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Original Article

Effects of Transcatheter Aortic Valve Implantation on Frailty and Quality of Life

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ABSTRACT

Background: Transcatheter aortic valve implantation (TAVI) is an effective alternative to surgical valve replacement in high-risk patients with severe aortic stenosis. Although measures of frailty have been used to attempt to predict outcomes in this population, few studies have demonstrated changes in these measures.

Methods: We performed a prospective, observational study of 171 patients undergoing TAVI, of whom 44 had maximal follow-up of 1 month and 50 had maximal follow-up of 1 year. Quality of life was assessed using the Minnesota Living With Heart Failure Questionnaire, Katz Index of Independence in Activities of Daily Living questionnaire,

RÉSUMÉ

Contexte : Le remplacement valvulaire aortique par cathéter (TAVI) est une solution de rechange efficace à la chirurgie de remplacement valvulaire chez les patients atteints de sténose aortique grave et présentant un risque élevé. Les mesures de la fragilité sont utilisées pour tenter de prévoir les résultats au sein de cette population. Néanmoins, peu d'études ont permis d'objectiver les variations de ces mesures.

Méthodologie : Nous avons réalisé une étude observationnelle prospective portant sur 171 patients ayant subi un TAVI, dont 44 suivis pendant un mois ou moins, et 50 durant un an ou moins. La qualité de

Transcatheter aortic valve implantation (TAVI) has become an established alternative to surgical aortic valve replacement (SAVR) in high-risk patients with severe aortic stenosis.[1-3] A systematic review of more than 60 studies has demonstrated that TAVI improves both physical function and quality of life.[4] In the inoperable patient population, TAVI has also been associated with a reduction in mortality and an improvement in New York Heart Association functional status.[5] Identification of appropriate patients to undergo TAVI has remained a challenge in the setting of publicly funded healthcare systems.[6] Frailty is defined as a clinical syndrome in which individuals exhibit reduced physiological capacity to adapt to stressors. Frailty has been demonstrated to be associated with worse clinical outcomes in the setting of acute myocardial infarction, heart failure, and cardiac surgery.[7] In the TAVI setting, frailty index scores have been used to predict functional decline post-TAVI and promises to be an important tool in patient selection for TAVI.[8] However, no studies to date have demonstrated longitudinal changes in frailty after TAVI.

Our study aimed to describe the short-term impacts of successful TAVI on markers of frailty in comparison with quality of life in patients with severe aortic stenosis.

Methods

Study population

The Mazankowski Alberta Heart Institute TAVI program serves a referral population of approximately 1.7 million people. Before referral for TAVI assessment, patients with symptomatic severe aortic stenosis are reviewed by a combined cardiac surgery and cardiology heart team for SAVR. If deemed to be prohibitive or high risk for SAVR, these patients are referred for TAVI assessment after completion of required additional cardiovascular imaging and clinical assessment. TAVI candidacy is then determined at a TAVI-specific multidisciplinary heart team meeting.[9] At the initial TAVI assessment, patients were prospectively recruited and provided informed consent between June 2012 and September 2017. A

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Ethics Statement: The research reported has adhered to the relevant ethical guidelines.

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and patient perception of overall well-being. Frailty was measured using the 10-m walk test and handgrip strength testing.

Results: In the overall cohort, participants demonstrated improvements in quality of life metrics, but deterioration in 10-m walk test and handgrip at 1 month. These trends continued at 1 year. However, patients in the lowest quintile of handgrip and 10-m walk test demonstrated a trend of improvements in these metrics during follow-up.

Conclusions: Despite improvements in quality of life after TAVI, no improvements in frailty were observed in patients at 1 year.

vie a été évaluée au moyen de questionnaires — *Minnesota Living With Heart Failure Questionnaire* et *Katz Index of Independence in Activities of Daily Living Questionnaire* — et en fonction de la perception du patient relativement à son bien-être général. La fragilité a été mesurée à l'aide d'un test de marche sur dix mètres et d'un test de force de préhension.

Résultats : Dans l'ensemble de la cohorte, une amélioration des mesures de la qualité de vie a été observée parallèlement à une détérioration des résultats au test de marche sur dix mètres et au test de force de préhension après un mois. Les tendances à cet égard se sont poursuivies au bout d'un an. Cependant, les résultats des patients du quintile inférieur au test de marche sur 10 m et au test de force de préhension ont eu tendance à s'améliorer au cours de la période de suivi.

Conclusions : Malgré une amélioration de la qualité de vie après le TAVI, la fragilité des patients ne s'est nullement améliorée après un an.

pragmatic approach was used, in which all participants who were offered TAVI after the multidisciplinary meeting were included. Of note, our TAVI program excludes patients with a Mini-Mental State Examination score of < 22. All participants were aged > 18 years. Participants who were referred for surgical valve replacement were excluded. Otherwise, no strict inclusion or exclusion criteria were used. After TAVI, all patients are routinely referred to cardiac rehabilitation. Ethical approval was obtained from the University of Alberta's Human Research Ethics Board.

Data collection

All participating patients referred for TAVI underwent a thorough baseline visit, which included a patient's history, physical examination, and measurement of left ventricular ejection fraction by transthoracic echocardiogram. In addition, patients completed the Minnesota Living with Heart Failure Questionnaire (MLHFQ) and Katz Index of Independence in Activities of Daily Living (ADL) questionnaire that were administered by study personnel. A higher score in the MLHFQ questionnaire indicates a higher burden on quality of life, whereas a high score on the ADL questionnaire indicates a lower burden of quality of life. A score of 6 of the Katz Index of ADL indicates full function. Patients were asked to self assess their overall health and well-being on a 1- to 100-point scale. Physical examination included a timed 10-m walk test (10MWT) and handgrip strength evaluation using a calibrated dynamometer. Handgrip was measured using a calibrated dynamometer with the patient in the seated position using the patient's dominant hand, and the mean of 3 measurements was calculated. Patients were followed up using routine clinic visits at a 1 month and 1 year. Baseline data were collected during the visit where the decision to proceed with TAVI was made. All data were prospectively collected.

Statistical analysis

The MLHFQ score (physical and emotional components) and Katz ADL questionnaires are reported using mean score $\pm$ standard deviation. Wilcoxon signed-rank tests were undertaken to describe changes in means of nonparametric variables, including quality of life score and frailty metrics among baseline, 1 month, and 1 year. One-way analysis of variance and Pearson's chi-square were used to compare baseline factors between groups of varying improvement in frailty metrics. All analysis was undertaken using SPSS v24 (SPSS Inc., Chicago, IL).

Results

Patient characteristics

Between June 2012 and September 2017, 215 consecutive TAVI procedures were completed at the Mazankowski Alberta Heart Institute, of which 171 participants had completed quality of life and frailty testing at baseline. Maximal duration of follow-up that included frailty testing was 1 year in 50 patients and 1 month in 44 patients. A total of 77 patients had no further documented frailty testing in routine follow-up. Survival data were available until January 2019, with a mean follow-up of 3.2 ± 1.6 years. During that period, 70 deaths (40.9%) were observed that occurred at a mean of 2.2 ± 1.5 years after TAVI. Cause of death was unknown in 15 cases (21.4%), noncardiac in 38 cases (54.3%), and cardiac in 16 cases (22.9%). There was 1 (1.4%) procedure-related death.

The mean age of these patients was 85.9 ± 6.9 years, and 57.3% ($n = 98$) were male. Mean body mass index at baseline was 27.9 ± 5.7 kg/m^2. Of participants, 25.1% ($n = 43$) had diabetes, 54.4% ($n = 93$) had coronary artery disease, 27.5% ($n = 47$) underwent previous coronary artery bypass grafting, 36.3% ($n = 62$) had documented atrial fibrillation, and 7.0% ($n = 12$) had previous valvular surgery. The majority of cases (91.2%, $n = 156$) were performed using a transfemoral approach, and the remainder (8.8%, $n = 15$) were done using a transapical approach. A minority of cases (3.5%, $n = 6$) were valve-in-valve procedures.

Quality of life metrics

Participants reported a baseline ADL disability mean score of 5.8 ± 0.6 and 5.8 ± 0.4 at 1 month and 5.8 ± 0.6 at 1 year (Fig. 1). At baseline, participants self-scored their overall baseline well-being at a mean of $64.0\% \pm 18.3\%$ and $73.2\% \pm 16.9\%$ at

Table 1. Paired analysis of quality of life and frailty metrics

	Baseline vs 1 mo				Baseline vs 1 y			
	N	Baseline	1 mo	*P* value	N	Baseline	1 y	*P* value
Katz ADL	49	5.6 ± 0.9	5.8 ± 0.4	0.856	50	5.9 ± 0.5	5.8 ± 0.6	0.236
Overall well-being (%)	44	60.2 ± 18.3	73.1 ± 17.4	< 0.001	48	66.8 ± 21.5	70.1 ± 17.8	0.307
MLHFQ Total	82	32.2 ± 15.6	13.2 ± 11.5	< 0.001	41	28.8 ± 15.0	17.3 ± 16.9	0.001
MLHFQ Physical	82	52.6 ± 23.6	13.2 ± 11.5	< 0.001	41	50.3 ± 25.2	25.1 ± 23.5	< 0.001
MLHFQ Emotional	82	13.4 ± 16.7	3.7 ± 7.7	< 0.001	41	7.7 ± 10.2	10.9 ± 18.2	0.531
Hand Grip (kg)	69	24.5 ± 7.7	23.1 ± 7.4	0.003	50	23.8 ± 8.2	20.3 ± 7.9	< 0.001
10MWT (s)	53	6.4 ± 1.9	6.3 ± 1.3	0.508	40	6.6 ± 1.9	8.1 ± 3.0	0.018

Of note, higher ADL score is interpreted as higher function, and higher MLHFQ scores are interpreted as a higher burden.
10MWT, 10-m walk test; ADL, activities of daily living, MSLHFQ, Minnesota Living with Heart Failure Questionnaire.

1 month and 70.1% ± 17.8% at 1 year. The MLHFQ total score at baseline was 30.3 ± 16.3 and 13.4 ± 12.5 at 1 month and 15.2 ± 16.4 at 1 year. The mean physical score component of the MLHFQ was 49.8 ± 24.0 at baseline, 21.3 ± 20.0 at 1 month, and 22.9 ± 24.1 at 1 year. The mean emotional score component of the MLHFQ was 13.5 ± 18.0 at baseline, 4.7 ± 9.9 at 1 month, and 9.25 ± 16.8 at 1 year. Paired analysis of quality of life metrics for baseline versus 1 month and baseline versus 1 year is shown in Table 1. Figure 2 illustrates quality of life metric scores using all available follow-up data.

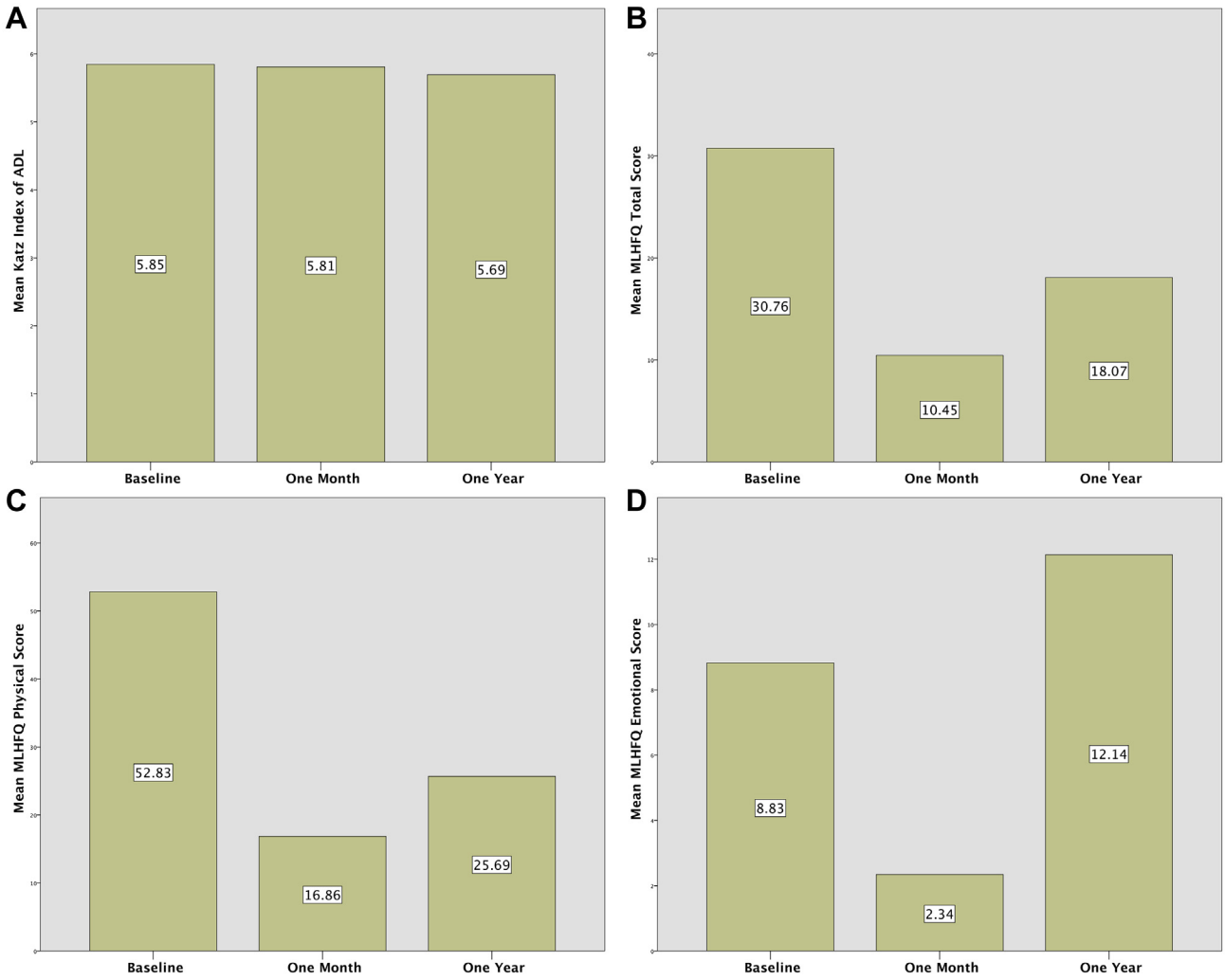

Figure 1. Quality of life metrics at baseline, 1 month, and 1 year using all available follow-up. (**A**) Katz index of ADL is displayed where a higher ADL score is interpreted as higher function. MLHFQ total score (**B**), physical score (**C**), and emotional score (**D**) were higher. MLHFQ scores are interpreted as higher burden. ADL, activities of daily living; CI, confidence interval; MLHFQ, Minnesota Living with Heart Failure Questionnaire.

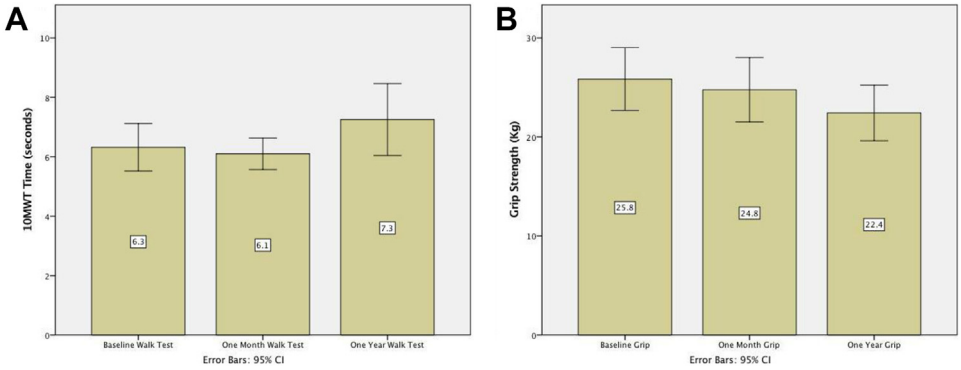

Figure 2. Frailty metrics at baseline, 1 month, and 1 year using all available follow-up. CI, confidence interval; 10MWT, 10-m walk test.

Frailty Metrics

Grip strength

The mean grip strength of participants was 23.6 ± 8.2 kg at baseline, 23.1 ± 7.4 kg at 1 month, and 20.3 ± 7.9 kg at 1 year. Male participants' baseline grip strength was 27.7 ± 7.9 kg compared with 18.1 ± 4.7 kg for female participants. The mean change in grip strength was −1.4 ± 4.2 kg at 1 month and −3.5 ± 5.3 kg at 1 year. At 1 month, 25 participants (36.2%) demonstrated an improvement in their grip strength from baseline. This is compared with only 12 participants (24.0%) who demonstrated improvement in their grip strength at 1 year from baseline.

When examining participants in the lowest quintile of the baseline handgrip assessment (<16 kg), we identified a baseline handgrip of 12.6 ± 2.5 kg. At 1 month, we observed a nonstatistically significant trend demonstrating improvement in their handgrip at 1 month (14.8 ± 5.9 kg; $P = 0.161$) and that returned to baseline at 1 year (12.6 ±3.5 kg; $P = 0.953$).

Ten-meter walk test

At baseline, the mean time to complete the 10MWT was 6.7 ± 2.0 seconds, 6.5 ± 1.9 seconds at 1 month, and 8.0 ± 3.0 seconds at 1 year. The mean change in time to complete the 10MWT at 1 month was a reduction of 0.2 ± 1.6 seconds and an increase of 1.5 ± 3.5 seconds at 1 year. At 1 month, only 18 participants (34.0%) reduced their time from baseline to complete the 10MWT, compared with 11 participants (27.5%) who reduced their time at 1 year. Figure 2 illustrates frailty metric scores using all available follow-up data. Table 2 demonstrates the baseline characteristics of patients when grouped into whether at 1 year they demonstrated an improvement in one of the frailty metrics, both, or none.

When examining participants in the lowest quintile of the baseline 10MWT (>8 seconds), the average baseline 10MWT time was 9.7 ± 01.6 seconds. At 1 month, we saw improvements in their 1-month 10MWT (7.5 ±1.7 s; $P = 0.018$), which persisted at 1 year, although they were not statistically significant (8.3 ± 2.9 seconds; $P = 0.153$).

Survival and length of stay

When comparing grip strength based on survival status at maximal follow-up, survivors demonstrated higher baseline grip strengths (24.8 vs 21.9 kg; $P = 0.02$) but relatively similar 10MWT times (6.6 vs 6.8 seconds; $P = 0.773$). The mean length of stay from TAVI to discharge was 4.5 ± 6.4 days. There was no association between hospital length of stay and baseline grip strength or 10MWT times.

Discussion

Our study demonstrated that patients undergoing TAVI experience significant improvements in quality of life using a

Table 2. Comparison of baseline characteristics by improvement category at 1 year

	Improvement in 2 frailty metrics (n = 9)	Improvement in 1 frailty metrics (n = 8)	No improvement in frailty metrics (n = 34)	*P* value
Age	87.0 ± 5.8	89.8 ± 4.7	84.5 ± 5.9	0.055
CAD	7 (77.8%)	7 (87.5%)	15 (44.1%)	0.024
Previous CABG	5 (55.6%)	5 (62.5%)	7 (20.6%)	0.028
Diabetes	2 (22.2%)	1 (12.5%)	6 (17.6%)	0.872
Atrial fibrillation	3 (33.3%)	1 (12.5%)	11 (32.4%)	0.499
Previous valvular surgery	0 (0.0%)	0 (0.0%)	3 (8.8%)	0.440
Baseline overall well-being (%)	87.0 ± 5.2	89.8 ± 4.7	84.5 ± 5.9	0.169
Baseline Katz ADL index	5.6 ± 1.0	6.0 ± 0.0	5.9 ± 0.4	0.155
Baseline total MLHFQ score	34.0 ± 14.8	32.4 ± 13.6	23.8 ± 15.3	0.196
Baseline grip (kg)	19.7 ± 9.6	24.6 ± 7.3	24.8 ± 7.9	0.251
10MWT (s)	7.9 ± 2.5	7.8 ± 2.5	6.0 ± 1.3	0.009

Higher ADL score is interpreted as higher function, and higher MLHFQ scores are interpreted as higher burden.

10MWT, 10-m walk test; ADL, activities of daily living; CABG, coronary artery bypass grafting; CAD, coronary artery Disease; MLHFQ, Minnesota Living with Heart Failure Questionnaire.

variety of different metrics after 1 month. Although these changes persisted at 1 year, they were less pronounced. Examining frailty using 10MWT and handgrip strength, we unexpectedly observed a deterioration in these metrics of frailty over the course of follow-up. However, participants in the lowest quintiles of baseline grip strength and the 10MWT demonstrated modest improvements in both during follow-up.

In concordance with other studies,[10] TAVI appears to demonstrably improve short-term quality of life using the MLHFQ[11-13] and Katz ADL score.[14] To our knowledge, serial measurements of 10MWT and grip strength results have not been described in the TAVI population. However, in the pretransplant/ventricular assist device population, grip strength was found to be reduced in 65% during the preprocedure assessment and only one-third of participants were reclassified as normal afterward.[15] This highlights the concept that physical strength is only a single domain of frailty, which is influenced by the accumulation of physical, cognitive, and psychological stressors. This concept is supported by a study that demonstrated that baseline grip strength was not found to be an independent predictor of mortality after TAVI.[16] However, when combined into a frailty score composed of grip strength, gait speed, ADL disability, and serum albumin, they were able to prognosticate patients undergoing TAVI at high risk of mortality. This suggests that frailty assessment requires a comprehensive assessment that encompasses functional and cognitive assessment, in addition to a physical assessment of frailty in an effort to standardize frailty assessment in the TAVI population.

From previous works, gait speed has been identified as an independent predictor of mortality after TAVI; however, the cutoff identified would be the equivalent of 26 seconds to complete the 10MWT, significantly slower than in the majority of our population, which may explain why we did not identify a relationship between baseline 10MWT times and survivorship.[17] Grip strength in the TAVI population has been described to be 22 to 25 kg in men and 13 to 15 kg in women, which is slightly worse than in our cohort.[16,18] This suggests that our population may be less frail than previously described TAVI populations.

Our study failed to demonstrate measurable improvements in 10MWT and grip strength in the entire cohort. However, when examining those in the lowest quintile of score, a trend emerged demonstrating improvements on repeat frailty measurements at 1 month and 1 year. Several explanations for this may be possible. The first is that our population was less frail to begin with when compared with previously reported populations as described earlier. Alternatively, we must consider that aortic stenosis may be only one of many accumulated comorbidities contributing to an individuals frailty. Undergoing TAVI may improve one aspect of frailty, but without addressing the concomitant risk factors, we may not see demonstrable improvements in frailty. This highlights the importance of a multidisciplinary that includes geriatrics to simultaneously identify and treat concomitant risk factors for frailty.

Further research is needed to assess whether TAVI can improve frailty using other indices than the 10MWT and handgrip or alternatively using an index score with multiple measures of frailty. Although there are a plethora of frailty indices, we examined handgrip and gait speed because these are relatively simple to use, objective measurements that can be easily introduced into routine clinical practice. Although subjective frailty scales such as the Canadian Study of Health and Aging Estimated Frailty Scale have been used in other populations, it was not found to be an independent predictor of short-term outcomes after TAVI.[19]

Study limitations

Our study is limited by the modest sample size from a single center and is susceptible to follow-up bias related to incomplete data on the full cohort of patients with TAVI. Incomplete follow-up was a result of incomplete data collection by the healthcare team, which was expected because this was an unfunded, pragmatic, resident-led study. Last, our study examined only physical metrics of frailty. Previously identified frailty metrics included cognitive domains and biochemical markers, which when added to physical metrics may improve the sensitivity and specificity of the frailty assessment.

Conclusion

Although TAVI has been demonstrated to improve quality of life, there remains uncertainty as to whether it improves frailty, and further evaluation is needed to ascertain long-term frailty effects.

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Disclosures

The authors have no conflicts of interest to disclose.

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