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Letters

Novel Computed Tomography Classification for Bioprosthetic Aortic Valve Degeneration

Guiding Trial of Anticoagulation or Reintervention

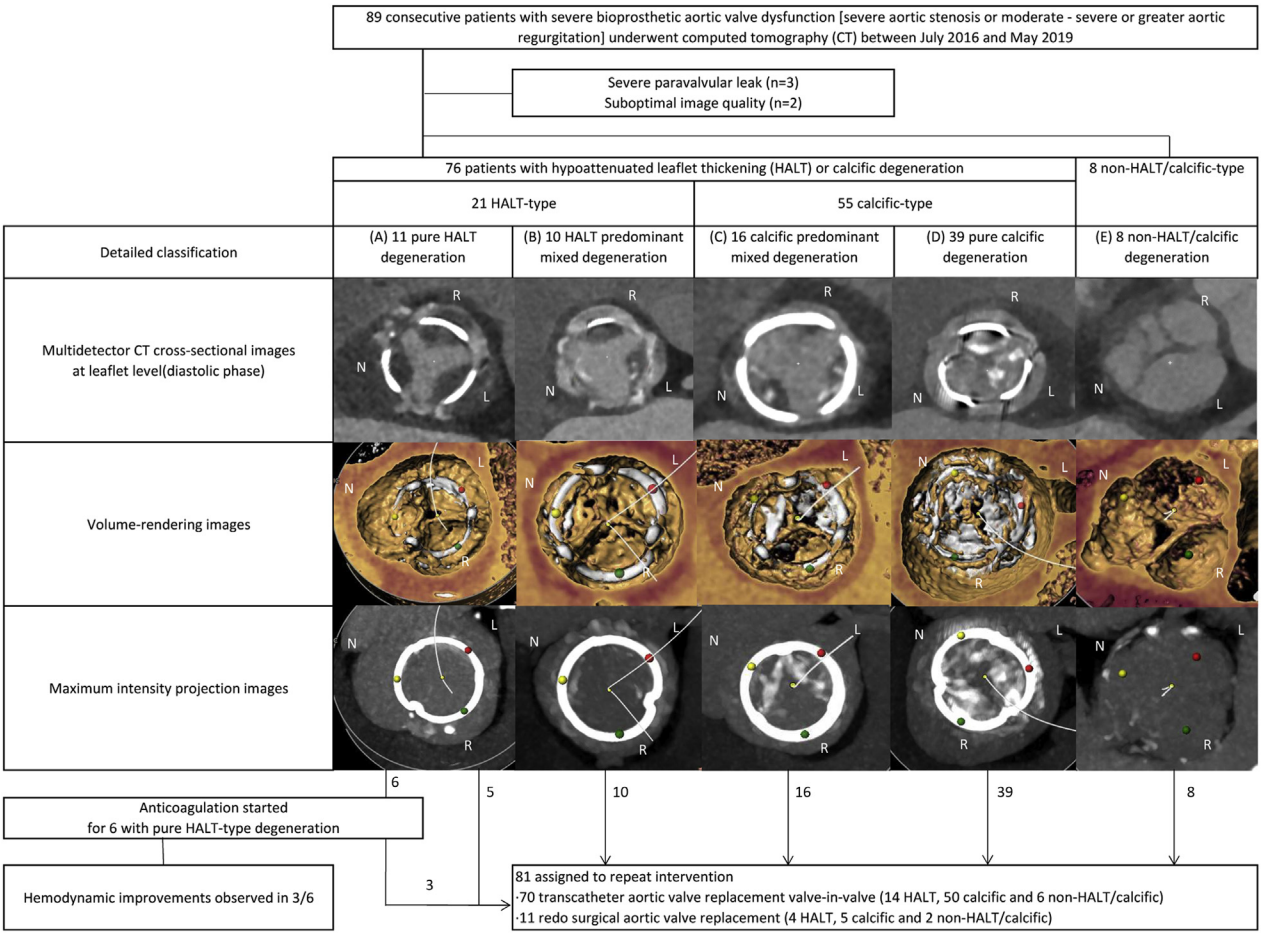
Earlier studies of valve-in-valve (V-in-V) with transcatheter aortic valve replacement for bioprosthetic aortic valve degeneration (BAVD) did not incorporate routine computed tomography (CT) as part of the preprocedural assessment (1). More recently, CT has been employed systematically for V-in-V to evaluate risk of coronary obstruction and to direct additional interventions to mitigate that risk (2). Cardiac CT may also readily detect hypoattenuated leaflet thickening (HALT) (3), leaflet calcification, and pannus. However, its utility for leaflet evaluation in patients presenting with BAVD for V-in-V has not been investigated. We sought to classify leaflet appearances in BAVD using detailed CT assessment and explore potential differences in mechanisms, presentation, and therapeutic implications for the respective subtypes.

This retrospective observational study included a total of 89 consecutive patients with symptomatic severe BAVD who underwent CT at NYU Langone Health between July 2016 and May 2019. Suboptimal image quality or paravalvular aortic insufficiency (AI) was excluded. The echocardiographic definition of severe valve dysfunction for aortic stenosis (AS) was a mean pressure gradient >40 mm Hg, a jet velocity >4.0 m/s, an effective orifice area <1.0 cm^2 (or an indexed effective orifice area <0.6 cm^2/m^2), or a Doppler velocity index <0.25, and for AI, was a regurgitation fraction ≥40%, regurgitation volume ≥45 ml, or effective regurgitant orifice area ≥0.2. The CT data were analyzed by a dedicated advanced imaging core laboratory using 3mensio software (Pie Medical Imaging, Maastricht, the Netherlands). The patients were visually divided into 3 groups based on CT findings: 1) HALT-type (including pure HALT degeneration without calcium and HALT-predominant mixed degeneration: HALT greater than calcium); 2) calcific-type (including pure calcific degeneration without HALT and calcific predominant mixed degeneration; calcium greater than HALT); and 3) non-HALT/calcific-type (neither HALT nor calcification present). The HALT-type and the calcific-type were statistically compared. The Student's *t*-test or Mann-Whitney *U* test for continuous variables and the chi-square test (or Fisher's exact test) for categorical variables were used. The study complies with the Declaration of Helsinki, and a locally appointed ethics committee confirmed its appropriateness.

We noted 21 HALT-type (25.0%), 55 calcific-type (65.5%), and 8 non-HALT/non-calcific type (9.5%) cases (**Figure 1**). HALT-type (vs. calcific-type) had a shorter time since surgery (7.8 ± 4.1 years vs. 12.0 ± 4.5 years; $p < 0.001$), fewer bovine valves (33.3% vs. 67.3%; $p = 0.007$) but more porcine valves (66.7% vs. 23.6%; $p < 0.001$). There were no significant differences in age (71.2 ± 14.5 years vs. 72.1 ± 12.8 years; $p = 0.803$), indices of renal dysfunction, valve size, the proportion of AS diagnosis (95.2% vs. 76.4%; $p = 0.095$), or use of direct oral anticoagulants (4.8% vs. 18.2%; $p = 0.272$). Serum calcium levels were higher in calcific-type (9.5 ± 0.5 mg/dl vs. 9.2 ± 0.6 mg/dl; $p = 0.034$). In the non-HALT/calcific-type, 6 of 8 were diagnosed as AI, and 2 were diagnosed as AS with patient-prosthesis mismatch.

Although HALT-type degeneration was more common in early-onset BAVD compared with calcific-type, HALT-type was also seen over a broad duration of time points (1 to 26 years) after surgery. Anticoagulation was started in 6 patients with pure HALT degeneration and 3 of 6 had hemodynamic improvement by echocardiography (1 nonresponder on apixiban, remainder warfarin); the 3 responders were 4, 7, and 10 years post-index surgery; mean gradients were reduced following 3 to 6 months of anticoagulation, from 34 to 24 mm Hg, from 37 to 22 mm Hg, and from 49 to 17 mm Hg, respectively; and the 3 nonresponders were 1, 3, and 8 years post-index surgery. The duration of anticoagulation until follow-up transthoracic echocardiography assessment (78 ± 19 days vs. 119 ± 44 days; $p = 0.212$), and therapeutic duration (70 ± 15 days

FIGURE 1 Study Workflow and Representative Images for Each Degeneration



(A) Pure HALT, **(B)** HALT predominant mixed, **(C)** calcific predominant mixed, **(D)** pure calcific, and **(E)** non-HALT/calcific degeneration. CT = computed tomography; HALT = hypoattenuated leaflet thickening.

vs. 89 ± 14 days; p = 0.264) appeared shorter in the nonresponder group, but did not reach statistical significance.

This study lacked power to evaluate interventional outcomes. However, some important preliminary conclusions may be made that merit further study to evaluate the clinical utility of this novel classification: 1) Even pure HALT-type BAVD may be due to heterogeneous causes and signify thrombus, fibrosis, or atherosclerosis; 2) Anticoagulation prevented reintervention in one-half of pure HALT cases regardless of time since surgery, and appeared more effective if given for at least 4 months; 3) Different prostheses appear to have different leaflet CT subtypes of BAVD; and 4) Current guidelines for annual follow-up commencing 10 years after surgery are insufficient, and annual transthoracic echocardiography from the index procedure may have a greater opportunity for the timely detection of hemodynamically significant (and potentially medically treatable) thrombotic degeneration.

Makoto Nakashima, MD
Mathew Williams, MD
Yuxin He, MD
Run Du, MD
Muhamed Saric, MD
Cezar Staniloae, MD
Michael Querijero, MSc
Illya Pushkar, MPH
Anna Kapitman, BA
***Hasan Jilaihawi, MD**

*Heart Valve Center
NYU Langone Health
Suite 9V
530 1st Avenue
New York, New York 10016, USA
E-mail: hasanjilaihawi@gmail.com

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The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

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