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RESEARCH ARTICLE

Durability of benefit after transcatheter tricuspid valve intervention: insights from actigraphy

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Aims Tricuspid regurgitation (TR) is associated with high mortality, morbidity and reduced physical capacity. This study was designed to examine the long-term impact of transcatheter tricuspid valve intervention (TTVI) on physical activity by using the method of actigraphy.

Methods and results Overall, we prospectively included 128 heart failure patients with severe TR (median age 79 years, 48% female) who were scheduled for TTVI. Patients were equipped with activity tracking devices for 1 week before TTVI, and again at 1–6 months and 1 year after TTVI. We compared continuous physical activity (CPA), defined as the mean number of steps/day with New York Heart Association class, quality of life assessments, and 6-min walk distance (all $p < 0.01$). TTVI reduced TR to grade ≤2+ in 94% of patients. Median (interquartile range [IQR]) CPA at baseline was 3108 (1350–4959) steps/day, which increased by 31.4% to 3958 (1823–5657) steps/day at 1–6 months and 4080 (2293–6514) steps/day at 1 year after TTVI ($p < 0.001$ for both comparisons). The impact of TTVI was significantly higher in advanced heart failure patients with low baseline activity (baseline CPA <1350 steps/day; 1-year CPA increase: +121.3%; $p < 0.001$), when compared to moderate activity patients (baseline CPA 1350–4959 steps/day; 1-year CPA increase: +27.5%; $p < 0.01$) or high activity patients (baseline CPA >4959 steps/day; 1-year CPA change: +2.6%; $p = 0.39$).

Conclusion One-week actigraphy demonstrates durable improvement of physical activity after TTVI. Fragile chronic heart failure patients with very low baseline activity, as determined by actigraphy in this study, significantly benefit from transcatheter intervention and should not be excluded from TTVI.

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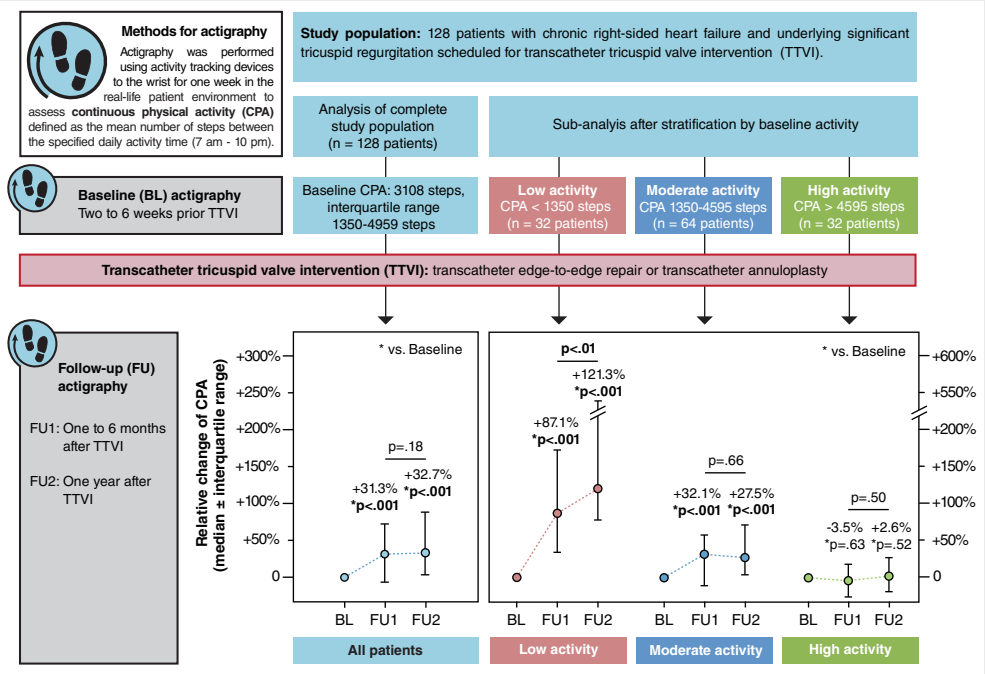
Graphical Abstract



Actigraphy demonstrates durable improvement of physical activity in heart failure patients with underlying significant tricuspid regurgitation after transcatheter tricuspid valve intervention.

Keywords Actigraphy • Activity tracking • Heart failure • Transcatheter tricuspid valve intervention • Tricuspid regurgitation

Introduction

Chronic heart failure with secondary tricuspid regurgitation (TR) is a serious and progressive disease.[1,2] In addition to its association with excess mortality, TR is also associated with a considerable reduction of physical activity,[3,4] which can markedly impact patients' quality of life. Until recently, patients with severe TR were markedly undertreated,[5] in part because isolated tricuspid surgery has been associated with high mortality rates and patients with severe TR are often deemed inoperable due to comorbidities and significant frailty.[1,6] In recent years, several percutaneous transcatheter tricuspid valve intervention (TTVI) techniques have been introduced, including tricuspid transcatheter annuloplasty and tricuspid transcatheter edge-to-edge-repair (T-TEER),[4] and early studies have suggested that TTVI improves functional outcomes.[7–10] Actigraphy devices can provide an objective assessment of physical activity in the real-life environment and are increasingly used in heart failure patient populations.[11–14] In an earlier study, we demonstrated the applicability of actigraphy in heart failure patients with underlying TR and observed improved physical capacity shortly after TTVI in a small group of heart failure patients.[7,15] However, the durability of these benefits has not yet been described.

In this study, we examined the time course of improvement in physical activity over the first year after TTVI in a sizable cohort of chronic heart failure patients with underlying TR. In addition to examining the durability of benefit, the enlarged patient population allowed us to analyse the impact of TTVI according to the baseline physical capacity to determine which patients may benefit most from the intervention. This might contribute to improve the patient selection process of an increasing heart failure patient population considered for TTVI.

Methods

Patient enrollment

Between February 2017 and October 2020, consecutive patients with heart failure and severe TR undergoing TTVI at our center were considered for participation in this study and prospectively enrolled. Patients who underwent simultaneous percutaneous treatment of both mitral and tricuspid valves were also included. Hospitalized inactive

patients before TTVI were not included. The local ethics committee approved the data analysis of patients treated with TTVI, and all patients signed informed consent.

Actigraphy

For the measurement of physical activity in heart failure, we used the concept of activity monitoring.[14] As previously described, patients were equipped with activity tracking devices to the wrist (Fitbit Charge 2, Fitbit, San Francisco, CA, USA).[7] The devices recorded the number of steps and the heart rate by accelerometry and photo-plethysmography, respectively. Patients were asked to wear the actigraphy devices at home in their real-life environment continuously until the battery of device was depleted – usually 7 to 12 days of activity tracking. Device re-charging, connection to a cell-phone or another device, and cellular data transmission were not performed to keep the methodology simple, which allowed for high device adherence. Actigraphy data were registered every 15 min, stored locally on the devices, and analysed using the Fitbit web-based application. An analysis algorithm was applied to the actigraphy data, which defined data (steps and heart rate) during 7:00 AM and 10:00 PM as activity hours. Continuous heart rate monitoring was used to control for the adherence of patients to device wearing. Sufficient adherence was set to a minimum of 10 activity hours per day (quality control for intraday device adherence).

Primary and secondary endpoints

The mean number of steps per day at each tracking period was referred to as continuous physical activity (CPA) and was defined as the primary outcome measure in this study. Additionally, we analysed the steps per day at the day with the highest activity (high-performance day) and the day with the lowest activity (low-performance day) in each tracking period. The resting heart rate was defined as the mean resting heart rate of all days within a tracking period. The high heart rate was defined as the mean value of all maximum daily heart rates within a tracking period.

Baseline and follow-up study visits

The baseline study visit was performed 2 to 6 weeks prior to TTVI. At baseline, out-of-hospital 1-week actigraphy as well as in-hospital heart failure examinations were assessed. In-hospital heart failure examination included New York Heart Association (NYHA) classification, estimation of health status using the Minnesota Living with Heart Failure Questionnaire (MLHFQ), 6-min walk distance test (6MWDT), N-terminal pro-B-type natriuretic peptide (NT-proBNP) and echocardiography with documentation of the left and right ventricular function as well as assessment of mitral regurgitation and TR according to the American and European guidelines for quantification of native valve regurgitation.[16,17] Regurgitation severity was assessed with grades of 0+ (none or trace), 1+ (mild), 2+ (moderate), 3+ (severe), or 4+ (massive). Patients with torrential TR were attributed to grade 4+. Actigraphy was performed at short-term (1 to 6 months after TTVI) and 1-year follow-up (± 3 months).

Statistical analysis

Variables are expressed as counts with percentages for categorical variables or as medians with interquartile ranges (IQRs) for continuous variables without normal distribution. Shapiro–Wilk normality test was used to test for normal distribution of continuous variables. Differences in actigraphy before and after TTVI were tested using the Wilcoxon matched-pairs signed rank test. Differences of variables between more than two groups were tested by the Kruskal–Wallis test. Univariate linear regression analysis was performed to identify echocardiographic predictors associated with the change in CPA after TTVI. Survival was analysed applying the Kaplan–Meier method. A p-value <0.05 was considered as statistically significant. Statistical analyses were performed using R version 3.4.1 (R Foundation for Statistical Computing, Vienna, Austria).

Results

Patient characteristics and transcatheter tricuspid valve intervention

During the enrollment period, we performed TTVI in 250 heart failure patients with underlying clinically leading significant TR according to the advice of an interdisciplinary heart team (online supplementary *Figure S1*). A total of 122 patients without baseline actigraphy were excluded (online supplementary *Table S1*). In this study, we prospectively included 128 patients with TTVI and available baseline actigraphy. Patient characteristics of the study population are listed in *Table 1*. Median age was 79 years, 48% were female, 96% patients were in NYHA class >II, and baseline TR was grade 3+ in 58% and grade 4+ in 40% of patients. Isolated T-TEER was performed in 67%, combined mitral and tricuspid intervention in 31%, and tricuspid annuloplasty in 2% of patients. TTVI led to significant reduction of TR in 94% of patients, as assessed by echocardiography at the day of discharge (TR ≤2+). At discharge from the hospital, residual TR was ≤1+ in 72 patients, 2+ in 48 patients and 3+ in 8 patients. Survival at 1 year after TTVI was 88% (113 of 128 patients).

Actigraphy methodology and correlation with standard heart failure measures

The median tracking phase of actigraphy assessments was 7 (IQR 6–9) days, and at least 5 days were recorded in 90% of actigraphy analyses (online supplementary *Figure S2A*). During the entire study period, actigraphy was assessed on 2303 days, and 32 818 activity hours (defined between 7.00 AM and 10.00 PM) were recorded in all patients (online supplementary *Figure S2B*). Device adherence was high; 94% of tracked days (2155 of 2303 days) passed the heart rate monitored quality control and were included for further analysis (online supplementary *Figure S2B*). At baseline, the assessed actigraphy parameter CPA correlated with NYHA functional class, formal quality of life assessment, and 6-min walk distance (all p <0.01; *Figure 1*).

Improvement of actigraphy results after transcatheter tricuspid valve intervention

All actigraphy results are listed in *Table 2*. Follow-up actigraphy was recorded and analyzsed in 113 of all 128 patients (96% actigraphy

Table 1 Patient characteristics ($n = 128$)

Age, years	79 (75–82)
Female sex	61 (48)
Body mass index, kg/m^2	24.7 (22.5–27.5)
EuroSCORE II, %	4.4 (3.0–6.9)
Transcatheter intervention	
Isolated tricuspid annuloplasty	3 (2)
Isolated T-TEER	85 (67)
Combined M + T-TEER	40 (31)
Medical history	
Coronary artery disease	59 (46)
Atrial fibrillation	111 (87)
Pacemaker or ICD lead	35 (27)
NYHA functional class	
I	0 (0)
II	5 (4)
III	101 (79)
IV	22 (17)
MLHFQ, points	37.5 (26.3–46.0)
6MWDT, m	202 (150–310)
NT-proBNP, ng/L	2378 (1310–4989)
eGFR, ml/min	47 (37–61)
LVEF, %	55 (47–62)
<40%	18 (14)
≥40%	110 (86)
RV TAPSE, mm	17 (15–21)
RV FAC, %	38 (32–43)
Estimated sPAP, mmHg	41 (32–51)
TR severity, grade	
1+, mild	0 (0)
2+, moderate	2 (2)
3+, severe	74 (58)
4+, massive	52 (40)
MR severity, grade	
No MR	9 (7)
1+, mild	56 (44)
2+, moderate	26 (21)
3+, severe	24 (19)
4+, massive	11 (9)

Values are *n* (%), or median (interquartile range). 6MWD, 6-min walk distance test; eGFR, estimated glomerular filtration rate; EuroSCORE, European System for Cardiac Operative Risk Evaluation; FAC, fractional area change; ICD, implantable cardioverter-defibrillator; LVEF, left ventricular ejection fraction; M + T-TEER, mitral and tricuspid transcatheter edge-to-edge repair; MLHFQ, Minnesota Living with Heart Failure Questionnaire; MR, mitral regurgitation; NT-proBNP, N-terminal pro-B-type natriuretic peptide; NYHA, New York Heart Association; RV, right ventricular; sPAP, systolic pulmonary artery pressure (estimated by echocardiography); TAPSE, tricuspid annular plane systolic excursion; TR, tricuspid regurgitation; T-TEER, tricuspid transcatheter edge-to-edge repair.

follow-up rate). Ten patients died before follow-up actigraphy. At short-term follow-up ($n = 100$ patients, median follow-up interval: 49 days), CPA significantly improved from 3108 (IQR 1350–4959) steps/day to 3958 (IQR 1823–5657) steps/day ($p < 0.001$; *Table 2*, *Figure 2A*, *Graphical Abstract*). At 1-year follow-up ($n = 91$ patients; 15 patients died before 1-year follow-up; median follow-up interval: 337 days), CPA increased to 4080 (IQR 2293–6514) steps/day ($p < 0.001$ compared with baseline CPA; *Table 2*, *Figure 2A*). Median CPA increased in 74 patients and decreased in 17 patients 1-year after TTVI – patient characteristics were similar between groups (online supplementary *Table S2*). Echocardiographic parameters for right ventricular function and load were not significantly associated with the change in CPA 1 year after TTVI in a linear regression model (online supplementary *Table S3*). To determine the number of patients with clinically significant improvement of CPA 1 year after TTVI, we set the effect size of CPA to 500 steps/day (effect size = 0.2 × standard deviation of baseline CPA). Clinically improvement of CPA by 500 steps/day was identified in 59% of all patients 1 year after TTVI.

The degree of residual TR after TTVI correlated with the extent of CPA improvement. In patients with residual TR grade ≤1+, 2+ and 3+, CPA improved by 40.0%, 26.0%, and 8.1% 1 year after TTVI, respectively (online supplementary *Figure S3*). Median CPA increased both in patients with reduced baseline left ventricular ejection fraction (LVEF <40%; 1-year CPA increase: +66.4%) and preserved baseline LVEF (>40%; 1-year CPA increase: +30.0%; both $p < 0.01$ compared to baseline CPA).

At 1-year follow-up, the high-performance days improved by 40.8% from 4756 (2584–7610) to 5156 (3211–9191) and the low-performance days improved by 75.1% from 1505 (529–2583) to 2172 (1048–3203), when compared with baseline actigraphy (both $p < 0.01$; *Table 2*, online supplementary *Figure S4*). The rate of patients with diuretic medication was similarly high before and after TTVI. The median furosemide equivalent dose remained unchanged between baseline evaluation and follow-up assessments (online supplementary *Table S4*).

To determine the extent to which our findings were driven by combined procedures, we repeated our analyses in the subgroup of patients ($n = 88$) who underwent isolated TTVI. Baseline characteristics of this subgroup are detailed in online supplementary *Table S5*. All actigraphy results of the complete study cohort were confirmed in the isolated TTVI subgroup (online supplementary *Table S6*). After isolated TTVI, median CPA significantly improved from 3184 (IQR 1473–5026) steps/day to 4018 (IQR 1938–5756) steps/day at short-term follow-up and 4140 (IQR 2111–6600) steps/day at 1 year after TTVI (both $p < 0.01$ when compared with baseline; online supplementary *Figure S5A*).

Improvement of activity after transcatheter tricuspid valve intervention according to baseline performance level

All patients were stratified according to their baseline CPA quartiles into low activity group (<Q1: <1350 steps/day), moderate activity group (IQR: 1350–4959 steps/day) and high activity group (>Q3: >4959 steps/day; *Graphical Abstract*). Patient characteristics of the different performance groups are detailed in *Table 3*. Patients with lower activity were at higher operative risk according to EuroSCORE II, were more symptomatic according to the NYHA classification (37% in NYHA class IV vs. 3% in high activity),

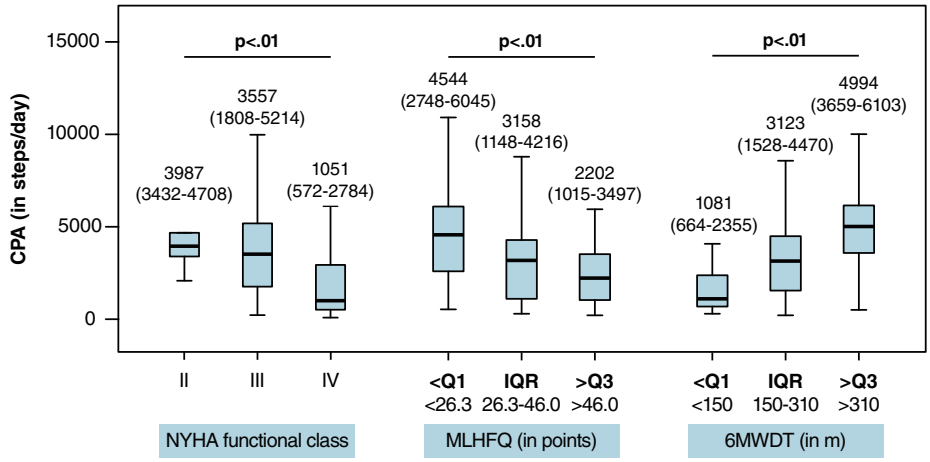


Figure 1 Actigraphy results are associated with conventional heart failure assessment. Continuous physical activity (CPA) in steps per day as assessed by actigraphy before transcatheter tricuspid valve intervention is significantly associated with New York Heart Association (NYHA) functional class (*left*), results from the Minnesota Living with Heart Failure Questionnaire (MLHFQ, *middle*) and 6-min walk distance test (6MWDT, *right*). MLHFQ and 6MWDT were stratified into three groups: below quartile 1 (<Q1), interquartile range (IQR), and above quartile 3 (>Q3). The middle horizontal line represents the median, the box shows the IQR, and error bars show the range of non-outlying data points (whiskers). The lower whisker shows the lowest data point within the 25th percentile minus 1.5 times IQR and the upper whisker shows the highest data point within the 75th percentile plus 1.5 times IQR.

Table 2 Actigraphy results

	Baseline (BL) (n = 128)	Short-term (FU1) (n = 100)	One-year (FU2) (n = 91)	p-value[a] (BL vs. FU1)	p-value[a] (BL vs. FU2)
Tracking period, days	7 (6–8)	7 (6–9)	7 (6–9)	0.11	0.40
CPA, steps/day	3108 (1350–4959)	3958 (1823–5657)	4080 (2293–6514)	**<0.001**	**<0.001**
High-performance day, steps/day	4721 (2078–7382)	5803 (3009–8408)	5166 (3510–8998)	**<0.01**	**<0.001**
Low-performance day, steps/day	1379 (565–2524)	1641 (819–3380)	2264 (1055–3570)	**<0.001**	**<0.001**
Resting heart rate, bpm	61 (57–66)	60 (57–63)	60 (57–64)	0.07	0.65
High heart rate, bpm	106 (99–116)	108 (99–118)	104 (96–114)	0.25	0.15

Values are median (interquartile range). BL, baseline; CPA, continuous physical activity; FU, follow-up.
[a]Wilcoxon matched-pairs signed rank test.

had a lower quality of life score and showed increased NT-proBNP levels (all p <0.05). Most patients stratified to the low activity group had TR grade 3+ (69%) and only 31% had TR grade 4+ before the intervention, and thus, there was correlation between TR severity at baseline and baseline actigraphy data.

Low activity <Q1 patients showed the greatest relative improvement of CPA after TTVI (change in short-term CPA: +87.1%, change in 1-year CPA: +121.3%, both p <0.001; *Figure 2B* red, *Graphical Abstract*). Clinically significant improvement of CPA 1 year after TTVI, defined as CPA improvement of 500 steps/day, was observed in 76% of patients of the low activity group (19 of 25 patients).

Moderate activity IQR patients also benefited from TTVI and CPA improved significantly, when compared to baseline CPA (change in short-term CPA: +32.1%, change in 1-year CPA: +27.5%, both p <0.001; *Figure 2B* blue, *Graphical Abstract*). Clinically significant improvement of CPA 1 year after TTVI was identified in 60% of patients of the moderate activity group (26 of 43 patients).

In contrast, CPA of high activity >Q3 patients remained unchanged after TTVI (change in short-term CPA: −3.5%, change in 1-year CPA: +2.6%; p = 0.63 and p = 0.52; *Figure 2B* green, *Graphical Abstract*). Clinically significant improvement of CPA 1 year after TTVI was determined only in 39% of patients of the high activity group (9 of 23 patients). However, patients of all performance groups showed significant and persistent symptomatic improvements after TTVI according to the NYHA functional class when compared to the baseline assessment (all p <0.001; *Figure 3*). Survival of all performance groups was similar within the first year after TTVI (*Figure 4*). A combined endpoint of mortality and heart failure hospitalization within the first year was similar between the performance groups (online supplementary *Figure S6*). The findings were confirmed in a sub-analysis of patients undergoing isolated TTVI (online supplementary *Figure S5B*).

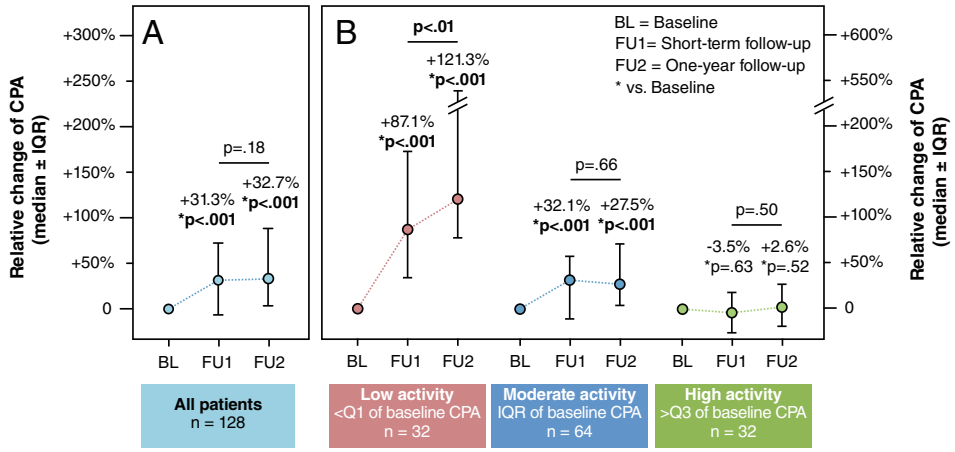


Figure 2 Improvement of physical activity following transcatheter tricuspid valve intervention (TTVI). (*A*) Relative change of continuous physical activity (CPA) in steps per day of all patients undergoing TTVI at short-term follow-up (FU1) and 1-year follow-up (FU2), compared to baseline (BL) assessment, respectively. (*B*) Relative change of CPA in steps per day according to different performance groups. Patients were stratified by baseline CPA before TTVI into low activity group (<quartile [Q] 1 of baseline CPA: <1350 steps/day, *red*), moderate activity group (interquartile range [IQR] of baseline CPA: 1350–4959 steps/day, *blue*) and high activity group (>Q3 of baseline CPA: >4959 steps/day, *green*). CPA at FU1 and FU2 after TTVI was analysed and compared to BL assessment. Dots represent the median and error bars show the IQR.

Table 3 Patient characteristics by performance group

	Low activity (<Q1 of baseline CPA) (*n* = 32)	Moderate activity (IQR of baseline CPA) (*n* = 64)	High activity (>Q3 of baseline CPA) (*n* = 32)	*p*-value
Age, years	80 (75–84)	79 (76–82)	78 (75–82)	0.89
Female sex	21 (66)	28 (44)	12 (38)	0.06
Body mass index, kg/m^2	26.4 (23.6–28.0)	24.8 (22.4–28.1)	24.1 (22.4–25.7)	0.07
EuroSCORE II, %	5.7 (4.4–8.3)	4.3 (2.9–6.0)	3.6 (2.2–5.5)	**<0.01**
Transcatheter intervention				0.59
Isolated tricuspid annuloplasty	1 (3)	1 (2)	1 (3)	
Isolated T-TEER	19 (59)	45 (70)	21 (66)	
Combined M + T-TEER	12 (38)	18 (28)	10 (31)	
NYHA functional class				**<0.001**
II	0 (0)	4 (6)	1 (3)	
III	20 (63)	51 (80)	30 (94)	
IV	12 (37)	9 (14)	1 (3)	
MLHFQ, points	41 (33–52)	38 (26–46)	31 (22–42)	**<0.05**
NT-proBNP, ng/L	5193 (2117–8028)	2046 (1115–4073)	1174 (1134–3185)	**<0.01**
LVEF, %	51 (43–60)	56 (50–62)	60 (50–64)	0.13
RV TAPSE, mm	17 (15–19)	18 (15–21)	17 (15–23)	0.58
Estimated sPAP, mmHg	42 (32–54)	41 (33–49)	36 (31–49)	0.58
TR severity, grade				0.55
1+, mild	0 (0)	0 (0)	0 (0)	
2+, moderate	0 (0)	2 (3)	0 (0)	
3+, severe	22 (69)	34 (53)	18 (56)	
4+, massive	10 (31)	28 (44)	14 (44)	

Values are *n* (%), or median (IQR). CPA continuous physical activity; EuroSCORE, European System for Cardiac Operative Risk Evaluation; IQR, interquartile range; LVEF, left ventricular ejection fraction; M + T-TEER, mitral and tricuspid transcatheter edge-to-edge repair; NT-proBNP, N-terminal pro-B-type natriuretic peptide; NYHA, New York Heart Association; Q1, first quartile; Q3, third quartile; RV, right ventricular; sPAP, systolic pulmonary artery pressure (estimated by echocardiography); TAPSE, tricuspid annular plane systolic excursion; TR, tricuspid regurgitation; T-TEER, tricuspid transcatheter edge-to-edge repair.

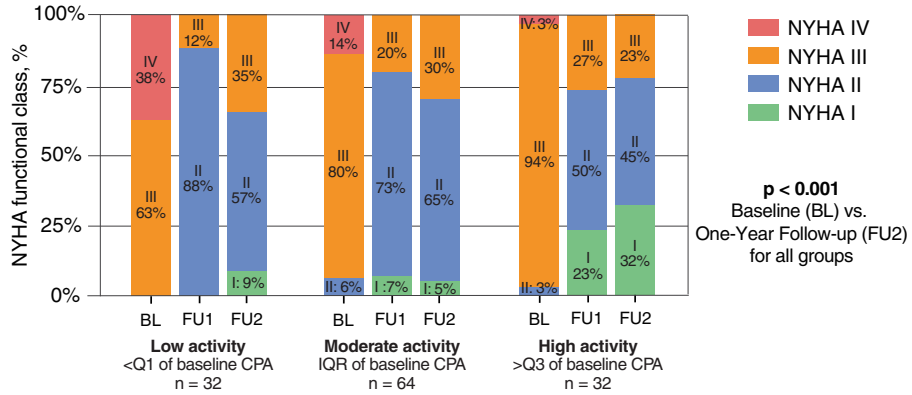


Figure 3 Improvement of New York Heart Association (NYHA) functional class after transcatheter tricuspid valve intervention according to different performance groups. Patients were stratified by baseline continuous physical activity (CPA) before TTVI into low activity group (<quartile [Q] 1 of baseline CPA: <1350 steps/day, *left*), moderate activity group (interquartile range [IQR] of baseline CPA: 1350–4959 steps/day, *middle*) and high activity group (>Q3 of baseline CPA: >4959 steps/day, *right*). NYHA functional class was assessed for each group at baseline (BL), short-term follow-up (FU1) and 1-year follow-up (FU2).

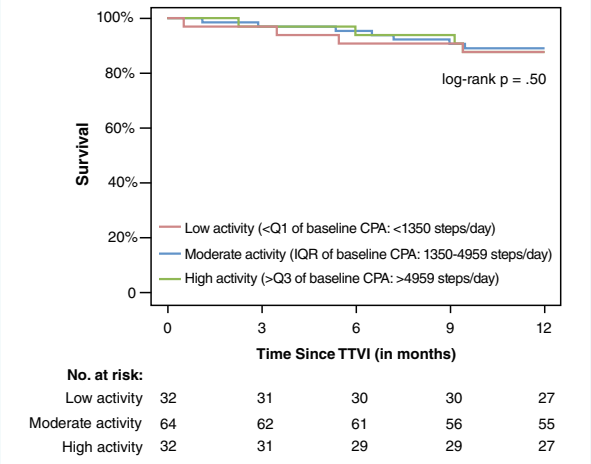


Figure 4 Survival after transcatheter tricuspid valve intervention (TTVI) according to different performance groups. Survival analysis of patients stratified by baseline continuous physical activity (CPA) into low activity (<quartile [Q] 1 of baseline CPA: <1350 steps/day, *red*), moderate activity (interquartile range [IQR] of baseline CPA: 1350–4959 steps/day, *blue*) and high activity (>Q3 of baseline CPA: >4959 steps/day, *green*).

Discussion

Heart failure patients with clinically significant TR are often deemed inoperable and suffer from high mortality as well as reduced activity levels and limited physical capacity.[3,18] This is the first study to report long-term actigraphy data from a cohort of patients with underlying significant TR treated with TTVI. Furthermore, the large cohort of patients undergoing TTVI allows for a patient stratification by baseline activity. In this study, we found that TTVI was associated with sustained functional improvement (as measured by actigraphy). In addition, we found that the greatest relative improvements occurred in patients with very low activity levels before the intervention. The results of this study are of high relevance for an increasing patient population treated with TTVI and may further improve the patient selection process.

An important finding of our study was demonstrating that 1-week actigraphy with a simplified patient protocol was associated with high device adherence rates and enabled assessment of the real-life physical capacity with significant association with NYHA functional class, quality of life and in-hospital physical performance tests. We aimed to assess at least five consecutive days for representative recording of the physical activity in the real-life environment. In this analysis, the median tracking period of all patients was 7 days and at least five consecutive days were recorded in 90% of all activity tracking phases. This finding as well as the high intraday device adherence (>90% at all time points) demonstrate the feasibility of our 1-week actigraphy approach with a simplified protocol, meeting the needs of an elderly and frail patient population.

The overall results from the entire patient population show that TTVI impacts physical capacity and is associated with early improvement of activity which is sustained at 1 year after the procedure. Improvement of heart failure symptoms in response to TTVI has been reported earlier.[8,9,19,20] However, most of these studies estimated the change in physical activity only by more subjective quality of life questionnaires and the assessment of NYHA functional class. Some studies also used the 6MWDT for the assessment of physical activity; however, the 6MWDT is recorded, by definition, during a short 6-min interval and is usually evaluated in an artificial in-hospital environment.[9] The 6MWDT is affected by the patient's intrinsic motivation and may be biased by hospital staff. We believe that actigraphy allows for a more unbiased, objective monitoring of physical capacity in everyday life, independent of in-hospital or outpatient visits. Using this method, we found that not only did the mean steps per day

of the entire tracking period increase significantly after TTVI, but also the measured low-performance and high-performance days showed a significant increase after TTVI. These findings demonstrate improvement of the general physical performance level in response to TTVI.

Importantly, we stratified patients into difference performance groups before TTVI using baseline actigraphy data. Patients stratified to the low baseline activity group (baseline CPA <1350 steps/day) were more severely diseased, when compared to the moderate or high baseline activity groups, as suggested by advanced heart failure symptoms, high NT-proBNP levels and high operative risk according to EuroSCORE II. Interestingly, this severely diseased advanced heart failure patient population with very low baseline activity showed the greatest relative benefit from TTVI with sustained post-procedural improvement of physical capacity. These findings are important, because a substantial proportion of heart failure patients with severe TR present with markedly reduced physical capacity and advanced heart failure symptoms, and thus, might be rejected by the heart team for tricuspid valve therapies due to reduced functional capacity. Our data strongly suggest that especially this extremely symptomatic patient population benefits from TTVI and their functional capacity might be improved. Patients with moderate baseline activity (baseline CPA 1350 to 4959 steps/day) also benefited from TTVI as demonstrated by an additional and significant increase of actigraphy results. In contrast, patients with already high baseline activity before the intervention (baseline CPA >4959 steps/day) showed no enhanced physical performance following TTVI in our study. However, TTVI was associated with similar durable symptomatic improvement as estimated by NYHA functional class in all performance groups – even in the high baseline activity group. Importantly, mortality during the first year after TTVI was similar in all performance groups, and thus, the differences between performance groups was not affected by different survival rates.

In an additional subgroup analysis with patients undergoing isolated TTVI, we demonstrate comparable improvement of physical activity suggesting that the results are induced by the intervention at the tricuspid valve. We identified a similar improvement of the physical capacity 1 year after isolated TTVI, when compared to the complete study cohort that included 31% of patients with combined mitral and tricuspid intervention. Similarly, patients with very low physical activity prior to the intervention showed the highest relative improvement of physical activity after isolated TTVI. The results from the subgroup analysis demonstrate that the observed improvement in physical activity was induced by the reduction of TR as clinically leading pathology and not simply dictated by concomitant mitral valve intervention.

Several limitations must be considered when interpreting the findings. Although the present study with actigraphy data in patients undergoing TTVI is the largest thus far, the number of patients is still limited. The study is based on a single-centre experience and does not include a control group of patients without TTVI. All patients were highly selected and evaluated by an interdisciplinary heart team, and thus, clinical considerations in the TTVI selection process might have led to the exclusion of certain patients.

Conclusions

In conclusion, the results from this study demonstrate that TTVI improves physical activity in patients with heart failure and underlying TR. The results further suggest that TTVI might reverse the functional progression of heart failure in selected patients. Importantly, patients with a remaining but significantly reduced activity as well as high morbidity before the procedure also significantly benefit from TTVI and should not be excluded from the intervention.

Supplementary Information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

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