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ORIGINAL ARTICLE

Risk factors of readmission and the impact of outpatient management in heart failure patients: A national study in Japan

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Abstract

Aims Heart failure is a significant disease, and its high readmission rate is a big concern. We must identify readmission risk factors and optimize outpatient management to prevent them. This study aims to investigate the readmission risk factors, including outpatient management represented by the number of outpatient visits, and to identify the factors related to frequent outpatient visits.

Methods and results We used the diagnosis-procedure-combination database between April 2016 and March 2022. Based on the number of outpatient visits within 60 days after discharge, we categorized patients into <1 visits/month, (1<, ≦2) visits/month, and <2 visits/month and observed the occurrence of 60 days readmission. We performed multiple logistic regression analyses to reveal the readmission risk factors and the association between the number of outpatient visits and readmission. As a subgroup analysis, we conducted the same research in the low- and high-readmission risk groups. We compared medical contents between (1<, ≦2) visits/month and <2 visits/month. We analysed 101 239 patients and identified the following factors as a risk of readmission: older age ($P < 0.001$), female ($P = 0.009$), longer length-of-hospital-stay ($P < 0.001$), artificial ventilator ($P < 0.001$), tolvaptan ($P < 0.001$), top 50% dosage of loop diuretics ($P = 0.036$), bottom 50% dosage of class III antiarrhythmic agents ($P < 0.001$), hypertension ($P = 0.005$), atrial fibrillation ($P < 0.001$), dilated cardiomyopathy ($P < 0.001$), valvular disease ($P = 0.021$), myocardial infarction ($P < 0.001$), diabetes ($P < 0.001$), and renal disease ($P < 0.001$). We revealed that the risk of readmission increases in <2 visits/month compared to (1<, ≦2) visits/month ($P < 0.001$), whereas the risk of readmission decreases in ≦1 visits/month compared with (1<, ≦2) visits/month ($P < 0.001$). In the subgroup analysis, we found the possibility that some risk factors are specific to the subgroup. We identified that the following factors were related to frequent outpatient visits: older age ($P < 0.001$), home medical care ($P = 0.007$), tolvaptan ($P < 0.001$), top 50% dosage of loop diuretics ($P < 0.001$), diabetes ($P < 0.001$), renal disease ($P = 0.009$), 0–2 weeks follow-up ($P < 0.001$), 2–4 weeks follow-up ($P < 0.001$), cardiac rehabilitation ($P < 0.001$), and echocardiography ($P < 0.001$).

Conclusions This study comprehensively identified risk factors for readmission and found outpatient visit is personalized by readmission risk. There is still room to optimize outpatient management. We suggest optimizing outpatient management according to our identified characteristics.

Keywords Diagnosis-procedure-combination; Heart failure; Outpatient care; Readmission

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Introduction

Heart failure is a common disease, with an estimated 26 000 000 patients worldwide.[1] And the number of heart failure patients is expected to increase globally and in Japan.[2] Also, it is known that the readmission rate in patients with heart failure is high because of its distinctive prognosis of repeated exacerbation.[3,4] Furthermore, earlier studies

have reported that repeated readmission impairs the patients' outcomes, including mortality, the activity of daily living, and quality of life, and increases the economic burden on society.[5–8] Thus, preventing readmission in patients with heart failure is a big concern from the point of individual and society. In particular, it is necessary to continue outpatient management after discharge to prevent readmission. However, regarding outpatient management after discharge, some studies evaluate the efficacy of early outpatient follow-up or introducing a heart failure clinic. Still, few studies have examined the association between readmission and the number of outpatient visits in patients with heart failure. Also, no study has comprehensively identified readmission risk factors using outpatient data from the Japanese national database. So readmission risk factors, including outpatient management represented by the number of outpatient visits, should be revealed.

Moreover, although the outpatient medical system differs from country to country, it is essential to optimize outpatient management from the burden on physicians and patients, financial resources, and so on in all countries. To maximize outpatient management, we should clarify the characteristics of frequent outpatient patients. In contrast, few studies described the characteristics of patients with frequent outpatient visits. Therefore, we need to establish evidence on factors related to frequent outpatient visits in patients with heart failure and optimize it.

This study aims to reveal the factors associated with 60 days readmission, including outpatient management represented by the number of outpatient visits within 60 days after discharge, and to identify the characteristics of patients with frequent outpatient visits.

Methods

Design and data source

This retrospective observational study used the inpatient and outpatient data from Diagnosis-Procedure-Combination (DPC) database.[9,10] The database includes sex, age, body mass index (BMI), diagnoses coded with the International Classification of Diseases 10th Revision (ICD-10) coded and written in Japanese, all medications administered daily during hospitalization, and medical procedures performed. The DPC database was collected from approximately 1100 facilities across Japan. The data reflect the actual clinical practice in the country, covering 92% of all tertiary-care emergency hospitals in Japan.[11] This database is used widely in medical and health research.[12,13] The institutional review board approved this study of Tohoku University (No. 2021-1-1082). Informed consent was not required because of the anonymous nature of the DPC database. The investigation conforms with the principles outlined in the Declaration of Helsinki (Br Med J 1964; ii: 177).

Patient selection

In the DPC data between April 2016 and March 2022, we included patients who met the following criteria: (i) patients admitted between April 2016 and March 2022; (ii) patients who were under the age of 20; and (iii) patients whose most resource-consuming diagnosis was heart failure. Based on the ICD-10 codes, we identified heart failure as I50.0, I50.1, and I50.9.[14] We excluded patients who met following criteria: (i) patients with planned readmission; (ii) patients who readmitted after 60 days or more from their discharge at index admission; (iii) patients whose readmission- precipitating diagnosis was not heart failure; (iv) patients who readmitted second or subsequent time to avoid reflecting the characteristics of same patient, defining first readmission in our study period as readmission if same patient readmitted multiple times; (v) patients whose index admission was between April 2016 and May 2016 to check the index admission was not 60 days readmission; (vi) patients whose index admission was between February 2022 and March 2022 for complete 60 days follow-up; (vii) patients who died in hospital at index admission; (viii) patients whose discharge disposition at index admission was not 'home, attending with their own hospital'; (ix) patients with cancer (ICD-10 codes; C00-C26, C30-C34, C37-C41, C43, C45-C58, C60- C76, C81-C85, C88, C90-C97); (x) patients with dialysis; (xi) patients with no outpatient visit for 60 days after discharge; (xii) patients who readmitted within 14 days because these patients are not the main beneficiaries of the number of outpatient visits and bias may be occurred in these patients in the calculation of the number of outpatient visits, which is articulated later; and (xiii) patients who visit hospital that outpatient data was not completely submitted. We also excluded patients with missing these data.

Variables

We determined variables to extract based on the former studies and existing knowledge. As for the baseline data at index admission, we extracted age, sex, BMI, Barthel index (BI) at discharge, smoking status, home medical care after discharge, length-of-hospital-stay (LOS), intensive care unit (ICU), artificial ventilator, and following co-morbidities: myocardial infarction (ICD-10 codes: I21, I22, and I252), dilated cardiomyopathy (ICD-10 codes: I420), hypertension (ICD-10 codes: I10–I15), valvular disease (ICD-10 codes: I05–I08, I091, I34–I38, I390, I391, I392, I393, and I394), diabetes (ICD-10 codes: E10–E14), renal disease (ICD-10 codes: N18, N19, N052, N053, N054, N055, N056, N057, N250, I120, I131, N032, N033, N034, N035, N036, N037, Z490, Z491, Z492, Z940, and Z992), atrial

fibrillation (ICD-10 codes: I48), chronic pulmonary disease (ICD-10 codes: J40–J47, J60–J67, I278, I279, J684, J701, and J703), and cerebrovascular disease (ICD-10 codes: G45, G46, I60–I69, and H340). As for the outpatient data, we extracted the number of outpatient visits within 60 days after discharge, outpatient cardiac rehabilitation within 60 days after discharge, outpatient brain natriuretic peptide (BNP) test within 60 days after discharge, outpatient echocardiography within 60 days after discharge, 0–2 weeks follow-up after discharge, 2–4 weeks follow-up after discharge, and following outpatient prescriptions and its maximum of the dosage in a day within 60 days after discharge: beta-blockers, angiotensin II receptor blockers/angiotensin-covering enzyme inhibitors (ARB/ACEI), mineralocorticoid receptor antagonists (MRA), tolvaptan, loop diuretics, and class III antiarrhythmic agents. As for the number of outpatient visits, the number in the readmission group seems to be lower than in the no-readmission group because the readmission group's observation period is shorter than the no-readmission group. To eliminate this bias, the number of outpatient visits is calculated as follows: the number of outpatient visits within readmission from discharge is divided by days within readmission from discharge in the readmission case, and the number of outpatient visits within 60 days is divided by 60 days in the no-readmission case. Then, we multiply these values by 30 days to calculate the number of outpatient visits per month.

The World Health Organization classified BMI as under 18.5 kg/m^2, between 18.5 and 30 kg/m^2, and over 30 kg/m^2.[15] Also, age was classified as under 64, between 65 and 74, and over 75. Smoking status was classified as smoking and no-smoking. BI at discharge was classified as under 59 and over 60. Age, smoking status, and BI were classified according to previous studies.[16–19] As for LOS, we used it as a continuous variable because there is no standard grouping method for LOS like BI and BMI. Outpatient prescriptions were classified as no-prescription, with a dosage between minimum and median (bottom 50%) and between median and maximum (top 50%). If there was little variation in the dosage, that was classified as no prescription and prescription. The number of outpatient visits was classified as less than or equal to one visit per month (≦1 visit/month), over one and less than or equal to two visits per month ((1<, ≦2) visits/month), and over two visits per month (<2 visits/month).

Outcomes

The primary outcome of this study was 60 days readmission. We defined 60 days readmission as an admission caused within 60 days from the discharge at index admission, and their readmission-precipitating diagnosis was heart failure.

Statistical analysis

We presented categorical variables as numbers and percentages and continuous variables as average and standard deviation. Using the χ^2 test and analysis of variance, we compared categorical and continual variables, respectively. We conducted multiple logistic regression analyses to identify the readmission risk factors, including the number of outpatient visits. We included all variables described in the part of variables as independent variables in the model. Also, we used the presence of readmission as a dependent variable. We checked the correlation coefficients between each variable to satisfy the independence of the variables. All the correlation coefficients were under 0.7, and we considered all variables independent. Then, we performed a complete case analysis. We conducted multiple logistic regression analyses in the low and high readmission risk groups as a subgroup analysis. We defined the low readmission risk group as a population consisting of patients who have no factors that met all of the following criteria in overall logistic regression analysis: (i) statistically significant variables; (ii) variables that have regression coefficients higher than 0.2 to select higher readmission risk factors; and (iii) variables that prevalence or using percentage is under 50% to prevent to be too small population. We defined the high readmission risk group as the population that excluded patients in the low readmission risk group.

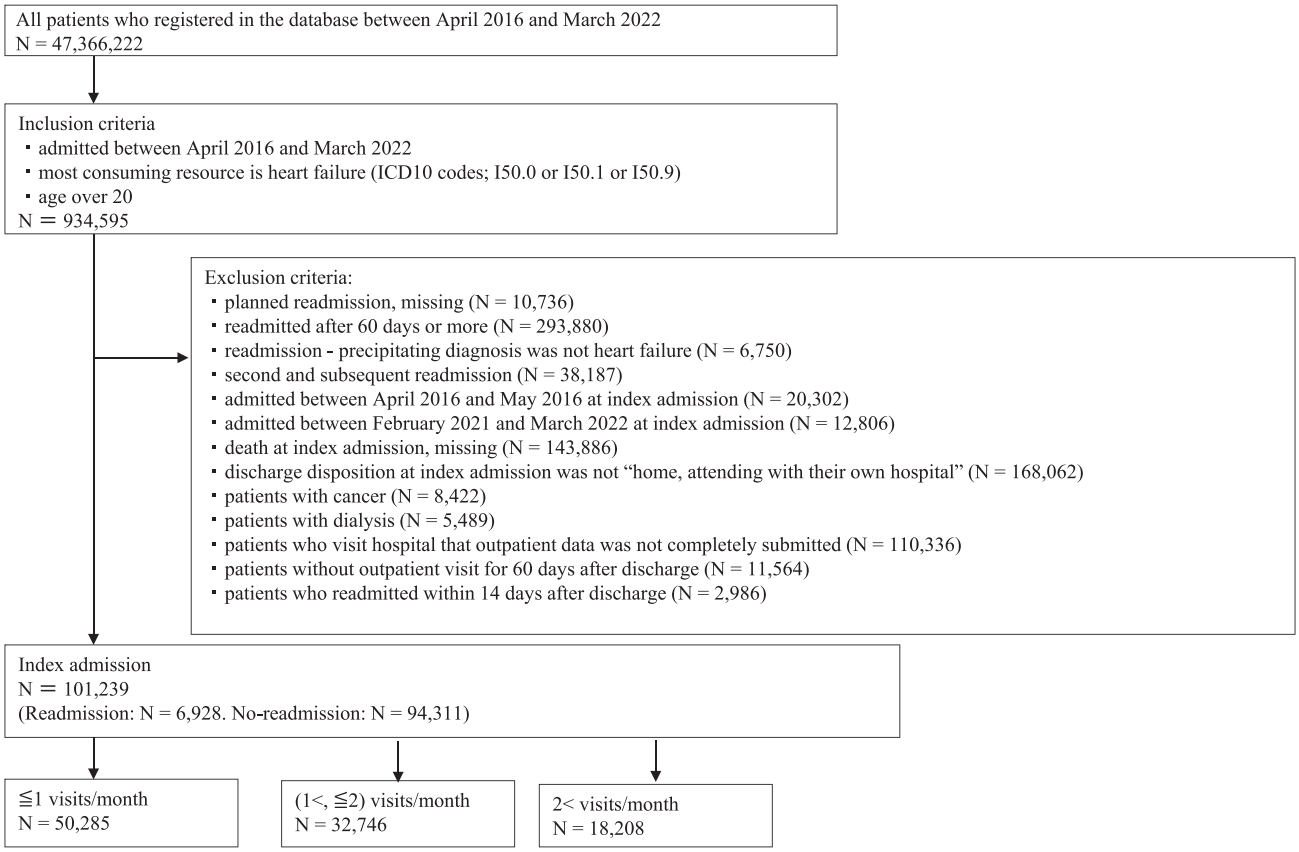
We also performed multiple logistic regression to compare medical contents between (1<, ≦2) visits/month and <2 visits/month. Again, we included all variables other than the number of outpatient visits as independent variables in the model. Also, we used the presence of (1<, ≦2) visits/month or <2 visits/month as a dependent variable.

All P values were two-tailed, and we considered $P < 0.05$ statistically significant. We performed all statistical analyses using SPSS version 28.0.0.0 for Windows (IBM Corp., Armonk, NY, USA).

Results

Figure 1 shows the patient selection flow. As a result, 101 239 cases were identified as index admission. Fifty thousand two hundred eighty-five patients, 32 746 patients, and 18 208 patients were categorized into ≦1 visits/month, (1<, ≦2) visits/month, and <2 visits/month, respectively. In total, 6928 patients were readmitted. As for the outpatient prescription, the dosages that include the median are the following: 2.5 mg for beta-blockers, 8 mg for ARB/ACEI, 7.5 mg for tolvaptan, 25 mg for MRA, 30 mg for loop diuretics, and 100 mg for class III antiarrhythmic agents. Regarding tolvaptan and MRA, 44.7% and 72.4% of patients were included in the median, respectively. Thus, we considered there was little variation in the dosage and classified these

Figure 1 Patient selection flow. ICD-10, International Classification of Diseases, 10th Revision, N, number of patients.



two drugs into no-prescription and prescription. Other drugs were classified into no-prescription, top 50%, and bottom 50%.

Table 1 shows the unadjusted characteristics of patients of each group. There were significant differences in age, sex, home medical care after discharge, BI, smoking status, BMI, ICU, beta-blockers, ARB/ACEI, tolvaptan, MRA, loop diuretics, class III antiarrhythmic agents, hypertension, atrial fibrillation, valvular disease, cerebrovascular disease, diabetes, renal disease, 0–2 weeks follow-up, 2–4 weeks follow-up, outpatient cardiac rehabilitation, outpatient BNP test, outpatient echocardiography, LOS, and 60 days readmission rate.

Table 2 shows the result of multiple logistic regression. We identified the following risk factors for readmission: older age, female, longer LOS, artificial ventilator, tolvaptan, top 50% dosage of loop diuretics, bottom 50% dosage of class III antiarrhythmic agents, hypertension, atrial fibrillation, dilated cardiomyopathy, valvular disease, myocardial infarction, diabetes, and renal disease. Higher BI, higher BMI, ICU, beta-blockers, ARB/ACEI, MRA, bottom 50% dosage of loop diuretics, 0–2 weeks follow-up, 2–4 weeks follow-up, outpatient cardiac rehabilitation, outpatient BNP test, and outpatient echocardiography were identified as factors that decrease the risk of readmission. As for the association between the number of outpatient visits and readmission, the risk of readmission increases in <2 visits/month compared with (1<,≦2) visits/month ($P < 0.001$), whereas the risk of readmission decreases in ≦1 visits/month compared to (1<, ≦2) visits/month ($P < 0.001$).

Table 3 shows the result of the subgroup analysis in the low readmission risk group. First, we defined the low readmission risk group according to how we articulated it in the Methods part. Then, we defined the low readmission risk group as the population that consists of patients with none of the following factors: artificial ventilator, tolvaptan, class III antiarrhythmic agents, atrial fibrillation, dilated cardiomyopathy, myocardial infarction, and renal disease. As a result, the risk factors identified in this group were older age, longer LOS, hypertension, diabetes, and the top 50% dosage of loop diuretics. Higher BI, higher BMI, top 50% dosage of beta-blockers, ARB/ACEI, MRA, 0–2 weeks follow-up, 2–4 weeks follow-up, outpatient cardiac rehabilitation, outpatient BNP test, and outpatient echocardiography decreased the risk of readmission. As for the association between the number of outpatient visits and readmission, the risk of readmission increases in <2 visits/month

Table 1 Unadjusted patients' characteristics

Number of outpatient visits per month	≦1		(1<, ≦2)		>2		
	Percentage (average)	Number (SD)	Percentage (average)	Number (SD)	Percentage (average)	Number (SD)	*P*-value
101 239	49.67%	50 285	32.35%	32 746	17.99%	18 208	
Age							<0.001
≦64	19.53%	9819	22.34%	7316	24.29%	4423	
65≦, <75	20.03%	10 073	22.16%	7256	25.09%	4569	
≦75	60.44%	30 393	55.50%	18 174	50.62%	9216	
Sex (male)	58.14%	29 238	60.65%	19 859	63.10%	11 490	<0.001
Length-of-hospital-stay	18.34	14	19.19	16	20.15	19	<0.001
Home medical care	3.76%	1883	4.15%	1352	4.50%	816	<0.001
Barthel index (≦60)	89.24%	41 409	90.88%	27 632	91.95%	15 665	<0.001
Smoking	38.26%	17 078	40.71%	11 832	42.27%	6799	<0.001
Body mass index							<0.001
<18.5	10.33%	4929	10.18%	3194	9.69%	1696	
≦18.5, <30	79.98%	38 171	79.26%	24 876	79.57%	13 922	
≦30	9.69%	4625	10.56%	3314	10.74%	1879	
Inpatient data							
Intensive care unit	7.87%	3958	8.54%	2796	9.49%	1728	<0.001
Artificial ventilator	14.45%	7267	14.37%	4707	15.05%	2740	0.090
Hypertension	61.49%	30 918	60.13%	19 689	58.94%	10 732	<0.001
Atrial fibrillation	35.47%	17 838	34.31%	11 235	32.33%	5886	<0.001
Dilated cardiomyopathy	2.50%	1259	2.52%	825	2.60%	474	0.760
Valvular disease	12.45%	6261	11.93%	3908	10.90%	1984	<0.001
Myocardial infarction	8.32%	4184	8.04%	2633	8.13%	1480	0.333
Cerebrovascular disease	6.24%	3139	6.10%	1997	5.52%	1005	0.002
Chronic pulmonary disease	7.21%	3626	7.35%	2406	7.54%	1372	0.340
Diabetes	28.34%	14 253	31.40%	10 281	33.50%	6099	<0.001
Renal disease	10.34%	5199	12.63%	4137	13.52%	2461	<0.001
Outpatient data							
Beta-blockers							<0.001
No-prescription	42.70%	21 472	33.20%	10 871	31.31%	5701	
Bottom 50%	30.78%	15 478	34.32%	11 237	35.41%	6447	
Top 50%	26.52%	13 335	32.49%	10 638	33.28%	6060	
ARB/ACEI							<0.001
No-prescription	49.93%	25 108	44.23%	14 482	43.87%	7987	
Bottom 50%	25.98%	13 066	28.54%	9345	28.62%	5211	
Top 50%	24.08%	12 111	27.24%	8919	27.52%	5010	
Tolvaptans	15.71%	7898	21.15%	6926	24.01%	4371	<0.001
MRA	38.87%	19 545	44.72%	14 643	45.39%	8264	<0.001
Loop diuretics							<0.001
No-prescription	35.42%	17 809	24.15%	7907	22.75%	4143	
Bottom 50%	45.41%	22 835	48.70%	15 946	47.09%	8574	
Top 50%	19.17%	9641	27.16%	8893	30.16%	5491	
Class III antiarrhythmic agents							<0.001
No-prescription	94.51%	47 522	92.23%	30 200	91.42%	16 646	
Bottom 50%	3.60%	1809	4.88%	1597	5.17%	942	
Top 50%	1.90%	954	2.90%	949	3.41%	620	
Cardiac rehabilitation	1.09%	548	3.13%	1024	18.83%	3428	<0.001
Echocardiography	10.75%	5405	16.97%	5556	21.91%	3989	<0.001
Brain natriuretic peptide	59.85%	30 094	72.28%	23 669	74.78%	13 616	<0.001
0–2 weeks follow-up	41.83%	21 033	72.58%	23 767	89.06%	16 216	<0.001
2–4 weeks follow-up	43.59%	21 917	68.41%	22 402	87.75%	15 977	<0.001
Readmission rate	4.76%	2392	7.76%	2542	10.95%	1994	<0.001

ARB/ACEI, angiotensin receptor blocker/angiotensin covering enzyme inhibitor; MRA, mineralocorticoid receptor antagonists; SD, standard deviation.

compared to (1<,≦2) visits/month ($P < 0.001$), whereas the risk of readmission decreases in ≦1 visits/month compared with (1<, ≦2) visits/month ($P < 0.001$).

Table 4 shows the results of the subgroup analysis in the high-readmission risk group. The high readmission risk group was defined as a population with the following factors: artificial ventilator, tolvaptan, class III antiarrhythmic agents, atrial fibrillation, dilated cardiomyopathy, myocardial infarction, and renal disease. Consequently, the following factors were identified as readmission risk factors: older age, female, longer LOS, artificial ventilator, tolvaptan, bottom 50% dosage of class III antiarrhythmic agents, atrial fibrillation, dilated cardiomyopathy, valvular disease, myocardial infarction, cerebrovascular disease, diabetes, and renal disease. Higher BI,

Table 2 Multiple logistic regression

	Coefficient	Odds ratio	95% CI		*P*-value
The number of outpatient visits					
≦1 visit/month	−1.384	0.251	0.232	0.271	<0.001
(<1, ≦2) visits/month	Reference				
<2 visits/month	0.984	2.674	2.471	2.894	<0.001
Age					
≦64	Reference				
≦65, <75	0.339	1.404	1.251	1.575	<0.001
≦75	0.828	2.290	2.063	2.541	<0.001
Sex (female)	0.091	1.095	1.023	1.173	0.009
Length-of-hospital-stay	0.005	1.005	1.004	1.007	<0.001
Home medical care	−0.078	0.925	0.810	1.057	0.253
Smoking	0.014	1.015	0.946	1.088	0.685
Barthel index (≦60)	−0.200	0.819	0.750	0.894	<0.001
Body mass index					
<18.5	Reference				
≦18.5, <30	−0.216	0.806	0.736	0.882	<0.001
≦30	−0.358	0.699	0.606	0.807	<0.001
Inpatient data					
Intensive care unit	−0.200	0.819	0.720	0.930	0.002
Artificial ventilator	0.287	1.333	1.216	1.461	<0.001
Hypertension	0.087	1.091	1.027	1.160	0.005
Atrial fibrillation	0.268	1.308	1.229	1.391	<0.001
Dilated cardiomyopathy	0.726	2.068	1.731	2.469	<0.001
Valvular disease	0.103	1.108	1.016	1.209	0.021
Myocardial infarction	0.380	1.462	1.324	1.615	<0.001
Cerebrovascular disease	0.099	1.104	0.988	1.233	0.080
Chronic pulmonary disease	0.099	1.104	0.994	1.227	0.066
Diabetes	0.161	1.175	1.102	1.253	<0.001
Renal disease	0.249	1.283	1.183	1.391	<0.001
Outpatient data					
Beta-blockers					
No-prescription	Reference				
Bottom 50%	−0.211	0.809	0.749	0.875	<0.001
Top 50%	−0.234	0.791	0.728	0.860	<0.001
ARB/ACEI					
No-prescription	Reference				
Bottom 50%	−0.450	0.638	0.586	0.694	<0.001
Top 50%	−0.578	0.561	0.517	0.608	<0.001
Tolvaptan	0.535	1.707	1.585	1.838	<0.001
MRA	−0.320	0.726	0.677	0.779	<0.001
Loop diuretics					
No-prescription	Reference				
Bottom 50%	−0.275	0.760	0.702	0.822	<0.001
Top 50%	0.092	1.097	1.006	1.195	0.036
Class III antiarrhythmic agents					
No-prescription	Reference				
Bottom 50%	0.465	1.592	1.394	1.819	<0.001
Top 50%	0.155	1.167	0.949	1.436	0.143
Cardiac rehabilitation	−0.923	0.397	0.330	0.478	<0.001
Echocardiography	−0.477	0.620	0.561	0.687	<0.001
Brain natriuretic peptide	−0.882	0.414	0.388	0.441	<0.001
0–2 weeks follow-up	−0.939	0.391	0.365	0.419	<0.001
2–4 weeks follow-up	−1.138	0.320	0.299	0.343	<0.001

ARB/ACEI, angiotensin receptor blocker/angiotensin covering enzyme inhibitor; CI, confidence interval; MRA, mineralocorticoid receptor antagonists.

higher BMI, ICU, beta-blockers, ARB/ACEI, MRA, bottom 50% dosage of loop diuretics, 0–2 weeks follow-up, 2–4 weeks follow-up, outpatient cardiac rehabilitation, outpatient BNP test, and outpatient echocardiography were identified as factors that decrease the readmission risk. As for the association between the number of outpatient visits and readmission, the risk of readmission increases in <2 visits/month compared with (1<,≦2) visits/month ($P < 0.001$), whereas the risk of readmission decreases in ≦1 visits/month compared to (1<, ≦2) visits/month ($P < 0.001$).

Table 5 compares medical contents between (1<, ≦2) visits/month and <2 visits/month. Multiple logistic regression analysis showed that the following factors were significantly related to <2 visits/month: older age, home medical care after discharge, tolvaptan, top 50% dosage of loop diuretics, diabetes, renal disease, 0–2 weeks follow-up,

Table 3 Multiple logistic regression in the low readmission risk group

	Coefficient	Odds ratio	95% CI		*P*-value
The number of outpatient visits					
≦1 visit/month	−1.331	0.264	0.228	0.306	<0.001
(<1, ≦2) visits/month	Reference				
<2 visits/month	0.961	2.614	2.228	3.066	<0.001
Age					
≦64	Reference				
≦65, <75	0.497	1.644	1.307	2.069	<0.001
≦75	0.976	2.655	2.170	3.249	<0.001
Sex (female)	0.020	1.020	0.895	1.162	0.765
Length-of-hospital-stay	0.008	1.008	1.005	1.012	<0.001
Home medical care	−0.039	0.962	0.750	1.233	0.759
Smoking	0.074	1.077	0.938	1.236	0.293
Barthel index (≦60)	−0.215	0.807	0.688	0.945	0.008
Body mass index					
<18.5	Reference				
≦18.5, <30	−0.209	0.811	0.688	0.956	0.012
≦30	−0.326	0.722	0.546	0.953	0.022
Inpatient data					
Intensive care unit	−0.085	0.918	0.667	1.264	0.602
Hypertension	0.223	1.250	1.110	1.407	<0.001
Valvular disease	0.096	1.100	0.926	1.308	0.279
Cerebrovascular disease	−0.019	0.982	0.790	1.219	0.866
Chronic pulmonary disease	0.112	1.118	0.928	1.348	0.240
Diabetes	0.244	1.276	1.128	1.444	<0.001
Outpatient data					
Beta-blockers					
No-prescription	Reference				
Bottom 50%	−0.094	0.910	0.779	1.063	0.235
Top 50%	−0.339	0.712	0.592	0.857	<0.001
ARB/ACEI					
No-prescription	Reference				
Bottom 50%	−0.550	0.577	0.484	0.688	<0.001
Top 50%	−0.687	0.503	0.427	0.593	<0.001
MRA	−0.303	0.739	0.639	0.854	<0.001
Loop diuretics					
No-prescription	Reference				
Bottom 50%	−0.020	0.980	0.847	1.134	0.785
Top 50%	0.362	1.437	1.207	1.710	<0.001
Cardiac rehabilitation	−1.134	0.322	0.202	0.513	<0.001
Echocardiography	−0.460	0.631	0.514	0.775	<0.001
Brain natriuretic peptide	−0.939	0.391	0.344	0.444	<0.001
0–2 weeks follow-up	−1.098	0.334	0.292	0.381	<0.001
2–4 weeks follow-up	−1.296	0.274	0.240	0.312	<0.001

ARB/ACEI, angiotensin receptor blocker/angiotensin covering enzyme inhibitor; CI, confidence interval; MRA, mineralocorticoid receptor antagonists.

2–4 weeks follow-up, outpatient cardiac rehabilitation, and outpatient echocardiography. Female, higher BMI, top 50% dosage of beta-blockers, bottom 50% dosage of ARB/ACEI, hypertension, atrial fibrillation, valvular disease, and myocardial infarction were factors related to (1<, ≦2) visits/month.

Discussion

In our study, we used the inpatient and outpatient data of the DPC database and investigated 101 239 heart failure patients nationwide. The DPC database mainly focuses on medical procedures. And we could evaluate the severity of the patients with heart failure using the data about medical procedures. However, it does not have data about cardiac functions like ejection fraction and brain natriuretic hormone. This study is the first in Japan to investigate the risk factors associated with readmission, including outpatient management represented by the number of outpatient visits, and identify the characteristics of patients with frequent outpatient visits in heart failure patients using outpatient data from the DPC database. The main results of this study are (i) readmission risk factors, including outpatient management, are comprehensively identified; (ii) each patient's readmission risk optimizes the number of outpatient visits; (iii) it had a possibility that the risk factors in high readmission risk group were different from those in low readmission risk group; (iv) the characteristics of patients with frequent outpatient visits are identified.

First, we identified the following risk factors for readmission: older age, female, longer LOS, artificial ventilator,

Table 4 Multiple logistic regression in the high readmission risk group

	Coefficient	Odds Ratio	95% CI		*P*-value
The number of outpatient visits					
≦1 visit/month	−1.411	0.244	0.223	0.267	<0.001
(<1, ≦2) visits/month	Reference				
<2 visits/month	0.987	2.682	2.448	2.938	<0.001
Age					
≦64	Reference				
≦65, <75	0.278	1.320	1.155	1.509	<0.001
≦75	0.764	2.146	1.900	2.424	<0.001
Sex (female)	0.127	1.135	1.048	1.229	0.002
Length-of-hospital-stay	0.004	1.004	1.003	1.006	<0.001
Home medical care	−0.099	0.906	0.774	1.061	0.220
Smoking	−0.004	0.996	0.919	1.080	0.925
Barthel index (≦60)	−0.185	0.831	0.748	0.923	<0.001
Body mass index					
<18.5	Reference				
≦18.5, <30	−0.222	0.801	0.719	0.892	<0.001
≦30	−0.371	0.690	0.583	0.816	<0.001
Inpatient data					
Intensive care unit	−0.223	0.800	0.697	0.920	0.002
Artificial Ventilator	0.292	1.339	1.212	1.479	<0.001
Hypertension	0.037	1.038	0.967	1.114	0.307
Atrial fibrillation	0.263	1.301	1.202	1.409	<0.001
Dilated cardiomyopathy	0.702	2.017	1.685	2.416	<0.001
Valvular disease	0.103	1.108	1.002	1.226	0.045
Myocardial infarction	0.385	1.470	1.324	1.632	<0.001
Cerebrovascular disease	0.141	1.151	1.012	1.310	0.033
Chronic pulmonary disease	0.087	1.091	0.960	1.240	0.184
Diabetes	0.121	1.129	1.047	1.217	0.002
Renal disease	0.248	1.282	1.174	1.399	<0.001
Outpatient data					
Beta-blockers					
No-prescription	Reference				
Bottom 50%	−0.244	0.783	0.716	0.857	<0.001
Top 50%	−0.212	0.809	0.736	0.889	<0.001
ARB/ACEI					
No-prescription	Reference				
Bottom 50%	−0.419	0.658	0.597	0.724	<0.001
Top 50%	−0.543	0.581	0.529	0.638	<0.001
Tolvaptan	0.555	1.742	1.606	1.890	<0.001
MRA	−0.332	0.718	0.663	0.778	<0.001
Loop diuretics					
No-prescription	Reference				
Bottom 50%	−0.396	0.673	0.612	0.740	<0.001
Top 50%	−0.024	0.976	0.883	1.078	0.632
Class III antiarrhythmic agents					
No-prescription	Reference				
Bottom 50%	0.463	1.588	1.389	1.815	<0.001
Top 50%	0.150	1.162	0.944	1.431	0.156
Cardiac rehabilitation	−0.893	0.410	0.334	0.502	<0.001
Echocardiography	−0.485	0.616	0.548	0.692	<0.001
Brain natriuretic peptide	−0.868	0.420	0.390	0.452	<0.001
0–2 weeks follow-up	−0.875	0.417	0.384	0.452	<0.001
2–4 weeks follow-up	−1.078	0.340	0.314	0.369	<0.001

ARB/ACEI, angiotensin receptor blocker/angiotensin covering enzyme inhibitor; CI, confidence interval; MRA, mineralocorticoid receptor antagonists.

tolvaptan, top 50% dosage of loop diuretics, bottom 50% dosage of class III antiarrhythmic agents, hypertension, atrial fibrillation, dilated cardiomyopathy, valvular disease, myocardial infarction, diabetes, and renal disease. Most of these results were consistent with earlier studies.[20–27] We identified that female is a risk factor for readmission. Studies on sex differences in patients with heart failure have been conducted, but their results may not be consistent. At least in Japanese tertiary-care emergency hospitals, females may be at risk for readmission because the DPC database has high representativeness in the setting. Patients with longer LOS and an artificial ventilator at index admission were considered more severe cases and more likely to readmit. Tolvaptan is a drug used in patients who are resistant to other diuretics, and such patients may have high readmission risk because of the difficulty of fluid management. We identified the top 50% dosage

Table 5 Comparison of medical contents between (1<, ≦2) visits/month and <2 visits/month

	Coefficient	Odds ratio	95% CI		*P*-value
Age					
≦64	Reference				
65≦, <75	0.194	1.215	1.136	1.299	<0.001
≦75	0.067	1.069	1.004	1.138	0.037
Sex (female)	−0.055	0.947	0.899	0.997	0.038
Length-of-hospital-stay	0.001	1.001	1.000	1.003	0.095
Home medical care	0.153	1.166	1.043	1.303	0.007
Smoking	0.006	1.006	0.956	1.058	0.832
Barthel index (≦60)	−0.027	0.974	0.897	1.057	0.525
Body mass index					
<18.5	Reference				
≦18.5, <30	−0.029	0.971	0.900	1.049	0.460
≦30	−0.124	0.884	0.796	0.980	0.020
Inpatient data					
Intensive care unit	0.029	1.029	0.943	1.123	0.520
Artificial ventilator	−0.027	0.974	0.907	1.045	0.461
Hypertension	−0.061	0.941	0.898	0.985	0.010
Atrial fibrillation	−0.066	0.937	0.892	0.983	0.009
Dilated cardiomyopathy	−0.133	0.875	0.757	1.013	0.073
Valvular disease	−0.120	0.886	0.826	0.951	<0.001
Myocardial infarction	−0.089	0.915	0.841	0.994	0.036
Cerebrovascular disease	−0.008	0.992	0.902	1.091	0.876
Chronic pulmonary disease	0.071	1.074	0.986	1.169	0.100
Diabetes	0.103	1.109	1.056	1.164	<0.001
Renal disease	0.090	1.094	1.023	1.170	0.009
Outpatient data					
Beta-blockers					
No-prescription	Reference				
Bottom 50%	−0.039	0.962	0.908	1.019	0.186
Top 50%	−0.087	0.917	0.863	0.973	0.005
ARB/ACEI					
No-prescription	Reference				
Bottom 50%	−0.134	0.875	0.827	0.926	<0.001
Top 50%	−0.030	0.970	0.918	1.026	0.290
Tolvaptan	0.123	1.131	1.070	1.196	<0.001
MRA	−0.046	0.955	0.911	1.002	0.060
Loop diuretics					
No-prescription	Reference				
Bottom 50%	0.019	1.019	0.961	1.082	0.526
Top 50%	0.182	1.199	1.122	1.281	<0.001
Class III antiarrhythmic agents					
No-prescription	Reference				
Bottom 50%	−0.009	0.991	0.893	1.101	0.871
Top 50%	0.009	1.009	0.884	1.152	0.889
Cardiac rehabilitation	1.886	6.594	6.054	7.181	<0.001
Echocardiography	0.320	1.378	1.302	1.457	<0.001
Brain natriuretic peptide	0.050	1.051	0.997	1.107	0.063
0–2 weeks follow-up	1.313	3.719	3.497	3.955	<0.001
2–4 weeks follow-up	1.343	3.832	3.613	4.063	<0.001

ARB/ACEI, angiotensin receptor blocker/angiotensin covering enzyme inhibitor; CI, confidence interval; MRA, mineralocorticoid receptor antagonists.

of loop diuretics as the readmission risk because patients with a high dosage of loop diuretics may be cases that have difficulty with fluid management and patients with tolvaptan. Regarding class III antiarrhythmic agents, patients using this drug may have a fatal arrhythmia, one of the main reasons for readmission. There was a significant difference only in the bottom 50% dosage of class III antiarrhythmic agents because patients who need a high dosage of class III antiarrhythmic agents visit a larger hospital which may provide better management. Co-morbidities we identified impair cardiac function or make fluid management difficult. Therefore, patients with these co-morbidities were more likely to exacerbate and readmit. We identified higher BI, higher BMI, ICU, beta-blockers, ARB/ACEI, MRA, bottom 50% dosage of loop diuretics, 0–2 weeks follow-up, 2–4 weeks follow-up, outpatient cardiac rehabilitation, outpatient BNP test, and outpatient echocardiography to decrease the risk of readmission. Patients who are admitted to ICU are more likely to readmit. However, our study shows adverse results. There is a possibility that we could not track the patient who was admitted to ICU after discharge because of the death out of the hospital or readmit other hospitals with diseases other than

heart failure. Although the top 50% dosage of loop diuretics was identified as a risk of readmission, we determined that the bottom 50% dosage of loop diuretics decreases the risk of readmission. These results suggest that a low dosage of loop diuretic improves fluid management status while increasing its dosage reflects the increase in patients' readmission risk. Outpatient BNP tests and outpatient echocardiography were important to understand patients' conditions. Implementing these medical procedures may allow outpatient care tailored to the patient's condition and decrease the readmission risk. Earlier studies have reported that beta-blockers reduce the risk of long-term readmission, which concurs with our result. However, some studies have reported that beta-blocker is a risk factor in the short term. So we should be careful about the effect of beta-blockers. Other factors that decreased the readmission risk were in concordance with earlier studies.[28,29,30–33]

Second, we examined the association between the number of outpatient visits and readmission using multiple logistic regression analysis. And we revealed that the risk of readmission increases in <2 visits/month compared to ($1<$,$\leqq 2$) visits/month ($P < 0.001$), whereas the risk of readmission decreases in $\leqq 1$ visits/month compared with ($1<$, $\leqq 2$) visits/month ($P < 0.001$). These results suggest that the number of outpatient visits for heart failure patients in Japan is personalized depending on each patient's readmission risk. One earlier study has reported no difference in the readmission risk in patients who contact two or more times within 30 days after discharge compared to no contact.[34] Considering this earlier study was conducted outside Japan, there may be room to optimize the number of outpatient visits based on the patient's readmission risk in countries other than Japan.

Third, we conducted subgroup analysis in the low and high readmission risk groups. And we found that there were risk factors specific to the subgroup. In the subgroup analysis of the low readmission risk group, we revealed that hypertension and the top 50% dosage of loop diuretics are the specific factors that increase the readmission risk. In the subgroup analysis of the high readmission risk group, we revealed that female, valvular disease and cerebrovascular disease were the specific factors that increase the readmission risk. And the top 50% dosage of beta-blockers and the bottom 50% dosage of loop diuretics were the specific factors that decreased the risk of readmission. These results suggest differences in risk factors between the low and high-readmission risk groups.

Fourth, we compared the medical contents between <2 visits/month and ($1<$, $\leqq 2$) visits/month. And we revealed the characteristics of patients with frequent outpatient visits. We identified that the following factors were the characteristics of patients with frequent outpatient visits: older age, home medical care after discharge, tolvaptan, top 50% dosage of loop diuretics, diabetes, renal disease, 0–2 weeks follow-up, 2–4 weeks follow-up, outpatient cardiac rehabilitation, and outpatient echocardiography. It is plausible that older patients need frequent outpatient visits because of the high readmission risk. Regarding home medical care, 0–2 weeks follow-up, 2–4 weeks follow-up, and outpatient echocardiography may reflect the patients' severity at index admission and allow more careful outpatient follow-up. Outpatient cardiac rehabilitation is conducted several times. Consequently, it is reasonable to increase outpatient visits. 0–2 weeks follow-up, 2–4 weeks follow-up, outpatient cardiac rehabilitation, and outpatient echocardiography are factors that decrease the readmission risk. Therefore, this medical care should be prioritized even if it increases the number of outpatient visits. As for tolvaptan, the top 50% dosage of loop diuretics, diabetes, and renal disease, we identified these factors as a risk of readmission. Thus, these results may imply that patients with these factors need more careful outpatient management to control the readmission risk. As for the factors that characterized patients with ($1<$, $\leqq 2$) visits/month, female, higher BMI, top 50% dosage of beta-blockers, bottom 50% dosage of ARB/ACEI, hypertension, atrial fibrillation, valvular disease, and myocardial infarction were identified. Higher BMI was identified as a factor that decreases readmission risk. So it is reasonable not to need frequent outpatient visits. Beta-blockers and ARB/ACEI reduce the risk of readmission and the number of outpatient visits. Therefore, these drugs may be better for improving patients' prognosis among drugs that have the effect of myocardial protection. However, there is a possibility that the dosage of these drugs may change the risks perceived by doctors and affects the number of outpatient visits. Female, hypertension, atrial fibrillation, valvular disease, and myocardial infarction were identified as readmission risks. Therefore, we should consider increasing the number of outpatient visits in patients with these factors to decrease the readmission risk. These results suggest that there is room to improve outpatient management to prevent readmission even though the patient's readmission risk personalized the number of outpatient visits.

Regarding generalizability, it is possible to generalize to the whole country considering the Japanese medical system and the strength of our study: the Japanese medical system is universal across the entire country, guidelines standardize medical care for heart failure, and the DPC database has high representativeness. On the other hand, considering the Japanese medical system allows free access to hospitals, and the general practitioner system is more underdeveloped than Europe and the United States, we should be careful about the generalizability to other countries. However, this is a study for heart failure patients, and drugs and medical procedures incorporated in this study are common worldwide. Thus, differences in medical systems would not impair the generalizability to other countries.

There are limitations in this study caused by the nature of the DPC database. The DPC database does not have laboratory data, including cardiac function like ejection fraction,

social data after discharge, data about visitation and transfer to other hospitals or clinics, and data about the clinical setting of outpatient visits. Several earlier studies have reported that laboratory data were predictors for readmission and prognosis.[35–37] Other studies have shown that the readmission rate increases depending on family composition and lifestyle, such as adherence to medication and diet management after discharge.[38,39] As for the visitation and transfer to other hospitals or clinics, to minimize these biases, we limited patients whose discharge disposition at index admission was 'home, attending with their own hospital' in the step of patient selection. As for the clinical setting of outpatient visits, it is important to measure which doctor sees the patients, whether the protocol exists, and whether the visitation is urgent or planned. However, because only the occurrence of patients' visits to the hospital is registered in the DPC database, we could not measure the details of the clinical setting.

In conclusion, although the patients' readmission risk personalizes the number of outpatient visits for heart failure patients in Japan, there is room to optimize outpatient management. Thus, we suggest optimizing outpatient management according to our identified factors and characteristics.

Conflict of interest

The authors declare that they have no competing interests.

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