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Original Article

Annual Increase of Acute Inpatients with Both Cancer and Cardiovascular Diseases in Japan 2011-2015: Analysis From National Database of Health Insurance Claims and Specific Health Checkups of Japan

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Summary: ***Background*:** Patients with cancer were able to live longer due to improvements in cancer treatment. Additionally, cardiovascular disease (CVD) is the second leading cause of mortality in cancer survivors. However, epidemiological data on onco-CVD have not been sufficiently provided. We aimed to investigate the clinical characteristics of cancer in CVD patients using the National Database of Health Insurance Claims and Specific Health Checkups of Japan (NDB).

***Method and Results*:** The NDB sampling dataset used in this study was randomly sampled 10% from the whole Diagnosis Procedure Combination (DPC) records from every January, April, July, and October from 2011 to 2015. The significance of the increase trend in the percentage of records in each disease group to the total number of all DPC records from 2011 to 2015 was checked with Chi-square test with a Bonferroni correction. The percentage of records in cancer with the CVD group to the total number of all DPC records significantly increased over time, and their average age also increased since 2011. Their proportion over 75 years was approximately 56 % in 2015. There was no difference in the cancer sites. However, the prevalence of heart failure dramatically elevated.

***Conclusion*:** We were able to assess the increase in cancer among CVD patients using DPC inpatient records obtained from the NDB. Both cardiologists and oncologists should be more aware of this phenomenon.

Keywords NDB, DPC, Onco-Cardiovascular diseases

INTRODUCTION

Cancer death rates have been increasing in Japan, becoming the leading cause of death in 1981 [1]. The estimated number of cancer deaths in 2019 was approximately 380,300 (222,500 males and 157,800 females) in Japan [1]. Given its hyper-aging society, Japan will likely face a substantial increase in the number of elderly cancer patients [2]. Approximately 36% of patients were older than 75 years of age in 2015 and it is estimated that the proportion will increase annually [1,3]. Additionally, patients with cancer are able to survive longer due to advanced cancer therapies [4,5]. Furthermore, it indicated that cardiovascular diseases (CVD) are the second greatest cause of mortality amongst cancer survivors [6]. Thus, onco-cardiology has several important tasks to establish an optimal care for cancer patients [7]. However, epidemiological data is still lacking in onco-cardiology, probably because oncologists and cardiologists have paid insuffi-

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Abbreviations: ACS, acute coronary syndrome; CVD, cardiovascular disease; DPC, diagnosis procedure combination; DVT, deep vein thrombosis; HIC, Health Insurance Claim; ICD-10, international classification of diseases, tenth revision; IHD, ischemic heart disease; NDB, National Database of Health Insurance Claims and Specific Health Checkups of Japan.

cient attention to each other.

To develop public health for both cancer and CVD, big data should be used [8]. Administrative databases are widely used in medical research studies [9]. Most Japanese citizens must participate in to one of the major insurance systems, including: the National Health Insurance, the Japan Health Insurance Association, health insurance arrangements provided by unions, employee insurance provided by mutual aid associations, and the Medical Care System for the Elderly, which covers people aged $\geq$75 years [10]. The National Database of Health Insurance Claims and Specific Health Checkups of Japan (NDB) is an administrative claims database that collects public health insurance data [10]. The NDB is a database for secondary use after anonymizing Health Insurance Claim (HIC) data originally used for the purpose of medical fee claiming. The NDB database includes all the processed HIC which can highly reflect the medical services of the whole country. The NDB database contains comprehensive HIC records regarding diagnosis procedure combination (DPC) inpatients care within the National Health Insurance system of Japan. DPC stands for diagnosis procedure combination per-diem payment system, a system in which provider reimbursement is calculated based on a flat-rate per-diem fee based on the diagnosis group.

In Japan, the DPC-based payment system was introduced in acute-care hospitals nationwide in 2003 [11]. It is a diagnostic group classification that was developed independently in Japan. DPC is based on the combination of the "name of injury or disease" for which the most medical resources were invested, such as medical treatment, surgery, procedures, and chemotherapy during the hospitalization period. Based on this, inpatient medical expenses are calculated as a comprehensive evaluation. Diagnoses are recorded by attending physicians using International Classification of Diseases, Tenth Revision (ICD-10) codes established by the WHO. The number of DPC medical institutions and DPC-calculated hospital beds from 2011, 2012, 2013, 2014 and 2015 were as follows: 1,449 institutions (467,511 DPC-calculated beds), 1,505 institutions (479,539 DPC-calculated beds), 1,496 institutions (474,981 DPC-calculated beds), 1,585 institutions (492,206 DPC-calculated beds) and 1,580 institutions (484,081 DPC-calculated beds), respectively [12]. As of April 2020, the payment system has been applied to 1,757 institutions with a total of 483,180 DPC calculated beds [12]. This number is thought to be enough to cover almost all acute inpatients and is about 30% of all hospitals with beds for general patients (including those in subacute care and rehabilitation, but excluding those with mental illness, infectious disease, tuberculosis, and long-term care) and about 54% of all beds of hospitals with beds for general patients across the country [12].

Diseases with high severity, such as CVD and cancer are likely to be treated in hospitals subject to DPC.

Therefore, the aim of this study was to investigate annual changes in the clinical characteristics of patients with cancer and/or CVD using DPC HIC records in Japan.

MATERIALS AND METHODS

Study design

In this study, we used datasets based on DPC inpatient HIC from the NDB. We used sampling NDB data sets in which 10% of DPC data were randomly extracted from every January, April, July, and October from 2011 to 2015 of Japan DPC data. The data was extracted by considering the proportions of gender and age groups, which should be close to all Japanese DPC inpatients. In each data set, age was provided in increments of 5 years, and information on infrequent injuries and diseases, medical practices, and drugs were anonymized. There is a serial number for each HIC record in each sampled dataset. Because IDs are not provided to identify individual patients, it is not possible to identify them within a data set. Furthermore, it is impossible to link them across multiple data sets. The analysis was conducted on the HIC record basis, not on a patient basis. In this situation, we collected only the cancer and CVD from all injury and disease in the records.

All HIC data used in our analysis were deidentified by the Ministry of Health, Labour and Welfare, and the guidelines on information security from the ministry were followed in the study. To use the NDB database, the opt-out method was applied from the Health and Welfare Ministry of Japan. Inspection by, and permission from the ministry for publication, are needed before the submission of the draft to ensure that patient privacy is respected.

The present study was approved by the Institutional Review Board at Kurume University (Approval Number 19147). The requirement for informed consent was waived because all the data were anonymized.

Study group definition

We classified these ICD-10 codes as follows: cancer and CVD included cerebrovascular diseases and peripheral vascular diseases. We selected patients

aged 20 years and older with their codes. We defined cancer patients when they had ICD-10 codes C00 - C96. We also defined by ICD-10 codes as the CVD (Supplementary Table 1). If a single record contained several disease names, it was counted as one record. We excluded suspicious diagnoses. We divided them into three groups: cancer, CVD, and cancer with CVD.

Statistical analyses

All randomly sampled records of each month were 10% of all DPC data aggregated by year. The numbers of records were divided into three groups : CVD, cancer, and cancer with CVD, and were counted in the same way. The significance of increase trend in the percentage of records in each disease group to the total number of all DPC records from 2011 to 2015 was checked with Chi-square test and a Bonferroni correction. As the number of DPC medical institutions and hospital beds in Japan have increased from 2011 to 2015, we adjusted the numbers of CVD, cancer, and cancer with CVD, which were divided by 10% number of all DPC medical institutions and hospital beds in Japan. The ranking of CVD and cancers of each group was calculated based on ICD-10 codes. The top 20 cancers were categorized and tabulated by cancer site. These were evaluated by each gender. Statistical significance was defined as $p<0.01$. All statistical analyses were performed using R version 3.5.0.

RESULTS

Annual changes in the number of all DPC records and distribution of patients according to age groups and sex (for 4 months, 2011-2015)

A total of 318,451, 333,641, 345,176, 336,949, 339,988 DPC records were examined respectively for 4 months: January, April, July, and October in 2011-2015. Their clinical characterization of age, age group and sex were shown in Table 1. The number of all DPC records and the average age of the records showed an annual increase over time.

Annual changes in the number of all CVD records and distribution of patients according to age groups and sex (for 4 months, 2011-2015)

A total of 106,168, 110,927, 115,208, 117,947, 123,116 CVD records were examined respectively for 4 months in 2011-2015. Their clinical characterization of age, age group, and sex were shown in Table 1. The number of all CVD records increased over time, and the average age increased from 2011 to 2015. (Table 1, Figure 1-A-1) The percentages of records in the CVD group to the total number of all DPC records were 33.3, 33.3, 33.4, 35.0, and 36.2%, and showed a trend of increasing with statistical significance since 2014. (Figure 1-A-2) The number of CVD records per one DPC medical institution (10% of whole institutions) (Figure 1-B) and per one DPC hospital bed (10% of whole institutions) (Figure 1-C) also showed an increasing trend over time. As shown in Figure 1-D, heart failure was the most commonly diagnosed in all CVD records, and the leading cause of CVD were followed by ischemic heart disease (IHD) except for acute coronary syndrome (ACS) and cerebral infarction.

Annual changes in the number of all cancer records and distribution of patients according to age groups and sex (for 4 months, 2011-2015)

A total of 85,762, 89,604, 90,868, 91,260, 93,905 cancer records were examined respectively for 4 months in 2011-2015. Their clinical characterization of age, age group, and sex were shown in Table 1. The number of all cancer records increased over time, and the average age increased from 2011 to 2015 (Table 1, Figure 2-A-1).

The percentage of records in the cancer group to the total number of all DPC records were 26.9, 26.9, 26.3, 27.1, and 27.6%, and showed a trend of increasing with statistical significance since 2015 (Figure 2-A-2). The number of cancer records per one DPC medical institution (10% of whole institutions) was unchanged (Figure 2-B). The number of cancer records per one DPC hospital bed (10% of whole institutions) showed a slightly increasing trend over time (Figure 2-C). Colorectal cancer was the most commonly diagnosed cancer and the leading cause of cancer, followed by bronchial/lung cancer and stomach cancer in all cancer records (Figure 3-A), indicating that colorectal cancer and bronchial/lung cancer increased over time. From the perspective of sex differences, bronchial/lung cancer and colorectal cancer in males (Figure 3-B) and colorectal cancer and breast cancer in females (Figure 3-C) increased.

Annual changes in the number of cancer with CVD patients and distribution of patients according to age groups and sex (for 4 months, 2011-2015)

Next, we examined cancer with CVD records. There were 17,709, 18,684, 19,262, 20,034, 22,620 cancer with CVD records examined for 4 months in 2011-2015. Their clinical characterization of age, age group, and sex were shown in Table 1. The number of cancer with CVD records increased over time, and the average age of the records also increased from 2011 to

2015 (Table 1, Figure 4-A-1). The percentages of records in the cancer with CVD group to the total number of all DPC records were 5.56, 5.60, 5.58, 5.95, and 6.65%, and showed a trend of increasing with statistical significance since 2014 (Figure 4-A-2). The number of cancer with CVD records per one DPC medical institution (10% of whole institutions) (Figure 4-B) and per one DPC hospital bed (10% of whole institutions) (Figure 4-C) also showed an increasing trend over time. The number of elderly patients aged over 75 years were 12,868 records for 4 months in 2015. These number of patients with both cancer and CVD had increased over time since 2011, the proportion of elderly patients aged over 75 years was approximately 56 % in 2015.

As shown in Figure 4-D, heart failure was the most commonly diagnosed CVD in 2015, and the leading cause of CVD were followed by IHD except for ACS

TABLE 1.
Change in the number of DPC records and distribution of patients according to age groups and sex over time (for 4 months, 2011-2015)

ALL		2011	2012	2013	2014	2015
Total		318,451	333,641	345,176	336,949	339,988
Age average		67.06	67.29	67.59	67.91	68.32
Age	20-64	116,812	120,205	120,164	113,498	110,536
	65-74	76,635	80,600	85,076	84,239	84,815
	75-	125,004	132,836	139,936	139,212	144,637
Male (rate:%)		166,200 (52.2)	173,923 (52.1)	179,623 (52.0)	173,377 (51.5)	174,050 (51.2)
CVD		2011	2012	2013	2014	2015
Total		106,168	110,927	115,208	117,947	123,116
Age average		74.29	74.46	74.62	74.88	75.08
Age	20-64	21,049	21,439	21,422	20,933	21,189
	65-74	25,918	26,898	28,162	29,409	30,435
	75-	59,201	62,590	65,624	67,605	71,492
Male (rate:%)		59,827 (56.4)	62,529 (56.4)	64,965 (56.4)	66,272 (56.2)	68,932 (56.0)
Cancer		2011	2012	2013	2014	2015
Total		85,762	89,604	90,868	91,260	93,905
Age average		69.26	69.4	69.97	69.99	70.36
Age	20-64	27,369	28,043	26,916	25,499	24,963
	65-74	26,408	27,864	29,074	30,162	31,233
	75-	31,985	33,697	34,878	35,599	37,709
Male (rate:%)		51,379 (59.9)	53,446 (59.6)	54,294 (59.8)	53,926 (59.1)	55,547 (59.2)
Cancer with CVD		2011	2012	2013	2014	2015
Total		17,709	18,684	19,262	20,034	22,620
Age average		74.4	74.56	74.7	74.97	75.07
Age	20-64	2,908	2,990	2,984	2,832	3,157
	65-74	5,052	5,253	5,524	5,909	6,595
	75-	9,749	10,441	10,788	11,293	12,868
Male (rate:%)		11,616 (65.6)	12,201 (65.3)	12,612 (65.4)	12,924 (64.5)	14,417 (63.7)

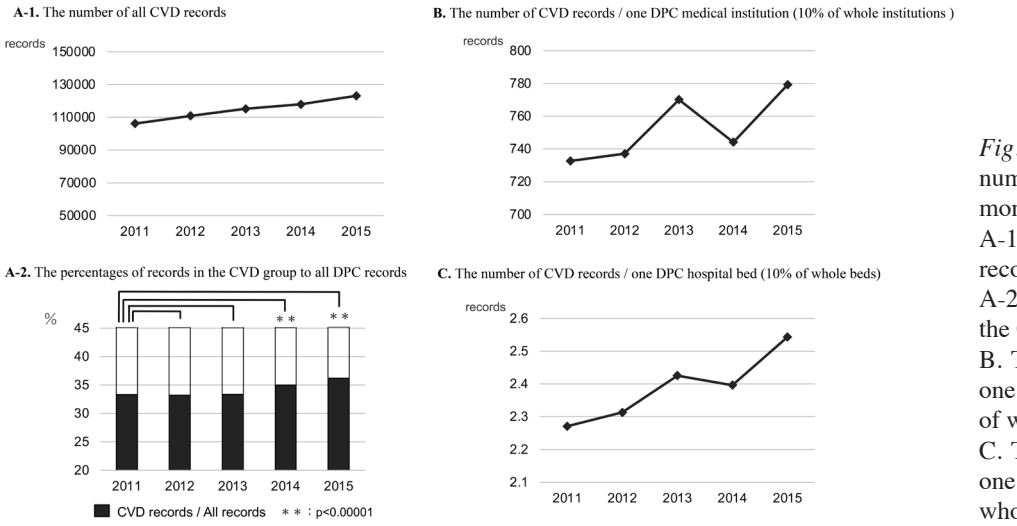
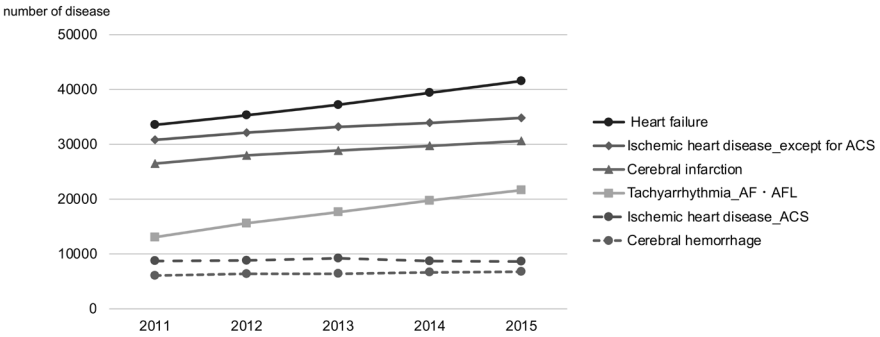


Fig. 1. Distribution in terms of the number of all CVD records for 4 months from 2011 to 2015.
A-1. The number of all CVD records
A-2. The percentages of records in the CVD group to all DPC records
B. The number of CVD records / one DPC medical institution (10% of whole institutions)
C. The number of CVD records / one DPC hospital bed (10% of whole beds)



	2011		2012		2013		2014		2015	
1	Heart failure	33550	Heart failure	35321	Heart failure	37196	Heart failure	39416	Heart failure	41554
2	IHD_except for ACS	30817	IHD_except for ACS	32134	IHD_except for ACS	33182	IHD_except for ACS	33922	IHD_except for ACS	34825
3	Cerebral infarction	26496	Cerebral infarction	27976	Cerebral infarction	28863	Cerebral infarction	29709	Cerebral infarction	30625
4	Tachyarrhythmia_AF・AFL	13077	Tachyarrhythmia_AF・AFL	15618	Tachyarrhythmia_AF・AFL	17646	Tachyarrhythmia_AF・AFL	19742	Tachyarrhythmia_AF・AFL	21645
5	IHD_ACS	8738	IHD_ACS	8823	IHD_ACS	9233	IHD_ACS	8723	IHD_ACS	8637
6	Cerebral hemorrhage	6074	Cerebral hemorrhage	6389	Cerebral hemorrhage	6414	Cerebral hemorrhage	6669	Cerebral hemorrhage	6770
7	vascular occlusion・stenosis	3784	vascular occlusion・stenosis	3783	vascular occlusion・stenosis	3924	vascular occlusion・stenosis	3975	vascular occlusion・stenosis	4044
8	Tachyarrhythmia_ventricular	2833	Tachyarrhythmia_ventricular	2756	Tachyarrhythmia_ventricular	2935	Tachyarrhythmia_ventricular	2981	Tachyarrhythmia_ventricular	2939
9	Tachyarrhythmia_other	1426	Tachyarrhythmia_other	1628	Tachyarrhythmia_other	1768	Tachyarrhythmia_other	1838	Tachyarrhythmia_other	1976
10	Cerebrovascular_dissection・aneurysm	1324	Cardiomyopathy	1415	Cardiomyopathy	1552	SAH	1645	SAH	1763

Fig. 1-D.
Time trends of type of CVD in all CVD patients (2011-2015)

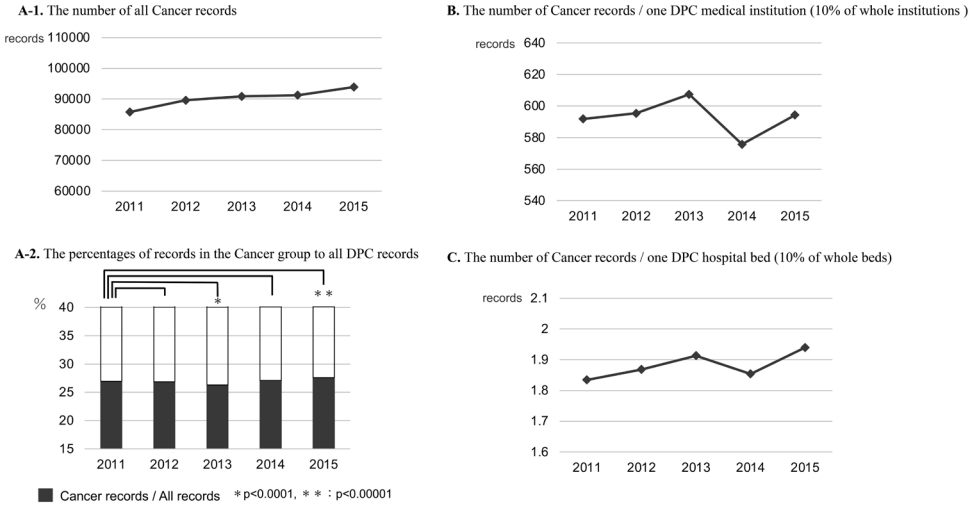
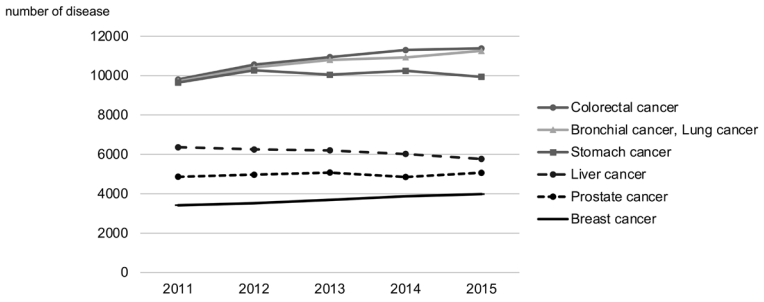
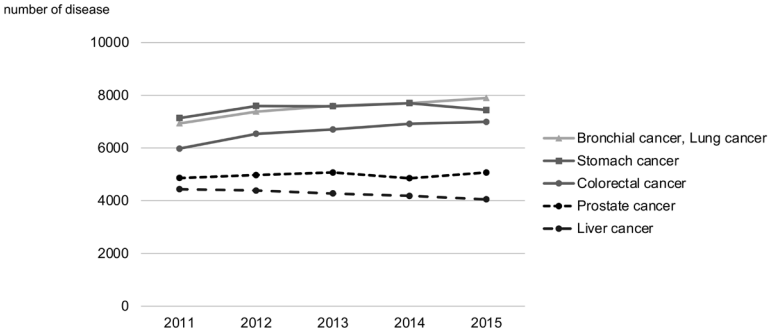


Fig. 2. Distribution in terms of the number of all cancer records for 4 months from 2011 to 2015.
A-1. The number of all Cancer records
A-2. The percentages of records in the Cancer group to all DPC records
B. The number of Cancer records / one DPC medical institution (10% of whole institutions)
C. The number of Cancer records / one DPC hospital bed (10% of whole beds)



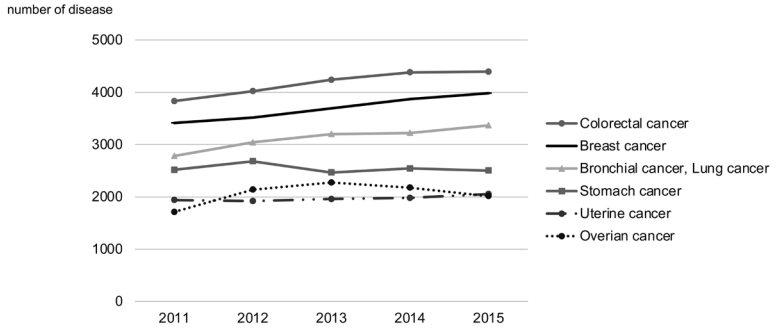
	2011		2012		2013		2014		2015	
1	Colorectal cancer	9811	Colorectal cancer	10560	Colorectal cancer	10941	Colorectal cancer	11300	Colorectal cancer	11388
2	Bronchial cancer, Lung cancer	9714	Bronchial cancer, Lung cancer	10420	Bronchial cancer, Lung cancer	10800	Bronchial cancer, Lung cancer	10926	Bronchial cancer, Lung cancer	11263
3	Stomach cancer	9650	Stomach cancer	10273	Stomach cancer	10048	Stomach cancer	10242	Stomach cancer	9942
4	Liver cancer	6367	Liver cancer	6250	Liver cancer	6206	Metastatic Liver cancer	6047	Metastatic Liver cancer	5846
5	Metastatic Liver cancer	5496	Metastatic Liver cancer	5563	Metastatic Liver cancer	5883	Liver cancer	6018	Liver cancer	5767
6	Prostate cancer	4862	Prostate cancer	4972	Prostate cancer	5072	Metastatic Bone tumor	4890	Prostate cancer	5067
7	Metastatic Bone tumor	4249	Metastatic Bone tumor	4563	Metastatic Bone tumor	4913	Prostate cancer	4851	Metastatic Bone tumor	4813
8	Metastatic Lung cancer	3414	Metastatic Lung cancer	3712	Metastatic Lung cancer	3747	Breast cancer	3869	Breast cancer	3982
9	Breast cancer	3413	Metastatic Peritoneal cancer	3538	Breast cancer	3692	Metastatic Lung cancer	3733	Metastatic Lung cancer	3725
10	Metastatic Peritoneal cancer	3280	Breast cancer	3516	Metastatic Peritoneal cancer	3605	Metastatic Peritoneal cancer	3611	Metastatic Peritoneal cancer	3644

Fig. 3-A Time trends of changes in cancer site in all cancer patients (2011-2015)



	2011		2012		2013		2014		2015	
1	Stomach cancer	7134	Stomach cancer	7594	Bronchial cancer, Lung cancer	7599	Bronchial cancer, Lung cancer	7704	Bronchial cancer, Lung cancer	7896
2	Bronchial cancer, Lung cancer	6932	Bronchial cancer, Lung cancer	7379	Stomach cancer	7583	Stomach cancer	7699	Stomach cancer	7439
3	Colorectal cancer	5979	Colorectal cancer	6540	Colorectal cancer	6703	Colorectal cancer	6919	Colorectal cancer	6993
4	Prostate cancer	4862	Prostate cancer	4972	Prostate cancer	5072	Prostate cancer	4851	Prostate cancer	5067
5	Liver cancer	4435	Liver cancer	4385	Liver cancer	4275	Liver cancer	4182	Liver cancer	4049
6	Metastatic Liver cancer	3454	Metastatic Liver cancer	3529	Metastatic Liver cancer	3711	Metastatic Liver cancer	3639	Metastatic Liver cancer	3585
7	Metastatic Bone tumor	2534	Metastatic Bone tumor	2805	Metastatic Bone tumor	3057	Metastatic Bone tumor	2984	Metastatic Bone tumor	2951
8	Metastatic Lung cancer	1946	Metastatic Lung cancer	2142	Metastatic Lung cancer	2133	Metastatic Lung cancer	2081	Metastatic Lung cancer	2072
9	Metastatic Peritoneal cancer	1586	Metastatic Peritoneal cancer	1679	Metastatic Peritoneal cancer	1701	Metastatic Peritoneal cancer	1713	Metastatic Peritoneal cancer	1781
10	Bladder cancer	1509	Metastatic Brain rumor	1352	Bladder cancer	1576	Bladder cancer	1662	Bladder cancer	1750

Fig. 3-B Time trends of changes in cancer site in male cancer patients (2011-2015)



	2011		2012		2013		2014		2015	
1	Colorectal cancer	3832	Colorectal cancer	4020	Colorectal cancer	4238	Colorectal cancer	4381	Colorectal cancer	4395
2	Breast cancer	3413	Breast cancer	3516	Breast cancer	3692	Breast cancer	3869	Breast cancer	3982
3	Bronchial cancer, Lung cancer	2782	Bronchial cancer, Lung cancer	3041	Bronchial cancer, Lung cancer	3201	Bronchial cancer, Lung cancer	3222	Bronchial cancer, Lung cancer	3367
4	Stomach cancer	2516	Stomach cancer	2679	Stomach cancer	2465	Stomach cancer	2543	Stomach cancer	2503
5	Metastatic Liver cancer	2042	Overian cancer	2139	Overian cancer	2275	Metastatic Liver cancer	2408	Metastatic Liver cancer	2261
6	Uterine cancer	1940	Metastatic Liver cancer	2034	Metastatic Liver cancer	2172	Overian cancer	2177	Uterine cancer	2053
7	Liver cancer	1932	Uterine cancer	1920	Uterine cancer	1959	Uterine cancer	1979	Overian cancer	2016
8	Metastatic Bone tumor	1715	Liver cancer	1865	Liver cancer	1931	Metastatic Bone tumor	1906	Metastatic Peritoneal cancer	1863
9	Overian cancer	1712	Metastatic Peritoneal cancer	1859	Metastatic Peritoneal cancer	1904	Metastatic Peritoneal cancer	1898	Metastatic Bone tumor	1862
10	Metastatic Peritoneal cancer	1694	Metastatic Bone tumor	1758	Metastatic Bone tumor	1856	Liver cancer	1836	Liver cancer	1718

Fig. 3-C Time trends of changes in cancer site in female cancer patients in (2011-2015)

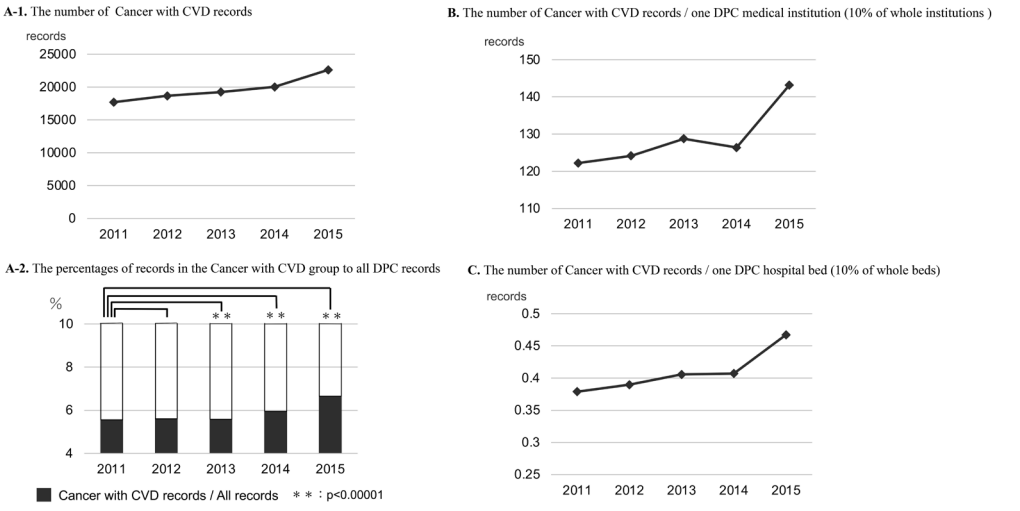
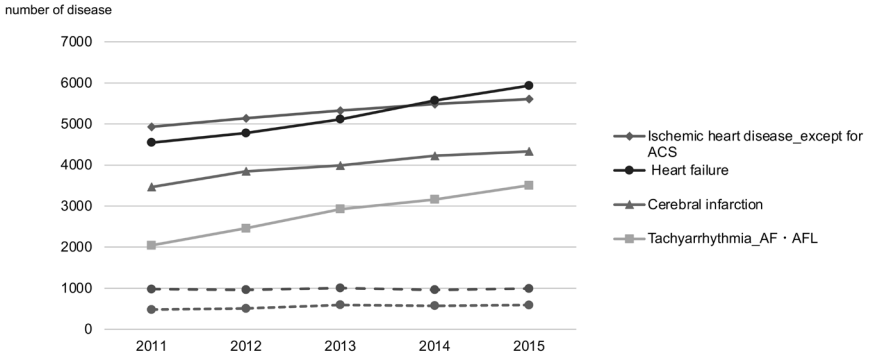


Fig. 4. Distribution in terms of the number of cancer with CVD records for 4 months from 2011 to 2015.
A-1. The number of Cancer with CVD records
A-2. The percentages of records in the Cancer with CVD group to all DPC records
B. The number of Cancer with CVD records / one DPC medical institution (10% of whole institutions)
C. The number of Cancer with CVD records / one DPC hospital bed (10% of whole beds)



	2011		2012		2013		2014		2015	
1	IHD_except for ACS	4930	IHD_except for ACS	5136	IHD_except for ACS	5324	Heart failure	5571	Heart failure	5932
2	Heart failure	4544	Heart failure	4778	Heart failure	5112	IHD_except for ACS	5484	IHD_except for ACS	5605
3	Cerebral infarction	3464	Cerebral infarction	3845	Cerebral infarction	3989	Cerebral infarction	4225	Cerebral infarction	4330
4	Tachyarrhythmia_AF・AFL	2044	Tachyarrhythmia_AF・AFL	2457	Tachyarrhythmia_AF・AFL	2927	Tachyarrhythmia_AF・AFL	3162	Tachyarrhythmia_AF・AFL	3505
5	IHD_ACS	976	IHD_ACS	960	IHD_ACS	1004	IHD_ACS	961	IHD_ACS	992
6	Cerebral hemorrhage	480	Cerebral hemorrhage	505	Cerebral hemorrhage	591	Cerebral hemorrhage	573	Cerebral hemorrhage	589
7	vascular occlusion・stenosis	436	vascular occlusion・stenosis	415	vascular occlusion・stenosis	460	vascular occlusion・stenosis	455	vascular occlusion・stenosis	490
8	Tachyarrhythmia_ventricular	379	Tachyarrhythmia_other	381	Tachyarrhythmia_other	424	Tachyarrhythmia_ventricular	434	Tachyarrhythmia_other	479
9	Tachyarrhythmia_other	342	Tachyarrhythmia_ventricular	332	Tachyarrhythmia_ventricular	401	Pulmonary thromboembolism	418	Pulmonary thromboembolism	451
10	Pulmonary thromboembolism	288	Pulmonary thromboembolism	315	Pulmonary thromboembolism	348	Tachyarrhythmia_other	410	Tachyarrhythmia_ventricular	435

Fig. 4-D. Time trends of type of CVD in cancer with CVD patient (2011-2015)

and cerebral infarction. Heart failure was on the rise surpassing ischemic heart disease in 2014.

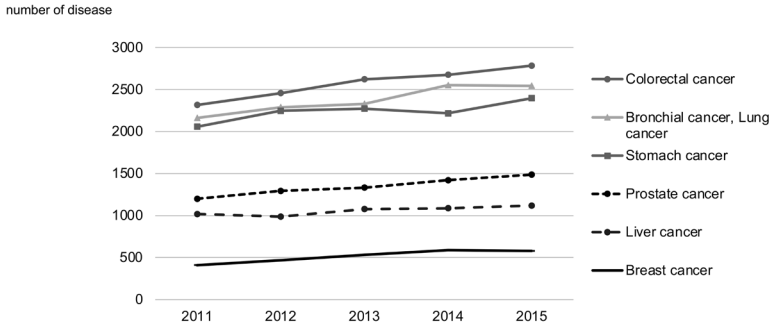
Colorectal cancer was the most commonly diagnosed cancer followed by bronchial/lung cancer and stomach cancer in patients with both cancer and CVD (Figure 5-A). These findings were similar to all cancer groups. Stomach cancer, bronchial/lung cancer and colorectal cancer in males (Figure 5-B) and colorectal cancer, bronchial/lung cancer and breast cancer in females (Figure 5-C) were commonly diagnosed.

DISCUSSION

Epidemiological data in onco-cardiology have not been sufficiently provided. In this study, we have shown the annual number of patients with cancer and/or CVD using DPC inpatient HIC records in Japan.

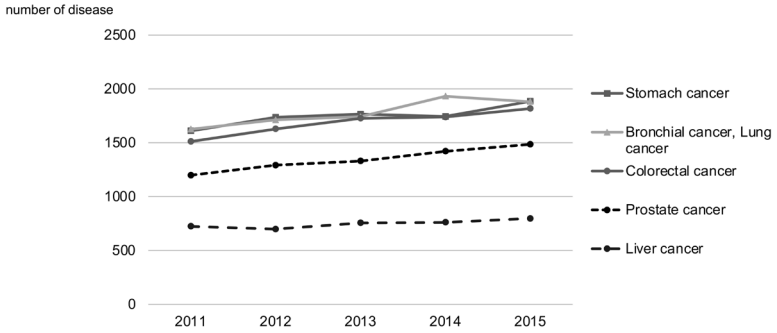
Cancer is one of the leading causes of death worldwide, estimated at nearly 10 million deaths in 2020 [13]. The estimated number of cancer deaths in 2019 was 380,300 (222,500 males and 157,800 females) in Japan [1]. Both the prevalence of cancer, and its deaths have been increasing, mainly due to the hyper-aging society in Japan. However, when looking at age-adjusted rates, after excluding the effects of population aging, cancer deaths peaked in the mid-1990s and have been declining since then [14]. In such situation, cancer survival rates have improved in many sites [14].

Our findings showed that the number of all cancer records statistically increased significantly over time and there was a similar trend in cancer sites. It suggested that a substantial increase in the number of elderly survivors were caused by aging, at least in part. In addition, patients with cancer have been able to sur-



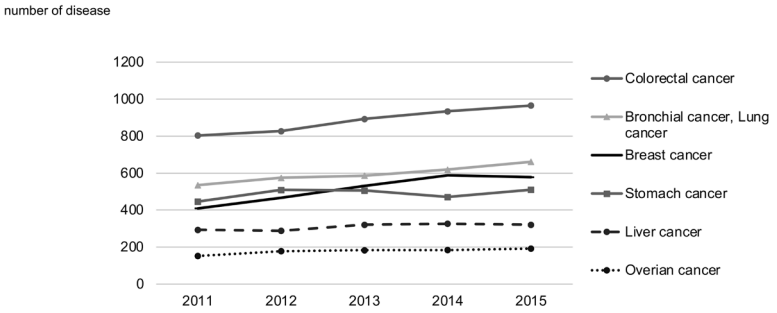
	2011		2012		2013		2014		2015	
1	Colorectal cancer	2315	Colorectal cancer	2456	Colorectal cancer	2620	Colorectal cancer	2674	Colorectal cancer	2783
2	Bronchial cancer, Lung cancer	2161	Bronchial cancer, Lung cancer	2288	Bronchial cancer, Lung cancer	2328	Bronchial cancer, Lung cancer	2551	Bronchial cancer, Lung cancer	2543
3	Stomach cancer	2056	Stomach cancer	2246	Stomach cancer	2272	Stomach cancer	2216	Stomach cancer	2395
4	Prostate cancer	1199	Prostate cancer	1293	Prostate cancer	1331	Prostate cancer	1421	Prostate cancer	1486
5	Liver cancer	1017	Liver cancer	987	Liver cancer	1077	Liver cancer	1087	Liver cancer	1119
6	Metastatic Liver cancer	743	Metastatic Liver cancer	847	Metastatic Liver cancer	913	Metastatic Liver cancer	920	Metastatic Liver cancer	952
7	Metastatic Bone tumor	559	Metastatic Bone tumor	650	Metastatic Bone tumor	704	Metastatic Bone tumor	699	Metastatic Bone tumor	736
8	Metastatic Lung cancer	481	Metastatic Lung cancer	508	Metastatic Lung cancer	549	Breast cancer	588	Breast cancer	578
9	Breast cancer	409	Breast cancer	467	Breast cancer	531	Metastatic Lung cancer	554	Metastatic Lung cancer	559
10	non-Hodgkin lymphoma	408	Metastatic Peritoneal cancer	438	Bladder cancer	487	Bladder cancer	513	Metastatic Peritoneal cancer	520

Fig. 5-A Time trends of changes in cancer site in cancer with CVD patients (2011-2015)



	2011		2012		2013		2014		2015	
1	Bronchial cancer, Lung cancer	1626	Stomach cancer	1737	Stomach cancer	1766	Bronchial cancer, Lung cancer	1932	Stomach cancer	1885
2	Stomach cancer	1610	Bronchial cancer, Lung cancer	1713	Bronchial cancer, Lung cancer	1742	Stomach cancer	1745	Bronchial cancer, Lung cancer	1882
3	Colorectal cancer	1512	Colorectal cancer	1629	Colorectal cancer	1727	Colorectal cancer	1740	Colorectal cancer	1818
4	Prostate cancer	1199	Prostate cancer	1293	Prostate cancer	1331	Prostate cancer	1421	Prostate cancer	1486
5	Liver cancer	724	Liver cancer	699	Liver cancer	756	Liver cancer	761	Liver cancer	798
6	Metastatic Liver cancer	506	Metastatic Liver cancer	583	Metastatic Liver cancer	624	Metastatic Liver cancer	607	Metastatic Liver cancer	639
7	Metastatic Bone tumor	383	Metastatic Bone tumor	451	Metastatic Bone tumor	504	Metastatic Bone tumor	493	Metastatic Bone tumor	510
8	Bladder cancer	334	Bladder cancer	335	Bladder cancer	400	Bladder cancer	410	Metastatic Lung cancer	334
9	Metastatic Lung cancer	308	Metastatic Lung cancer	319	Metastatic Lung cancer	356	Metastatic Lung cancer	335	Metastatic Peritoneal cancer	277
10	non-Hodgkin lymphoma	237	non-Hodgkin lymphoma	250	non-Hodgkin lymphoma	249	Metastatic Peritoneal cancer	271	Bladder cancer	426

Fig. 5-B Time trends of changes in cancer site in male cancer with CVD patients (2011-2015)



	2011		2012		2013		2014		2015	
1	Colorectal cancer	803	Colorectal cancer	827	Colorectal cancer	893	Colorectal cancer	934	Colorectal cancer	965
2	Bronchial cancer, Lung cancer	535	Bronchial cancer, Lung cancer	575	Bronchial cancer, Lung cancer	586	Bronchial cancer, Lung cancer	619	Bronchial cancer, Lung cancer	661
3	Stomach cancer	446	Stomach cancer	509	Breast cancer	531	Breast cancer	588	Breast cancer	578
4	Breast cancer	409	Breast cancer	467	Stomach cancer	506	Stomach cancer	471	Stomach cancer	510
5	Liver cancer	293	Liver cancer	288	Liver cancer	321	Liver cancer	326	Liver cancer	321
6	Metastatic Liver cancer	237	Metastatic Liver cancer	264	Metastatic Liver cancer	289	Metastatic Liver cancer	313	Metastatic Liver cancer	313
7	Metastatic Peritoneal cancer	193	Metastatic Peritoneal cancer	204	Metastatic Peritoneal cancer	212	Metastatic Peritoneal cancer	224	Metastatic Peritoneal cancer	243
8	Metastatic Bone tumor	176	Metastatic Bone tumor	199	Metastatic Bone tumor	200	Metastatic Lung cancer	219	Metastatic Bone tumor	226
9	Metastatic Lung cancer	173	Metastatic Lung cancer	189	Metastatic Lung cancer	193	Metastatic Bone tumor	206	Metastatic Lung cancer	225
10	non-Hodgkin lymphoma	171	Overian cancer	178	Overian cancer	183	Overian cancer	184	Overian cancer	192

Fig. 5-C Time trends of changes in cancer site in female cancer with CVD patients (2011-2015)

vive longer due to advanced cancer therapies [4,5]. Similarly, the increase in the number of records with CVD may be related not only to the aging population but also to the introduction of new drugs for cardiovascular disease and catheterization for the elderly [15,16].

Moreover, we have shown that the number of patients with cancer with CVD has been increasing annually in Japan, which is the most important thing. Okura Y. et al. showed that the total number of Japanese cancer patients with CVD is expected to increase rapidly by 30,000 by 2020, peaking at 313,000 in 2030–2034 [17]. Additionally, it was reported that the CVD population would be predominantly men ≥ 75 years of age [17], which was consistently observed in the present study.

Our results show that there were 22,620 records observed as cancer with CVD in 2015, which means that there were actually about 226,200 records as cancer with CVD in four months of 2015 in all of Japan. These findings included the possibility that the same patients may be admitted more than once, suggesting that we need to treat 678,600 inpatient treatments as cancer with CVD patients annually in Japan.

Furthermore, according to the Niigata Cancer CVD Study, 10-year (2005–2014) cancer registry, the survival rate was 64.0% for all cancer patients and 44.2% for cancer patients with CVD [18]. The number of cancer survivors also increased in the United States. More than 16.9 million Americans with a history of cancer have survived on 2019 and would, reach more than 22.1 million by 2030 [19]. The deaths from CVD mainly occur in patients with breast, prostate, or bladder cancer [20]. According to Canadian longitudinal study, the odds of several CVD risk factors were higher in middle-aged cancer survivors than the general Canadian population [21].

It is mentioned that patients with cancer and cancer survivors are at risk of CVD for several reasons [22]. First, many new cancer therapies, are associated with vascular and metabolic complications [22]. There are many recognized and unrecognized adverse cardiovascular effects caused by cancer therapies [23]. As cancer survivors live longer, they would be at risk of complications of heart disease, partially due to the effects of cardiotoxicity of chemotherapy and radiotherapy [6,24-26].

Next, cancer patients have an increased risk of thromboembolic events [22]. Venous thrombosis, including deep vein thrombosis (DVT), catheter–associated thrombosis, and pulmonary embolism are known [22,27,28]. Our finding in the present study also indicated that pulmonary thromboembolism was more common in both cancer with CVD patients compared to all CVD patients.

Finally, it is suggested that common risk factors relate to both cancer and CVD [22]. Smoking has been well known to be associated with lung cancer and CVD [29].

Until now, cardiologists and oncologists have treated patients independently, however in the near future, both specialists have to be aware of the above and should both enhance their knowledge as well as collaborate with each other.

Strength and Limitation

The NDB is a very large database constructed by the Ministry of Health, Labour and Welfare by collecting anonymized HIC information collected from insurers across all of Japan. It is a near-universal database that covers most of the insurance treatments conducted in Japan and is highly representative of the population. Therefore, the traceability at the individual level is ensured even when patients visit different hospitals or clinics. In this study, we used datasets based on DPC inpatient HIC from the NDB.

In studies using medical HIC, it has often been pointed out that they do not always provide accurate information because they are originally designed to be used for insurance claims [30]. However, it is considered that the DPC HIC are more accurate due to medical institutions usually being subject to a review of their requests for insurance payments. Yamana et al. reported the validity of the DPC HIC data in Japan [31]. According to the study, the specificity of diagnoses in the DPC data exceeded 96%, while the sensitivity was variable across diseases [31]. Chronic pulmonary diseases and liver disorders had low sensitivity in the 30% range [31]. The sensitivity of heart failure and malignant diseases was high at 68.8% and 83.5%, respectively [31]. In the JROADDPC dataset, ICD-10 codes showed acceptable concordance between DPC and clinical data for the diagnosis of AMI or HF among hospitalized patients [32]. These studies supported that the diagnostic accuracy rate of DPC is considered to be high.

Even more, as of April 2020, there are 1,757 DPC medical institutions and 483,180 DPC-calculated beds, which is more than half of the total number of hospital beds in Japan [12]. DPC inpatient HIC data are thought to be enough to cover almost all acute inpatients who required acute care for special procedures, treatments, or surgeries. On the other hand, they do not reflect what would be seen in primary care or

patients in the recovery ward. Furthermore, there is no data of non-insurance practices. Also, public medical care such as high-cost medical care, welfare recipients, and designated intractable diseases are excluded. Currently, we are not able to account for cases outside of DPC treatment, such as unapproved anti-cancer drug treatment, in the DPC study.

In the present study, because IDs were not provided to identify individual patients, it was not possible to identify the patients within a data set, or to link across the multiple data sets. Thus, the analysis in the present study was conducted on a HIC record basis, not on a patient basis. Additionally, DPC records include the inability to track patients due to insurance withdrawals. It means that it is not only impossible to examine the causal relationship between cancer and CVD, but also, we were not able to analyze trends over time. However, the impact of this on our findings is negligible.

Although DPC HIC contain information of the main diseases for hospitalization and the required medical resources, we collected only the cancer and CVD from all injury and disease in the records. Although it may cause some bias for the analyses of combined cancer and CVD, we consider that this bias should occur with the same probability in each dataset.

It might be difficult in determining outcomes due to the lack of data to adjust for patient severity of illness. Although it was not done in this study, due to the limited time for the data availability, it is possible to evaluate the definition of severity and comorbidity by scoring using the Charlson comorbidity index (CCI) [33].

The DPC records have the following characteristics: If a patient is discharged and re-hospitalize within 7 days of the same month with the same disease in a DPC-calculated hospital, the readmission will be considered as a series of admissions with the previous admission, which means that the patient has only a HIC. If more than 7 days, two or more HIC may exist in the same month even with the same disease. In the case of chemotherapy for a patient with malignant tumors, readmission for the same disease is not considered as a series of hospitalizations, even if the readmission is within 7 days, indicating that multiple HIC may exist in the same patient in the same month, who takes chemotherapy. As described above, there may be multiple HIC for the same patient in the same month. However, the sampling dataset used in this study randomly sampled 10% of all DPC records in Japan. We consider that this bias should occur with the same probability in each month and each year.

Finally, in this study, the number of DPC medical institutions and hospital beds were taken into account to compare the changes in the number of records. Furthermore, we should have added a comparison by different age groups to consider the aging of the population. In addition, to consider the advances in treatment and technology, the type of medication, with or without chemotherapy, radiotherapy and surgery should be added to the evaluation items. We were not able to examine these issues due to the limited time for the data availability. We would add these analyses in our next study.

CONCLUSION

We were able to assess the increase in cancer among CVD patients using DPC inpatient records obtained from the NDB. Both cardiologists and oncologists should be more aware of this phenomenon.

IRB INFORMATION: The present study was approved by the Institutional Review Board at Kurume University (Approval Number 19147).

DATA AVAILABILITY: The deidentified participant data will not be shared.

DISCLOSURES: The authors declare no conflict of interest.

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TABLE S1.
Definition of Cardiovascular diseases

		ICD10 codes
Cardiovascular diseases		
①	Heart failure	I11.0, 11.9, 50.0, 50.1, 50.9, 51.7, 51.9
② -1	Ischemic heart disease:ACS	I20.0, 21.0, 21.1-21.4, 21.9, 22.0, 22.1, 22.8, 22.9, 23.0-23.6, 23.8, 24.0, 24.1, 24.8, 24.9
② -2	Ischemic heart disease_except for ACS	I20.1, 20.8, 20.9, 25.1-25.6, 25.8, 25.9
③	Cardiopulmonary arrest	I46.0, 46.1, 46.9
④	Pulmonary thromboembolism	I26.0, 26.9
⑤ -1-a	Tachyarrhythmia_ventricular	I47.0, 47.2, 49.0, 49.3
⑤ -1-b	Tachyarrhythmia_AF･AFL	I48.0-48.2, 48.9
⑤ -1-c	Tachyarrhythmia_other	I47.1, 49.1
⑤ -2	Bradyarrhythmia	I44.0-44.7, 45.1-45.6, 45.8, 45.9, 49.5
⑤ -3	Arrhythmia_other	I47.9, 49,2, 49.4, 49.8, 49.9
⑥	Valvular disease	I05.0-05.2, 05.8, 05.9, 06.0-06.2, 06.9, 07.0-07.2, 07.8, 07.9, 08.0-08.3, 08.8, 08.9, 09.0-09.2, 09.8, 09.9, 34.0-34.2, 34.8, 35.0-35.2, 35.8, 35.9, 36.0-36.2, 36.9, 37.0-37.2, 37.9
⑦	Pulmonary hypertension	I27.0, 27.2, 27.8, 27.9, 28.0, 28.1, 28.8, 28.9
⑧	Pericarditis･Myocarditis	I30.0, 30.1, 30.8, 30.9, 31.0-31.3, 31.8, 31.9, 33.0, 33.9, 38, 40.0, 40.1, 40.8, 40.9, 51.4
⑨	Takotsubo cardiomyopathy･Carditis	I51.8
⑩ -1	Cardiomyopathy_except for drug-induced	I42.0-42.6, 42.8, 42.9
⑩ -2	Cardiomyopathy_drug-induced	I42.7
Cerebrovascular diseases		
①	Subarachnoid hemorrhage	I60.0-60.9, I69.0
②	Cerebral hemorrhage	I61.0, 61.1, 61.3-61.6, 61.8, 61.9, 62.0, 62.1, 62.9, 69.1
③	Cerebral infarction	I63.0-63.6, 63.8, 63.9, 69.3
④	Vascular occlusion･stenosis	I65.0-65.3, I66.0-66.3, 66.8, 66.9
⑤	Dissection･Aneurysm	I67.0, 67.1
⑥	Other	I67.2-67.9
Vascular diseases		
①	Aortic aneurysm, dissection	I71.0-71.6, 71.8, 71.9
②	Aneurysm, dissection_Other	I72.0-72.6, 72.8, 72.9
③	Peripheral vascular disease	I70.2, 70.8, 70.9, 73.0, 73.1, 73.8, 73.9, 74.0-74.5, 74.8, 74.9, 77.1
④	Venous thrombosis	I80.2, 81, 82.0-82.3, 82.8, 82.9
⑤	Phlebitis	I80.0, 80.1, 80.3, 80.8, 80.9
⑥ -1	Arteriosclerosis	I70.0
⑥ -2	Renal arteriosclerosis	I70.1

Abbreviations: ACS, Acute Coronary Syndrome; AF, atrial fibrillation;AFL, atrial flutter;