valve leaflets could be adequately visualized to assess leaflet restriction in all cases. However, TTE was able to visualize significant HALT in only 3 of 7 patients with grade 4 HALT, and although the long-term or clinical significance of milder HALT is not well understood, TTE was also insensitive to detect grade 1 to 3 HALT. Although RLM_{CT} was significantly associated with higher valve gradients, this was not seen for RLM_{echo}, which may be due to the small cohort size, as well as the underdetection of RLM by echocardiography. Despite this, RLM_{echo} was also associated with less improvement in heart failure symptoms, on the basis of improved NYHA

functional class at 30-day follow-up. Although TTE can detect some cases of severe HALT and RLM, it is not as sensitive as CT imaging. CT imaging is therefore important to enable early diagnosis, especially if mild to moderate HALT precedes valve degeneration and dysfunction.

Finally, although the HALT score used in this study was developed on the basis of the scoring system for TAVR, there are some key differences in the anatomy and hemodynamic parameters of these valves. The first of these is that the tricuspid valve is a larger valve, with lower gradients and greater surface area, which may be more likely to promote thrombosis.[8] Lower gradients also offer less granularity in the hemodynamic assessment of these valves. It also was interesting to note asymmetry of thrombosis in 2 cases in this cohort, and such a disparity has not been reported on aortic valves. The scoring system for HALT was applied to the most heavily thickened or thrombosed valve in this cohort on the basis of the tendency for patients to be treated accordingly to the highest grade of observed thrombosis, and this may have resulted in lack of correlation between HALT severity and valve gradient.

Findings from this initial cohort suggest that HALT is a common finding in TTVR, with an impact on leaflet mobility, which is associated with functional recovery from heart failure symptoms. Although HALT and RLM_{CT} were not associated with a specific anticoagulation or antiplatelet strategy, this study was not powered to draw firm conclusions, and this should be investigated in future, larger cohorts. Importantly, all cases of severe HALT regressed, including in patients in whom there was no change in anticoagulation strategy.

STUDY LIMITATIONS. This was an initial exploratory cohort, not powered for clinical endpoints such as mortality, and the findings and correlations are hypothesis generating. Nonetheless, the observed associations with NYHA functional class suggest that HALT may be clinically meaningful and potentially related to subsequent TTVR prosthetic valve dysfunction. Larger prospective studies with systemic surveillance evaluation and prespecified anticoagulation regimens are required to characterize the natural history of HALT after TTVR and to define the optimal antithrombotic strategy.

CONCLUSIONS

HALT and RLM are common findings after TTVR, with important associations with transvalvular gradient and resolution of heart failure symptoms. As a more sensitive investigation for HALT and RLM than TTE, routine postprocedural CT assessment (eg, 1 month after the procedure) may play an increasingly important role for the diagnosis and subsequent management of HALT. Larger, prospective studies are required to define the natural history and clinical implications of HALT after TTVR, in particular with respect to progression to RLM and valve dysfunction, and to optimize the anticoagulation strategy in this population.

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PERSPECTIVES

WHAT IS KNOWN? HALT and RLM are recognized complications after TAVR, associated with valve thrombosis and impaired function. Similar findings have been observed after TTVR, but their classification and clinical implications remain undefined.

WHAT IS NEW? This study proposes a dedicated grading system for HALT and RLM_{CT} after TTVR, demonstrating that both are common and associated with elevated transvalvular gradients and less symptomatic alleviation and are underappreciated on echocardiography.

WHAT IS NEXT? Routine postprocedural CT imaging may be warranted to improve early detection of valve thrombosis after TTVR. Larger, prospective studies are needed to clarify the natural history of HALT and RLM and their impact on long-term valve durability and valve and right heart function and to optimize antithrombotic management in this population.

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APPENDIX For supplemental tables, please see the online version of this paper.