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Letters

RESEARCH LETTER

Opportunistic CT-Derived Periaortic Fat Attenuation as a Novel Marker of Mortality in Patients Undergoing TAVR

Mortality after transcatheter aortic valve replacement (TAVR) remains high, and with its expanding use in lower-risk patients, novel markers of long-term risk are needed to improve patient management.[1] Periaortic adipose tissue (PAAT) attenuation marks periaortic inflammation,[2] and can be opportunistically quantified on preprocedural computed tomography (CT) for TAVR planning, but its prognostic relevance in TAVR populations is unclear. Using data from our multicenter TAVR cohort, we investigated whether higher PAAT attenuation quantified on routine preprocedural CT is associated with increased long-term all-cause mortality after TAVR.

We performed a retrospective multicenter cohort study of consecutive adults undergoing TAVR between 2014 and 2023 across 4 Mass General Brigham hospitals with routine preprocedural CT imaging. The study was approved by the institutional review board with waiver of informed consent. Demographic and clinical data, including the STS (Society of Thoracic Surgeons) risk score,[3] were obtained from institutional registries and electronic health records. Preprocedural noncontrast CT scans were analyzed using a validated deep learning algorithm (TotalSegmentator v2.6.0) to segment the entire aorta from the sinotubular junction to the aortic bifurcation,[4] with PAAT defined as adipose voxels (−190 to −30 HU) within a 10-mm periaortic mask, enabling quantification of PAAT attenuation and volume. Mortality was ascertained over a median follow-up of 22 months (Q1-Q3: 14-36 months).

Cumulative event rates between PAAT attenuation groups were assessed using Kaplan-Meier curves and log-rank tests. Associations between PAAT attenuation and mortality were assessed using Cox regression with restricted cubic splines with 5 knots to model nonlinearity, adjusting for body-surface-area indexed PAAT volume, CT technical parameters, STS risk score, and obesity (body mass index ≥30 kg/m^2). Results are reported as HRs with 95% CIs. Model discrimination was assessed using Harrell's C-statistic. Patients were additionally categorized by median PAAT attenuation (high vs low), and restricted mean survival time ≤5 years was estimated using flexible parametric models. Analyses were exploratory, used a 2-sided $\alpha = 0.05$, and performed in Stata 18.0 (StataCorp LLC).

Among 928 included patients (mean age: 81 ± 8 years; 58% male), mortality was 23.9% (222/928). Mean PAAT attenuation was −77.3 ± 7.2 HU and was higher in women (+2.1 ± 0.5 HU), nonobese patients (+4.7 ± 0.5 HU), and those with moderate or high STS risk score (+1.7 ± 0.5 HU) (all $P < 0.001$). Kaplan-Meier analysis demonstrated significantly lower survival in patients with PAAT attenuation above the cohort median (−78 HU) compared with those below (log-rank $P < 0.001$) (**Figure 1A**). In multivariable Cox models, PAAT attenuation remained independently associated with mortality (per 10 HU: adjusted HR: 1.79 [95% CI: 1.33-2.41]; $P < 0.001$), with consistent findings across thoracic and abdominal aortic segments.

PAAT attenuation modestly but significantly improved discrimination beyond the STS score alone, increasing Harrell's C from 0.686 to 0.691 when STS was modeled continuously and from 0.668 to 0.703 when STS risk categories (<4%, 4%-8%, >8%) were used (both $P < 0.001$). Restricted cubic splines demonstrated a nonlinear, exponential risk increase at higher attenuation levels (≥90th percentile: adjusted HR: 3.71 [95% CI: 2.05-6.78]) (**Figure 1B**), corresponding to a 0.58-year (95% CI: −0.83 to −0.32; $P < 0.001$) reduction, ie, ∼7 months of life lost, in restricted mean survival over 5 years.

In this multicenter cohort of 928 patients undergoing TAVR, we found that higher preprocedural CT-derived PAAT attenuation was independently associated with long-term mortality beyond STS risk and other clinical and technical factors. These findings support PAAT attenuation as a novel imaging biomarker with potential to refine risk stratification in patients undergoing TAVR.

Our findings extend prior work linking adipose tissue attenuation to adverse cardiovascular outcomes. Higher perivascular fat attenuation has been associated with vascular inflammation and disease activity in the coronary and abdominal aortic beds, supporting its role as an imaging biosensor of vascular pathology. Although PAAT is a local perivascular compartment, its attenuation likely reflects the cumulative effects of systemic atherosclerosis, chronic inflammation, and vascular aging ("inflammaging") rather than isolated regional disease.

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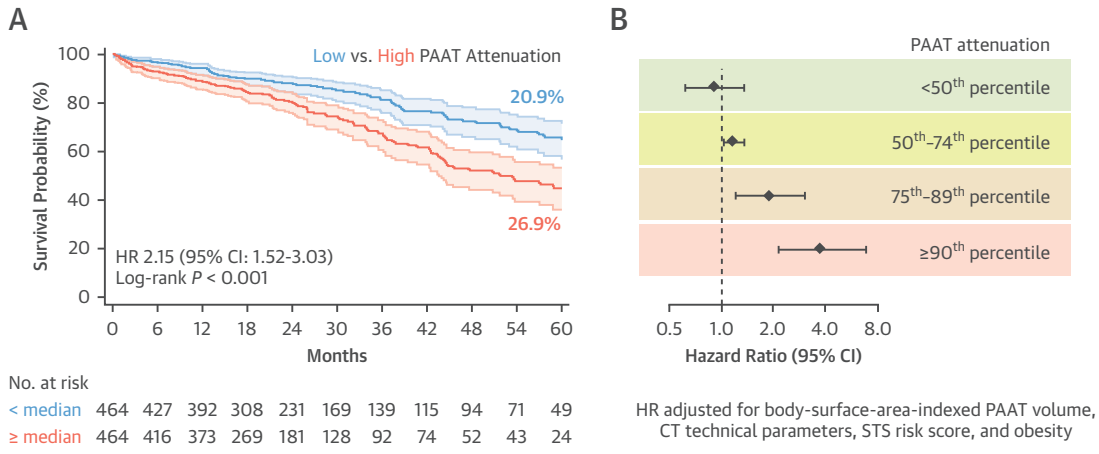
FIGURE 1 **Periaortic Fat Attenuation on Preprocedural CT as a Novel Marker of Mortality After TAVR**



(A) PAAT attenuation measured on planning CT marks periaortic inflammation and is independently associated with mortality after TAVR. Patients were divided at the cohort median into low (blue) and high (red) PAAT attenuation groups. (B) Risk accelerated exponentially at higher PAAT attenuation (≥90th percentile: adjusted HR: 3.71 [95% CI: 2.05-6.78]). CT = computed tomography; PAAT = periaortic adipose tissue; STS = Society of Thoracic Surgeons; TAVR = transcatheter aortic valve replacement.

Among TAVR patients, who tend to have significant comorbidity and systemic atherosclerosis, high PAAT attenuation may represent a surrogate of broader biological vulnerability. The consistency of this signal with prior TAVR studies on epicardial adipose tissue density[5] strengthens the biological plausibility that qualitative adipose characteristics contribute to long-term outcomes. In this context, PAAT attenuation may serve as an imaging readout of a broader inflammatory state that predisposes individuals to adverse events despite procedural success. Longitudinal studies should examine whether inflammation-modifying agents alter PAAT attenuation and whether such changes translate into improved outcomes.

This retrospective study precludes causal inference, and PAAT attenuation should be interpreted as an imaging-derived surrogate rather than a direct measure of periaortic inflammation; additionally, noncontrast CT may not be routinely acquired in all TAVR pathways.

To conclude, CT-derived PAAT attenuation is independently associated with long-term mortality after TAVR and may represent an adjunctive, potentially modifiable imaging marker of risk that merits further validation.

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Data generated or analyzed during the study are available from the corresponding author by request.

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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