

**Supplementary material:****Table S1.** Pattern of Beta-blocker use among patients discharged with a diagnosis of Takotsubo syndrome

	<b>Full cohort (n=519)</b>	<b>Survival free of recurrence (n=402)</b>	<b>Death or recurrence (n=117)</b>	<b>P value</b>
<b>Baseline use:</b> <b>Beta-blocker prescription prior to index admission*</b>	102 (19.7)	77 (19.2)	25 (21.4)	0.60
<b>First year of diagnosis:</b> <b>At least one beta-blocker prescription filled within one year of index admission</b>	447 (86.1)	356 (88.6)	91 (77.8)	0.003
<b>Persistent use after one year of diagnosis:</b> <b>At least one beta-blocker prescription filled one-year after index admission</b>	337 (64.9)	272 (67.7)	65 (55.6)	0.016
<b>Persistent use at the end of follow-up:</b> <b>Beta-blocker use at the end of the follow-up period †</b>	260 (50.1)	211 (52.5)	49 (41.9)	0.043
<b>Proportion of days covered (PDC):</b> <b>Beta-blocker PDC during the entire follow-up period ‡</b>	0.57 ± 0.41	0.59 ± 0.41	0.50 ± 0.39	0.047
<b>Adherence:</b> <b>Beta-blocker PDC ≥ 80% ^</b>	254 (48.9)	212 (52.7)	42 (35.9)	0.001
<b>Dose:</b> <b>Medium to high beta-blocker dose §</b>	94 (18.1)	72 (17.9)	22 (18.8)	0.83

values are n(%) or mean ± standard deviation

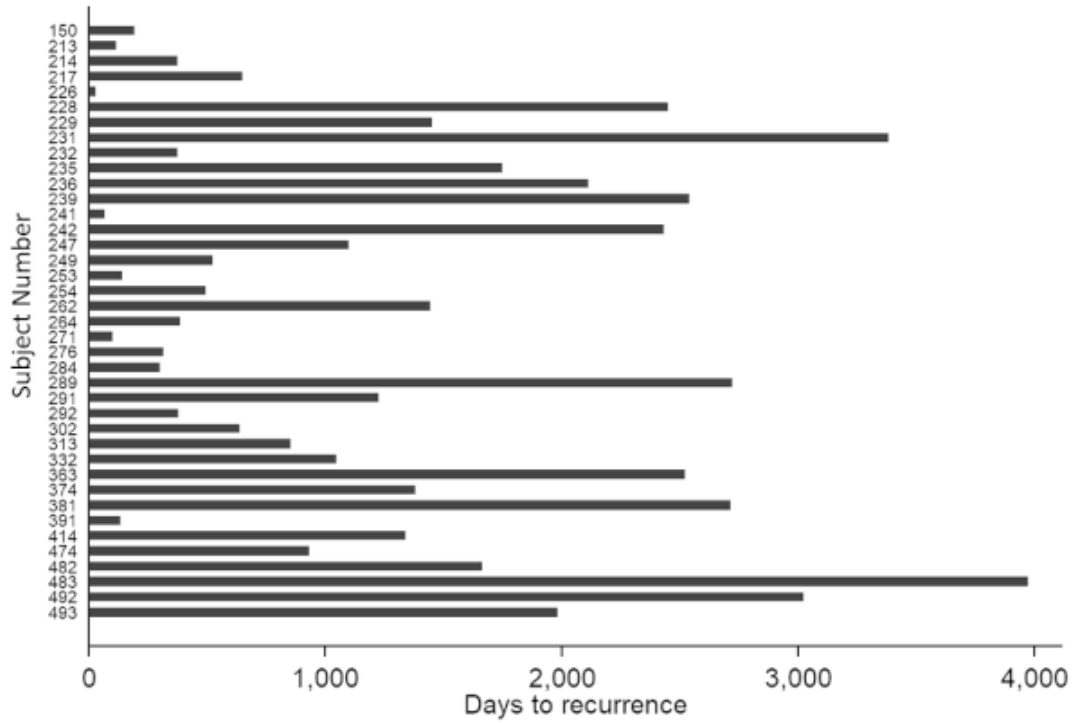
\* defined as at least one beta-blocker prescription filled within 3 months prior to the index admission.

† defined as having a least one beta-blocker prescription filled within 3 months prior to the end of follow-up (follow-up ends at the time of death, time of recurrence or the end of the study).

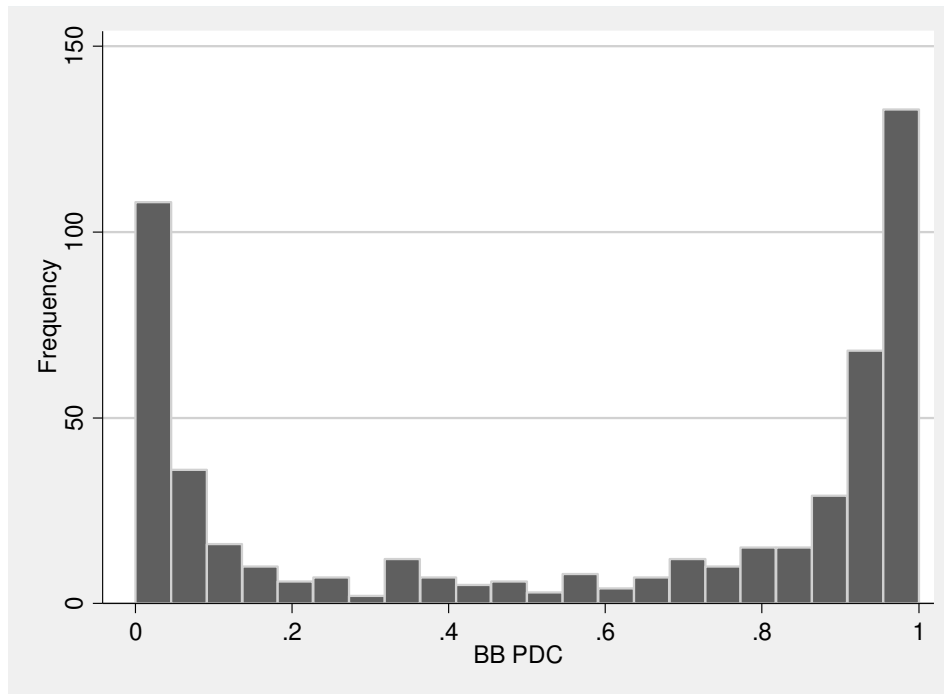
‡ defined as the “days supply of medication dispensed to the patient” divided by the “total follow-up time”

^ defined as number of patients whose proportion of days covered is >80%

§ Medium to high beta-blocker dose is defined as the equivalent or higher than carvedilol 12.5mg twice a day.

**Figure S1.** Number of days to first recurrence of takotsubo syndrome.

**Figure S2.** Beta-blocker prescription pattern based on proportion of days covered during the entire follow-up period



**Table S2.** Association between beta-blocker use and recurrence or death.

	Univariable		Multivariable*	
	HR (95% CI)	P value	HR (95% CI)	P value
<b>BB use within 1 year of diagnosis (all patients)</b>	0.53 (0.35-0.83)	0.005	0.46 (0.29-0.72)	0.001
<b>BB use within 1 year of diagnosis (excluding patients with baseline BB use)</b>	0.54 (0.33-0.88)	0.013	0.53 (0.32-0.86)	0.011
<b>BB proportion of days covered (PDC) <math>\geq</math> 80%</b>	0.51 (0.35-0.74)	0.001	0.40 (0.27-0.59)	<0.001
<b>BB proportion of days covered (per 10% increase)</b>	0.95 (0.91-0.99)	0.018	0.92 (0.88-0.96)	<0.001

\* Multivariable analyses were adjusted for age, sex, diabetes, chronic obstructive pulmonary disease / asthma, and chronic kidney disease.

† BB dose measured per mg increase in carvedilol dose.

BB = beta-blockers

**Table S3.** Univariable and Multivariable Models using Joint Survival and Longitudinal (Time-Varying) Exposure Modeling for Assessing the Association of Beta-Blocker Proportion of Days Covered with Recurrence or Death

	Univariable		Multivariable Model*	
	HR (95% CI)	P Value	HR (95% CI)	P Value
<b>Beta-blocker proportion of days covered (per 10% increase)</b>	0.84 (0.77-0.92)	<0.001	0.78 (0.71-0.85)	<0.001

HR=hazard ratio; CI=confidence interval. \* multivariable modeling included the following variables: age, male, diabetes, chronic kidney disease and pulmonary disease.

**Table S4.** Characteristics of stress cardiomyopathy cohort stratified by beta-blocker proportion of days covered (BB PDC) <80% vs. ≥80%. unadjusted and IPTW-adjusted.

Characteristic	Unweighted Cohorts			IPTW-weighted cohorts		
	BB PDC < 80% (n = 265)	BB PDC ≥ 80% (n = 254)	Std Diff, %	BB PDC < 80% (n = 265)	BB PDC ≥ 80% (n = 254)	Std Diff, %
Age, Mean (SD)	66.5 (11.73)	70.0 (10.74)	30.6	68.3 (11.49)	68.5 (11.23)	1.7
Male, n (%)	21 (7.9%)	14 (5.5%)	9.6	19 (7%)	18 (7%)	0.1
White, n (%)	168 (63.4%)	164 (64.6%)	2.4	170 (64%)	161 (63.4%)	1.4
Income ≤ \$45k, n (%)	66 (24.9%)	55 (21.7%)	7.7	62 (23.2%)	60 (23.5%)	0.7
Diabetes, n (%)	47 (17.7%)	64 (25.2%)	18.2	59 (22.3%)	56 (22.2%)	0.4
Pulmonary Disease, n (%)	73 (27.5%)	62 (24.4%)	7.2	4 (1.3%)	3 (1%)	0.2
Chronic kidney disease, n (%)	38 (14.3%)	43 (16.9%)	7.1	43 (16.1%)	42 (16.4%)	0.9
Hyperlipidemia, n (%)	134 (50.6%)	165 (65%)	29.5	153 (57.8%)	148 (58.2%)	0.8
History of stroke, n (%)	23 (8.7%)	30 (11.8%)	10.3	29 (10.9%)	28 (11%)	0.4
Hypertension, n (%)	153 (57.7%)	195 (76.8%)	41.4	179 (67.6%)	173 (68.3%)	1.5
Dementia, n (%)	2 (0.8%)	3 (1.2%)	4.4	2 (0.8%)	2 (0.9%)	1.5
Pulmonary Disease, n (%)	73 (27.5%)	62 (24.4%)	7.2	69 (26%)	66 (25.9%)	0.2
Rheumatic Disease, n (%)	16 (6%)	10 (3.9%)	9.7	13 (4.9%)	12 (4.6%)	1.5
Neurologic Disorder, n (%)	19 (7.2%)	20 (7.9%)	2.7	22 (8.3%)	19 (7.5%)	3
Hypothyroidism, n (%)	44 (16.6%)	44 (17.3%)	1.9	45 (17%)	41 (16.2%)	2.3
Liver Disease, n (%)	7 (2.6%)	10 (3.9%)	7.3	7 (2.8%)	9 (3.6%)	4.7
Obesity, n (%)	50 (18.9%)	61 (24%)	12.6	58 (22%)	56 (21.9%)	0.2
Depression, n (%)	78 (29.4%)	75 (29.5%)	0.2	80 (30.1%)	74 (29.3%)	1.8

**Table S5.** Association between beta-blocker use and recurrence or death.

	<b>Unadjusted</b>		<b>IPTW-adjusted</b>	
	<b>HR (95% CI)</b>	<b>P value</b>	<b>HR (95% CI)</b>	<b>P value</b>
<b>BB proportion of days covered (PDC) <math>\geq</math> 80%</b>	0.51 (0.35-0.74)	<0.001	0.45 (0.31-0.66)	<0.001

BB = beta-blockers