

Relationship of moderate metabolic risk factor clustering to cardiovascular disease mortality in non-lean Japanese: A 15-year follow-up of NIPPON DATA90

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ARTICLE INFO

Article history:

Received 10 December 2009

Received in revised form

21 November 2010

Accepted 25 November 2010

Available online 4 December 2010

Keywords:

Metabolic risk factor

Cardiovascular disease

Mortality

Epidemiology

ABSTRACT

Objective: The individual components of metabolic syndrome are defined as levels ranging from moderate to high level as to require medication. We investigated the impact of moderate metabolic risk factor clustering on cardiovascular disease (CVD) mortality.

Methods: We followed up 6758 non-lean Japanese in randomly selected areas from all over the country who had no history of CVD for 15 years. The multivariate-adjusted hazards ratio (HR) and 95% confidence interval (CI) for CVD mortality according to the number of moderate metabolic risk factors (BMI ≥ 25 kg/m², 130/85 mmHg \leq systolic/diastolic BP $<$ 140/90 mmHg, 140 mg/dl \leq casual blood glucose $<$ 200 mg/dl, triglycerides ≥ 150 mg/dl and/or HDL cholesterol $<$ 40 mg/dl [men], 50 mg/dl [women]) were estimated using the Cox proportional hazards model. The population-attributable risk fraction of moderate metabolic risk factor clustering was also estimated.

Results: During the follow-up, 282 participants died of CVD. CVD mortality tended to increase with the number of moderate metabolic risk factors. However, they were not statistically significant. The multivariate-adjusted HRs were 1.82 (95%CI: 0.89–3.73) for having any moderate metabolic risk factors and 2.87 (95%CI: 1.46–5.64) for having any medication-required metabolic risk factors, compared with participants without any moderate metabolic risk factors. The population-attributable risk fractions were 7.3% and 52.4% for any moderate and medication-required metabolic risk factors, respectively.

Conclusions: We did not find the statistically significant increase of CVD mortality for moderate metabolic risk factor clustering. Its attribution was relatively small in this Japanese population. More efforts would be required to detect and control medication-required risk factors.

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1. Introduction

Metabolic syndrome is the concept of metabolic risk factor clustering, which is an appropriate target for therapeutic lifestyle changes [1–4]. Several cohort studies have revealed that metabolic syndrome is associated with an increased risk of cardiovascular disease (CVD) [5–11]. However, the individual component risk factors

in the present criteria for metabolic syndrome are not graded by severity but they are defined as levels ranging from moderate to high requiring medication [12–17]. Because individual established risk factors such as hypertension or diabetes strongly and independently increase the risk of CVD [8,18,19], the risk of moderate metabolic risk factor clustering on CVD might escape detection. Individuals with established risk factors often require medication in addition to therapeutic lifestyle changes, whereas moderate risk factors can be controlled with such lifestyle changes [17]. However, the CVD risk for individuals with moderate risk factor clustering has rarely been reported.

Here we investigated the association between clustering of moderate metabolic risk factors and CVD mortality among people with normal weight or more in a 15-year follow-up of a cohort of

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representative general Japanese, who participated in the National Survey of Circulatory Disorders of Japan in 1990.

2. Methods

2.1. Study population

NIPPON DATA (National Integrated Project for Prospective Observation of Non-communicable Disease and Its Trends in the Aged) is a cohort study of participants in the National Survey on Circulatory Disorders of Japan, which has been conducted by the Ministry of Health, Labor and Welfare of Japan. NIPPON DATA includes two cohort studies of which the baseline data were surveyed in 1980 and in 1990 (NIPPON DATA80 and NIPPON DATA90) and the details of the studies have been described [8,18–20]. Here, we investigated the data from NIPPON DATA90 because some important metabolic risk factors such as HDL cholesterol were not included in the NIPPON DATA80 baseline survey.

A total of 8384 residents (3504 men and 4880 women, aged ≥ 30 years) from 300 randomly selected districts from all over Japan participated in the baseline survey and were followed up until November, 2005. The participation rate in this survey was 76.5%. Of the 8384 participants, 1626 were excluded because of a history of coronary heart disease or stroke ($n=261$), information missing at the baseline survey ($n=649$), withdrawal due to incomplete residential access information ($n=255$) and a low BMI ($\text{BMI} < 18.5 \text{ kg/m}^2$) ($n=461$). We excluded these lean participants because they also have a higher CVD mortality risk in Japan as well as in western studies [21,22]. The remaining 6758 participants (2828 men and 3930 women) were analyzed in this study. The Institutional Review Board of Shiga University of Medical Science (No. 12-18, 2000) approved this study.

2.2. Baseline examination

Body mass index (BMI) was calculated as weight (kg) divided by the square of height (m). Trained observers measured baseline blood pressure using a standard mercury sphygmomanometer on the right arm of seated participants. Non-fasting blood samples were obtained at the baseline survey. Serum was separated and centrifuged soon after blood coagulation. Plasma samples were collected into siliconized tubes containing sodium fluoride and shipped to a central laboratory (SRL, Tokyo) for blood measurements. Plasma glucose was measured enzymatically. Serum triglycerides (TG) and total cholesterol were also measured enzymatically and high-density lipoprotein (HDL) cholesterol was measured after heparin-calcium precipitation.

Public health nurses collected the information about smoking, alcohol consumption and medical history. We divided participants into four categories of smokers (never-smoked; ex-smoker; current smoker of <20 or ≥ 20 cigarettes/day) and six categories of drinking (never-drink; ex-drinker; current drinker of 1–4 and more *gou* of sake/day); 1 *gou* (180 ml) is equivalent to 23 g of alcohol.

2.3. Endpoints

We previously reported that participants who had died in each area were confirmed by computer matching with data from the National Vital Statistics database, using area, gender, date of birth and death as key codes [19,23]. The underlying causes of death in the National Vital Statistics were coded according to the 9th International Classification of Diseases (ICD-9) until 1994 and according to the 10th International Classification of Disease (ICD-10) from 1995. Details of these classifications are described elsewhere [18–20,23]. Deaths coded from 393 to 459 according to

ICD-9 and from I00 to I99 according to ICD-10 were defined as CVD deaths in this study.

2.4. Definition of metabolic risk factors

Based on the modified NCEP (National Cholesterol Education Program) metabolic syndrome criteria [12], moderate metabolic risk factors were defined as follows: obesity ($\text{BMI} \geq 25 \text{ kg/m}^2$), moderate high blood pressure ($130 \leq$ systolic blood pressure [SBP] $< 140 \text{ mmHg}$ and/or $85 \leq$ diastolic blood pressure [DBP] $< 90 \text{ mmHg}$), dyslipidemia ($150 \text{ mg/dl} \leq$ non-fasting triglycerides and/or HDL-cholesterol $< 40 \text{ mg/dl}$ for men, and $< 50 \text{ mg/dl}$ for women). We also defined moderate high blood glucose ($140 \text{ mg/dl} \leq$ non-fasting blood glucose $< 200 \text{ mg/dl}$). Because our samples were non-fasting, post load blood glucose of $\geq 140 \text{ mg/dl}$ indicated impaired glucose tolerance [24]. Furthermore, we defined medication-required metabolic risk factors as follows: high blood glucose (non-fasting blood glucose $\geq 200 \text{ mg/dl}$ and/or medication), high blood pressure (SBP $\geq 140 \text{ mmHg}$ and/or DBP $\geq 90 \text{ mmHg}$ and/or medication) according to the criteria of hypertension stage 1 in JNC7 (The Seventh Report of the Joint National Committee of Prevention, Detection, Evaluation, and Treatment of High Blood Pressure) [25]. We divided the participants into five categories of metabolic risk factor condition (none, moderate metabolic risk factor [1, 2 and ≥ 3 factors], any medication-required metabolic risk factor). Participants with any one or more of the medication-required metabolic risk factors were categorized as “any medication-required metabolic risk factor” irrespective of the number of moderate metabolic risk factors.

2.5. Statistical analysis

Differences in the baseline characteristics of participants were examined using the analysis of variance for continuous variables and χ^2 -test for dichotomized variables according to metabolic risk factors. The multivariate-adjusted hazard ratio (HR) of all CVD mortality for each group was estimated using the Cox proportional hazards model adjusted for age, sex, total cholesterol, smoking and drinking categories. Participants without metabolic risk factors were established as the reference group. Population-attributable risk fraction (PAF) for CVD deaths were estimated using the following equation: proportion of CVD death with moderate metabolic factors among total CVD death $\times (\text{HR} - 1)/\text{HR}$ [26]. All CI values were estimated at the 95% level. A *P*-value of < 0.05 was considered statistically significant. The Statistical Package for the Social Sciences, version 11.0J (SPSS Japan, Inc., Tokyo, Japan) was used for all analysis.

3. Results

Table 1 shows the baseline characteristics of the study participants according to the categories of metabolic risk factors. The mean age of participants was higher and the proportion of women was lower among those with more advanced metabolic risk factors. The proportion of participants with any moderate metabolic risk factors was 33.6%. The total number of person-years was 94,817 and the mean follow-up period was 14.0 years. During the follow-up, 1007 participants died of all causes, 282 of all CVD, 119 of stroke and 63 of coronary heart disease.

Table 2 shows the number of deaths, adjusted HRs and 95% CIs according to metabolic risk factors. Crude HR values for CVD mortality ranged from 2.32 to 5.17 among participants with moderate metabolic risk factors. The trend was statistically significant among the four categories of moderate and the five categories up to medication-required metabolic risk factors (*P* for trend < 0.001). Multivariate-adjusted HRs among participants with moderate

Table 1

Baseline characteristics of 2828 men and 3930 women aged ≥ 30 years according to number of moderate or medication-required metabolic risk factors. NIPPON DATA90, 15-year follow-up.

Baseline characteristics	Number of moderate metabolic risk factors ^a				Any medication-required metabolic risk factors ^b
	0	1	2	3 and 4	
Number of participants	1297	1393	683	199	3186
Women (%)	69.1	58.8	56.5	45.7	54.5
Age (years)	44.0 \pm 10.5	47.0 \pm 11.8	50.0 \pm 12.4	50.8 \pm 12.8	58.6 \pm 12.5
BMI (kg/m ²)	21.3 \pm 1.7	22.5 \pm 2.3	24.5 \pm 2.8	26.9 \pm 2.6	23.9 \pm 3.1
Systolic blood pressure (mmHg)	115.1 \pm 8.8	122.4 \pm 10.4	127.7 \pm 8.2	132.1 \pm 4.9	151.7 \pm 16.6
Diastolic blood pressure (mmHg)	71.8 \pm 7.5	75.6 \pm 7.7	78.1 \pm 7.4	81.2 \pm 6.4	89.1 \pm 10.9
Blood glucose (mg/dl)	92.6 \pm 13.2	96.3 \pm 15.4	100.1 \pm 19.6	108.9 \pm 25.2	110.3 \pm 42.0
HbA1c (%)	4.69 \pm 0.34	4.78 \pm 0.36	4.89 \pm 0.44	5.01 \pm 0.52	5.13 \pm 0.95
Total cholesterol (mg/dl)	193.7 \pm 31.7	195.4 \pm 35.8	207.8 \pm 38.8	217.1 \pm 37.2	210.3 \pm 39.5
Triglycerides (mg/dl)	80.0 \pm 28.3	123.4 \pm 76.7	168.9 \pm 93.2	213.9 \pm 112.8	150.2 \pm 103.2
HDL-cholesterol (mg/dl)	63.6 \pm 12.7	52.8 \pm 14.2	45.9 \pm 12.1	43.2 \pm 12.2	52.2 \pm 15.3
Drinking					
Never-drink (%)	75.8	69.8	71.6	67.8	63.7
Ex-drinker (%)	1.9	2.2	2.6	1.5	3.7
Current drinker (%)	22.3	28.0	25.8	30.7	32.6
Smoking					
Never-smoked (%)	68.8	61.3	57.8	47.7	57.9
Ex-smoker (%)	9.0	8.4	9.4	10.6	14.0
Current smoker (%)	22.2	30.3	32.8	41.7	28.1
Moderate or medication-required metabolic risk factors (%)					
Obesity	0	12.1	45.1	91.0	33.1
Triglycerides/HDL cholesterol	0	48.8	82.9	97.0	51.4
Blood glucose	0	1.5	5.7	17.1	11.1
Blood pressure	0	37.5	66.3	99.0	97.3

BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; HDL, high density lipoprotein.

^a Moderate metabolic risk factors were defined as follows: moderate high blood glucose (140 mg/dl \leq non-fasting blood glucose < 200 mg/dl), moderate high blood pressure (130 \leq SBP < 140 mmHg and/or 85 \leq DBP < 90 mmHg), moderate dyslipidemia (150 mg/dl \leq non-fasting triglycerides and/or (HDL-cholesterol < 40 mg/dl in men or HDL-cholesterol < 50 mg/dl in women), obesity (BMI \geq 25 kg/m²).

^b Medication-required metabolic risk factors were defined as follows: high blood glucose (non-fasting blood glucose \geq 200 mg/dl and/or on medication), high blood pressure (SBP \geq 140 mmHg and/or DBP \geq 90 mmHg and/or on medication).

metabolic risk factors ranged from 1.61 to 2.26 with a statistically significant increase. The trend in the multivariate-adjusted model was statistically significant ($P < 0.001$) among the five categories of metabolic risk factors, although it did not reach statistical significance among the four categories of moderate metabolic risk factors. These relationships were similar in gender-specific analyses.

Table 3 shows multivariate adjusted HRs and 95% CIs according to the three categories of metabolic risk factors (none, any moderate metabolic risk factors and any medication-required metabolic risk factors). Crude HR was 2.98 times higher in participants with any moderate metabolic risk factor than in those with none, and multivariate-adjusted HR was 1.82. PAFs calculated by multivariate

adjusted HRs were 7.3% and 52.4% for any moderate and medication-required metabolic risk factors, respectively.

4. Discussion

This 15-year follow-up of a representative Japanese cohort did not find the statistically significant increase of CVD mortality for the moderate metabolic risk factor clustering. In addition, PAF was relatively small (7.3%) in people with any moderate factors compared with those with any medication-required factors (52.4%). To the best of our knowledge, this would be the first report to clarify the CVD risk of moderate metabolic risk factor clustering.

Table 2

Multivariate adjusted hazard ratios of cardiovascular deaths according to number of moderate or medication-required metabolic risk factors. NIPPON DATA90, 15-year follow-up.

	Number of moderate metabolic risk factors ^a				Any medication-required metabolic risk factors ^b
	0	1	2	3 and 4	
Number of participants	1297	1393	683	199	3186
Person-years	19,082	20,148	9835	2883	42,869
Cardiovascular deaths	9	22	17	7	227
Mortality per 1000 person-years	0.47	1.09	1.73	2.43	5.30
Crude HR (95%CI)	1	2.32 (1.07–5.05)	3.68 (1.64–8.26)	5.17 (1.93–13.88)	11.46 (5.89–22.30)
Age and sex adjusted HR (95%CI)	1	1.58 (0.73–3.43)	1.92 (0.85–4.31)	2.04 (0.76–5.49)	2.70 (1.38–5.30)
Multivariate adjusted HR ^c (95%CI)	1	1.61 (0.74–3.50)	2.02 (0.90–4.54)	2.26 (0.84–6.10)	2.88 (1.47–5.65)

BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; HDL, high density lipoprotein; HR, hazard ratio; CI, confidence interval.

^a Moderate metabolic factors were defined as follows: moderate high blood glucose (140 mg/dl \leq non-fasting blood glucose < 200 mg/dl), moderate high blood pressure (130 \leq SBP < 140 mmHg and/or 85 \leq DBP < 90 mmHg), moderate dyslipidemia (150 mg/dl \leq non-fasting triglycerides and/or (HDL-cholesterol < 40 mg/dl in men or HDL-cholesterol < 50 mg/dl in women), obesity (BMI \geq 25 kg/m²).

^b Medication-required metabolic factors were defined as follows: high blood glucose (non-fasting blood glucose \geq 200 mg/dl and/or on medication), high blood pressure (SBP \geq 140 mmHg and/or DBP \geq 90 mmHg and/or on medication).

^c Multivariate hazard ratios were estimated by Cox proportional hazard model adjusted for sex, age, total cholesterol, smoking habits and drinking habits.

Table 3
Multivariate adjusted hazard ratios of cardiovascular deaths for having any moderate or medication-required metabolic risk factors. NIPPON DATA90, 15-year follow-up.

	None	Any moderate metabolic risk factors ^a	Any medication-required metabolic risk factors ^b	P for trend
Number of participants	1297	2275	3186	
Person-years	19,082	32,866	428,69	
Cardiovascular deaths	9	46	227	
Mortality per 1000 person-years	0.47	1.40	5.30	
Crude HR (95%CI)	1	2.98 (1.46–6.09)	11.46 (5.88–22.30)	<0.001
Age and sex adjusted HR (95%CI)	1	1.75 (0.86–3.58)	2.70 (1.38–5.29)	<0.001
Multivariate adjusted HR ^c (95%CI)	1	1.82 (0.89–3.73)	2.87 (1.46–5.64)	<0.001

BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; HDL, high density lipoprotein; HR, hazard ratio; CI, confidence interval.

^a Moderate metabolic factors were defined as follows: moderate high blood glucose (140 mg/dl < non-fasting blood glucose < 200 mg/dl), moderate high blood pressure (130 ≤ SBP < 140 mmHg and/or 85 ≤ DBP < 90 mmHg), moderate dyslipidemia (150 mg/dl ≤ non-fasting triglycerides and/or (HDL-cholesterol < 40 mg/dl in men or HDL-cholesterol < 50 mg/dl in women), obesity (BMI ≥ 25 kg/m²).

^b Medication-required metabolic factors were defined as follows: high blood glucose (non-fasting blood glucose ≥ 200 mg/dl and/or on medication), high blood pressure (SBP ≥ 140 mmHg and/or DBP ≥ 90 mmHg and/or on medication).

^c Multivariate hazard ratios were estimated by Cox proportional hazard model adjusted for sex, age, total cholesterol, smoking habits and drinking habits.

especially in Asia, where stroke is the predominant cause of CVD mortality.

The influence of metabolic syndrome on CVD risk has been reported [5–11]. McNeil et al. used NCEP criteria and found that the adjusted HR for coronary heart disease incidence was 1.46 for men and 2.05 for women, and that for ischemic stroke incidence was 1.42 for men and 1.96 for women in the Atherosclerosis Risk in Communities Study [5]. Katzmarzyk et al. investigated the relationship between metabolic syndrome diagnosed by NCEP criteria and CVD mortality among 19,223 men in the USA and found that the adjusted HR was 1.23 [6]. Iso et al. reported in a study using the modified NCEP criteria found that the adjusted HR for the incidence of ischemic heart disease was 2.4 and that of ischemic stroke was 1.8 among 9087 Japanese in five communities [9]. Ninomiya et al. found using modified NCEP criteria that the adjusted HR of CVD incidence among 2452 Japanese in Hisayama Study was 1.86 for men and 1.70 for women [10]. All of these previous studies demonstrate a CVD risk associated with metabolic syndrome irrespective of the severity of the individual component. For example, high blood pressure is defined according to the NCEP criteria as ≥ 130/85 mmHg, a value that covers a range of blood pressure from high-normal to severe hypertension. However, the CVD risk for individuals with moderate risk factor clustering, which is not usually treated by medication, has rarely been reported.

In the present study, moderate metabolic risk factor clustering tended to increase CVD mortality, however, they were not statistically significant. Several epidemiological studies have revealed that the CVD risk factors included in the criteria for metabolic syndrome are incrementally associated with CVD risk and do not have any threshold [27,28]. Therefore, combined moderate metabolic risk factors might increase the CVD risk. Further studies are required to clarify the relationship of moderate metabolic risk factor clustering and CVD risk.

In the present study, the prevalence of participants with any moderate metabolic risk factor was 33.6% and the PAF of moderate metabolic risk factors on CVD mortality was 7.3%. The impact of moderate metabolic factors on a population should be assessed by estimating population-attributable risk fraction of moderate metabolic factors, which has been seldom reported yet. Vasan et al. investigated the relative contribution of borderline (suboptimal but below current treatment thresholds) and elevated risk factors among US population using five traditional vascular risk factors (blood pressure, low-density lipoprotein cholesterol level, high-density lipoprotein cholesterol, glucose tolerance and smoking status) [29]. They found that the prevalence of the isolated borderline risk factors decreased with age and ranged from 19% to 32.6% in men and from 28.6% to 55.2% in women. They also indicated that isolated borderline risk factors without elevated

risk factors accounted for only about 10% of hard CHD events. Although different risk factors and different ranges were applied in their study, their results would be comparable to our results. Our smaller PAF in people with moderate metabolic risk factors would be partly due to smaller range of moderate BP elevation (SBP/DBP 130–139/85–89 mmHg) in the criteria of metabolic syndrome.

The present study indicated that HR of CVD deaths was near 3-folds among participants with any medication-required metabolic risk factor and their PAF was over 50%. Previous studies have shown that almost 80% of patients with coronary heart disease had at least one major risk factor [30,31]. Our findings among participants with any medication-required metabolic risk factors were comparable with these results and emphasize the importance of focusing upon individuals with any severe risk factor to prevent CVD. The statement of the American Heart Association and National Heart, Lung and Blood Institute recommends that established risk factors such as elevated blood pressure ≥ 140/90 mmHg and elevated glucose ≥ HbA1c 7% should be medicated in addition to undergoing therapeutic lifestyle changes [17]. However, many people with any medication-required metabolic risk factor are neither yet detected nor controlled. Further efforts are required to identify and control established risk factors.

Several limitations should be noted about this study. Firstly, analysis of non-fasting blood samples and no consideration of treatment for dyslipidemia might have resulted in misclassifications of serological abnormalities. Secondly, we used BMI because information about waist circumference was unavailable. Since waist circumference might more precisely enhance the effect of obesity on CVD than BMI, we might have under- or overestimated the effect of obesity. However, BMI is closely related to waist circumference.

In conclusion, we did not find the statistically significant increase of CVD mortality for moderate metabolic risk factor clustering in a representative Japanese population. Further studies are required to clarify the relationship of moderate metabolic risk factor clustering and CVD risk. In addition, its attribution to CVD deaths was relatively small compared with having any medication-required risk factors in this Asian population. People with moderate metabolic risk factors should modify their lifestyle mainly to reduce weight, but more efforts would be required to detect and control medication-required risk factors for CVD prevention.

Conflict of interest

None.

Acknowledgements

This study was supported by the grant-in-aid of the Ministry of Health, Labor and Welfare under the auspices of Japanese Asso-

ciation for Cerebro-cardiovascular Disease Control, the Research Grant for Cardiovascular Diseases (7A-2) from the Ministry of Health, Labor and Welfare, and the Health and Labor Sciences Research Grant, Japan (Comprehensive Research on Aging and Health [H11-Chouju-046, H14-Chouju-003, H17-Chouju-012, H19-Chouju-Ippan-014] and Comprehensive Research on Life-Style Related Diseases including Cardiovascular Diseases and Diabetes Mellitus [H22-Jyunkankitou-Seisyu-Sitei-017]). We appreciate the members of the NIPPON DATA80/90 Research Group which is listed in the Appendix.

Appendix A. The NIPPON DATA80/90 Research Group

Chairperson: Hirotsugu Ueshima (Department of Health Science, Shiga University of Medical Science, Otsu, Shiga).

Co-Chairperson: Akira Okayama (The First Institute for Health Promotion and Health Care, Japan Anti-Tuberculosis Association, Tokyo) for the NIPPON DATA80, Tomonori Okamura (Department of Preventive Medicine and Public Health, Keio University, Tokyo) for the NIPPON DATA90.

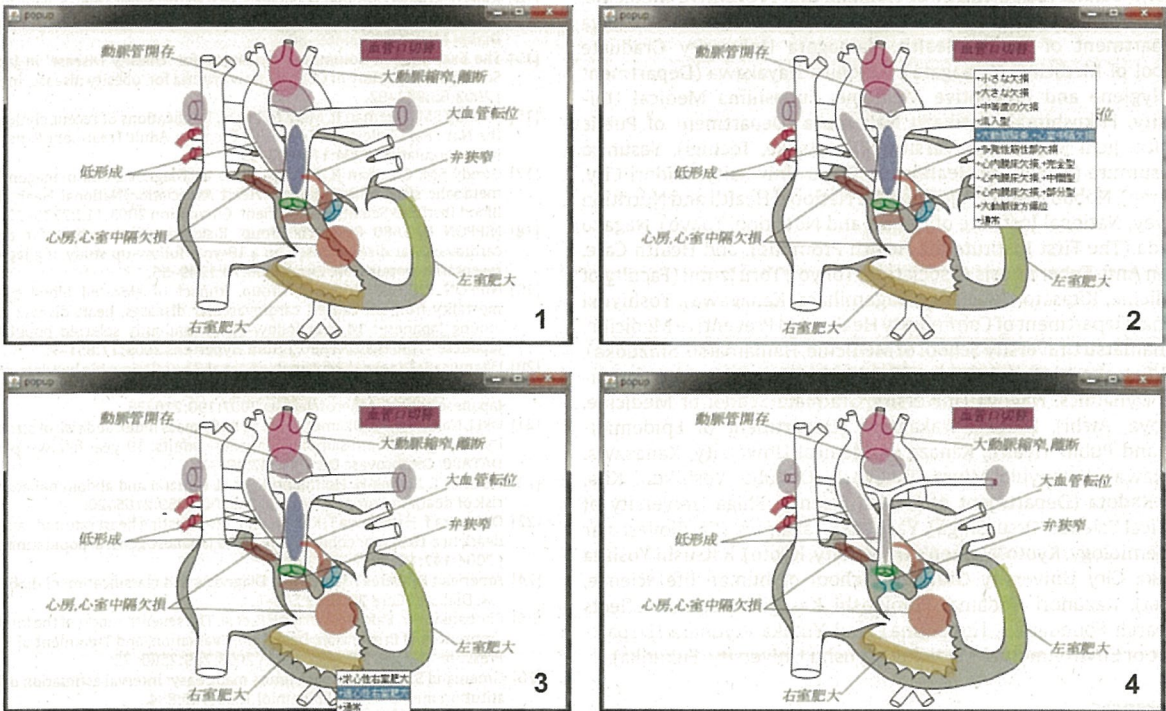
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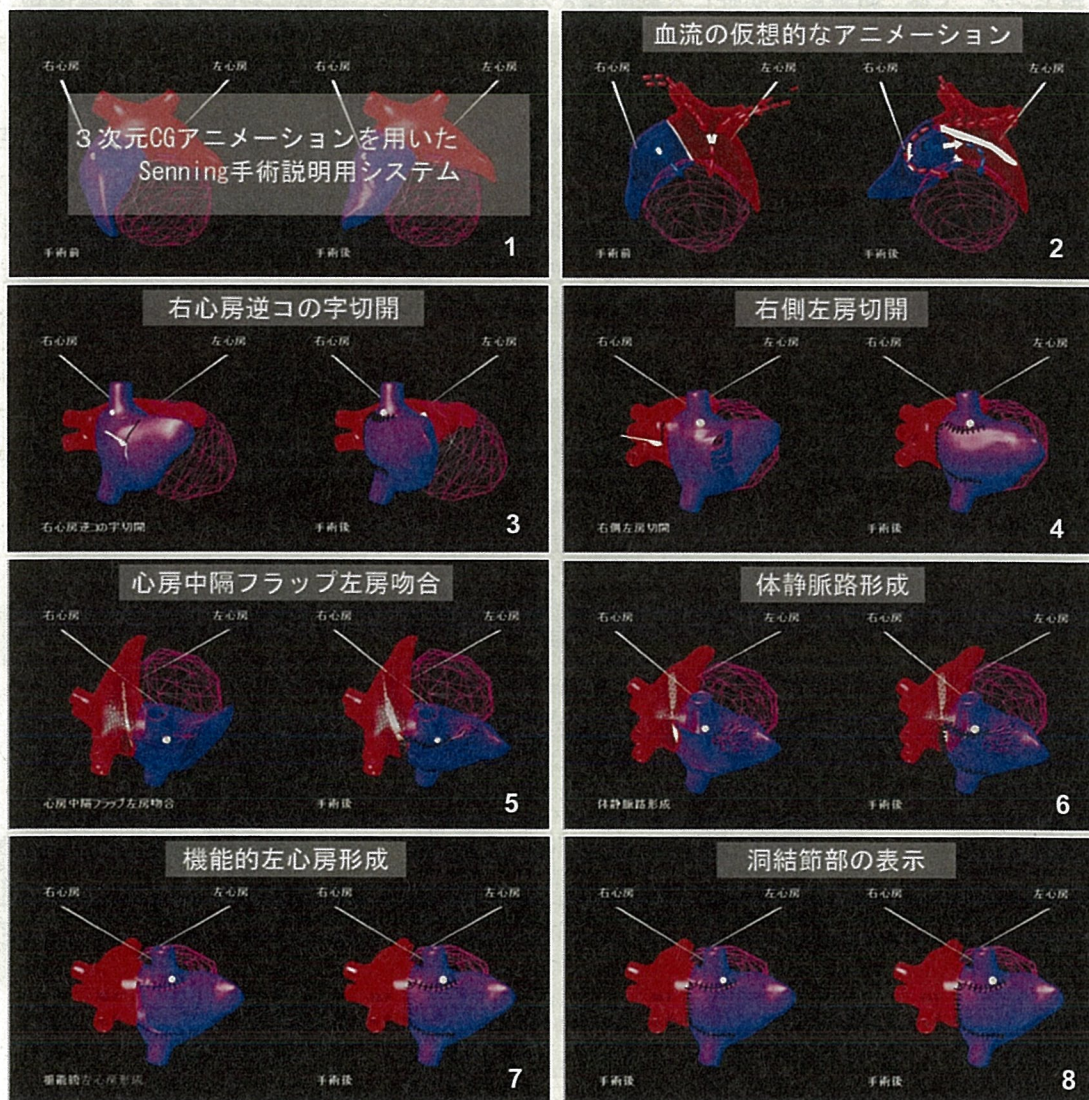
SVG 形式によるシエマ作成支援インタフェースに関する研究

先天性心疾患のための2次元イラスト(シエマ)を Scalable Vector Graphics (SVG) 形式で記述し、様々な形態を表現することができるインタフェースの開発を行っている。従来、患児家族への説明、医療スタッフ間の情報共有には、手書きシエマが用いられている。しかし、様々な形態があり、個人差も大きい先天性心疾患において、わかりやすく、高品質なシエマを個人ごとに手作業で作成することは容易ではない。開発したインタフェースでは、各シエマにキーワードとして登録した情報(位置情報、形状的異常、病名、手術名など)をもとに、求めるシエマを見つけ出すことができる。さらに、正常な心臓のシエマを起点に、心臓の各部位をパーツ化し、典型的なパーツを数種類用意して組み合わせることで、基本的な先天性心疾患の形態を表現することもできる。この研究は、治療に関連する人々の理解共有への貢献や、電子カルテへの応用が期待される。



先天性心疾患外科手術のための3次元CGモデル開発に関する研究

先天性心疾患における様々な病態とその治療法である外科手術を立体的に表現することができる3次元 Computer Graphics (CG) モデルの開発を行っている。従来、各疾患は2次元イラスト(シェーマ)によって表現されている。しかし、2次元シェーマのみでは、心臓の複雑かつ立体的な構造を正確に表現することは困難であり、各個人の立体認識能力も異なるため、治療法を正確に理解することには限界がある。作成した3次元CGモデルでは、アニメーション技術を用いた手術過程における血流の経過的な表現、任意の位置での断面図処理、ワイヤーフレーム(立体を線だけで表現する手法)による透過などを可能とする。このようにCGの特性を利用した説明展開を充実させれば、先天性疾患の外科手術に対して、患児家族の理解度が向上すると考えられる。さらに、医療従事者の理解・教育に大きな成果が期待される。



1) 疾病に着目した研究 ①循環器病の本態解明

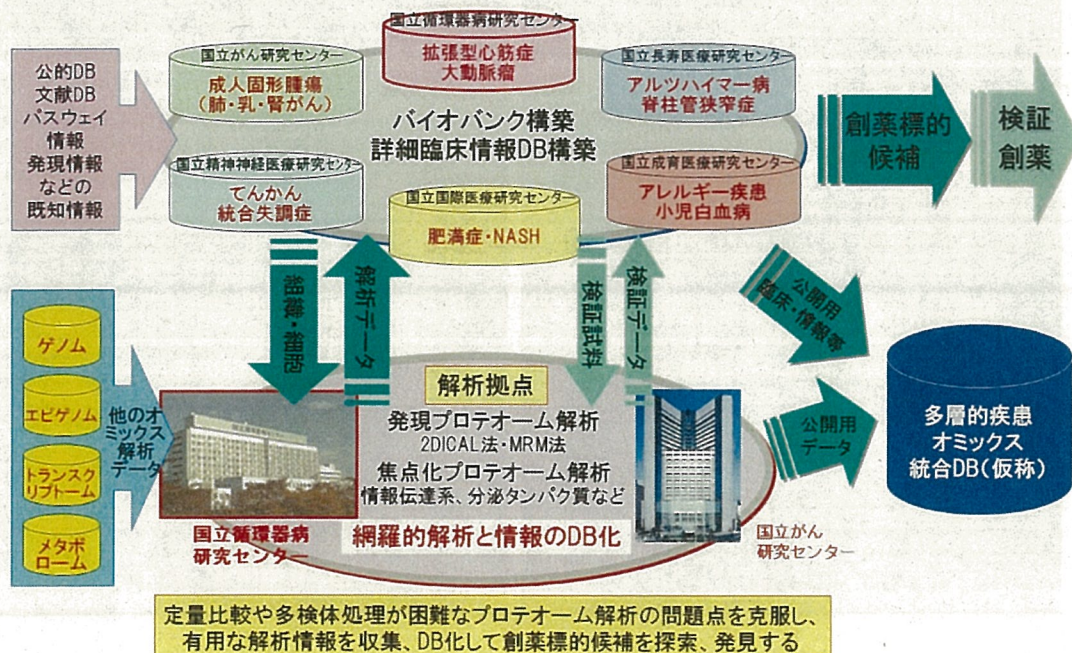
「多層的疾患オミックス解析に基づく創薬標的の網羅的探索を目指した研究」

当センターは、拡張型心筋症と大動脈瘤を対象疾患とし、プロテオーム解析拠点として参加。分子薬理部と研究所、病院、基盤センターの多部門が研究に参加。

健康長寿社会の実現は国民の最大の願いである。死亡率や罹患率が高く、その最大の障害となっている心血管疾患、がん、アレルギー疾患、認知症、生活習慣病等の11疾患を対象として、ゲノム・トランスクリプトーム・プロテオームなどの5種類のオミックス解析技術を駆使して、革新的な創薬標的候補分子の発見を目指す研究を、医薬基盤研究所の支援により平成22年度より開始した。この「多層的疾患オミックス解析研究」を実施するために、6ヶ所の国立高度医療研究センターとオミックス解析研究者とが研究共同体を構築し、同じ病変組織試料を用いて5種類のオミックス解析を行うことにより、疾患発症や病態形成の機序に基づく新しい創薬標的候補分子の発見を目指す。得られた情報や成果はデータベースに収録、公開し、創薬研究などに活用される予定である。

当センターでは、拡張型心筋症と大動脈瘤を対象疾患として、組織試料の収集、病情報、臨床情報の収集を行い、解析に適する試料や情報を他機関に提供する。22年度には基本的な試料、情報収集体制を構築し、大動脈瘤の収集を開始した。

研究所分子薬理部はプロテオーム解析拠点を担当し、1000検体以上の試料について解析を行う計画である。各国立高度医療研究センターで収集された組織試料について、2DICAL法を用いたプロテオーム解析、リン酸化タンパク質などの焦点化プロテオーム解析を実施し、予防・診断・治療法の開発に利用できる創薬標的候補タンパク質の発見を目指す。大動脈瘤組織のタンパク質は溶解が困難であるが、22年度は可溶化して多くのタンパク質を解析可能とする手法を作成し、23年度には解析を実施する。他の研究部門や病院、基盤センターでは、5種のオミックス解析の結果と臨床情報や病情報との比較解析を実施し、創薬標的候補となる遺伝子やタンパク質を見出し、その機能や創薬標的としての意義を検証する予定である。



当センターが総括する「プロテオーム情報に基づく創薬標的の網羅的探索を目指した研究」の概要

五大新聞に疾病、検査、治療、予防等について、医師等が寄稿又は取材により掲載された回数。(時事ニュース除く)

掲載日	新聞社	朝・夕	題名	医師名
1	朝日	朝	医療 薬減ったら血圧下がった	生活習慣病部門長 河野
2	朝日	朝	論点 新しい日本医師会	名誉総長 川島
3	毎日	夕	近刊 心臓移植にかけた40年の鼓動	名誉総長 川島
4	朝日	夕	心筋梗塞、治療までに3.9時間	心臓血管内科部門長 野乃木
5	朝日	夕	家族承諾での臓器移植	名誉総長 北村
6	朝日	夕	妊婦に薬 胎盤通じ効果	周産期・婦人科部長 池田
7	朝日	夕	医療 油断できない失神	不整脈部長 鎌倉
8	日経	夕	Do It ユア・ヘルス	研究所副所長 妙中
9	朝日	朝	医療 脳卒中正しい知識で備え	副院長 峰松
10	産経	夕	突然死予防 病院外がカギ	心臓血管内科部門長 野乃木
11	産経	朝	心臓移植40年 闘いの軌跡	名誉総長 川島
12	毎日	朝	くらしナビ 健康 Health	心臓リハビリ部長 後藤
13	産経	朝	震災ストレス…注意	心臓血管内科部門長 野乃木

平成22年度循環器病研究開発費実績報告書（主任研究者分）

1. 主任研究者 所属・職名 看護部 看護部長
氏名 山田 泰子
2. 研究課題名 循環器病看護の質とアウトカムの向上に関する定量的評価方法の開発

3. 研究実績の概要

下欄には、当該年度に実施した研究の成果について、その具体的内容、意義、重要性等を、事業計画書に照らし、800-1000字程度で、できるだけ分かりやすく記述すること。図表を使用する場合は、報告書の最後にファイルが一つになるように添付して下さい。

循環器看護の質とアウトカムの向上の観点から、看護提供体制（構造）、看護実践（過程）、患者の転帰（アウトカム）を包括的に捉え、循環器看護における新たな評価基準を再構築するため、各分担班（診療、医療連携、安全や感染対策）において、データ集積および解析に取り組んだ。

総括班の「急性期循環器病看護の評価基準に関する研究」では、特定集中治療室において、5 症例（成人2症例、小児3症例）に対して直接的・間接的に行った看護行為を、録音・録画によりデータを集積した。延べ 600 時間のデータ解析を進め、看護業務内容をコード化中である。「脳卒中の地域連携における脳卒中看護の構築に関する研究」では、各都道府県の人口密度がもっとも高い二次医療圏と最も低い二次医療圏に位置する病院・施設（1137 施設）を対象に、地域連携の内容・情報提供の伝達ツールについてデータを収集した。「心拍監視モニターアラーム誤作動の低減化と方策の提言のための研究」は、難治性不整脈患者から慢性期安定期にわたる多様な循環器疾患患者が入院している一般病棟におけるアラームの発生内容と医療者の行動及びアラーム発生時の心電図波形に関する調査を実施した。アラーム分析システムを用いて不整脈アラームの種別についての詳細把握及びアラーム発生からアラーム音消去までの時間を調査し、データ解析を実施中である。「急性期循環器疾患の褥瘡発生要因と治癒因子に関する検討」は、過去1年分の診療録から有効なデータが得られた対象 106 名を早期治癒群と長期化群に分類し、褥瘡治癒に影響を及ぼす検査データ、発生部位、栄養状態、心機能等の 14 項目についてロジスティック解析分析を用いてデータ解析を実施した。結果、%FC、アルブミン、クレアチニンの項目で心機能の低下に伴い、創治癒遅延リスクが5～8 倍高くなることが示唆された。「在宅におけるヒックマンカテーテルの管理方法と患者教育の内容の再構築」は、皮下トンネル型カテーテル管理方法に関する問題点の抽出より改善方法を検討し、管理手順を改定した。また、Micrococcus luteus が検出された症例のデータを集積した。

研究組織一覽

課題番号	22-4-10	研究課題名	研究課題名 (フリガナ) 氏名	所属施設名	所属部署名・職名	他施設研究者の 参加理由	経歴		
							現在の主な 研究領域	卒業学校 及び学部	卒業年次 (西暦)
		分担研究課題							
		急性期循環器看護の評価基準に関する研究	カクチ ケイ 川口 桂子	独立行政法人国立循環器病研究センター	看護部・看護師長		循環器看護、看護管理	放送大学	2002
		脳卒中地域連携における脳卒中看護の構築に関する研究	ヤマグチ リエコ 山口 理恵子	独立行政法人国立循環器病研究センター	看護部・看護師		脳卒中看護	大阪府立看護大学 医療技術短期大学 看護第1科	2002
		心拍監視モニターアラーム誤動作の低減化と方策の提言のための研究	タカサカ 高田 幸千子	独立行政法人国立循環器病研究センター	看護部・看護師長 (医療安全管理者)		医療安全、循環器看護	人間総合科学大学	2004
		急性期循環器疾患の褥瘡発生要因と治癒因子に関する検討	ナカヤ ヨシコ 中屋 貴子	独立行政法人国立循環器病研究センター	看護部・副看護師長 (褥瘡管理者)		創傷管理、急性期循環看護	国立療養所宇多野病院附属看護学校	1991
		在宅におけるヒックマンカテーテルの管理方法と患者教育の内容の再構築	マキウチ ユウコ 牧内 優子	独立行政法人国立循環器病研究センター	看護部・副看護師長 (感染管理認定看護師)		感染管理	大阪府立千里看護専門学校	1999

『入院患者さまへのアンケート』集計結果表

■ 国立循環器病センター

	当院得点	全国平均点	21' 当院
		NC	
入院アンケート総合得点	4.4	4.4	4.4
I. 入院でのできごと	4.4	4.4	4.4
1. 入院時	4.3	4.3	4.3
● 医師の説明について不満	4.5	4.4	4.4
① 説明時、検査結果等を見せてくれなかった	4.5	4.5	4.4
② 検査・治療内容を教えてくれなかった	4.5	4.6	4.5
③ 検査、治療、手術等の日程の説明なし	4.5	4.5	4.5
④ 一方的な説明で意思を尋ねなかった	4.6	4.5	4.5
⑤ 聞きたいことを質問できなかった	4.5	4.5	4.5
● 入院の手続きについて不満	4.4	4.3	4.3
① パンフレットや資料が不十分	4.4	4.3	4.4
② 入院するまで長く待った	4.4	4.4	4.3
③ 入院手続きに手間がかかった	4.5	4.4	4.4
④ どのくらい費用がかかるのか、わからず入院	3.4	3.4	3.3
⑤ 入院の際に相談できなかった	4.2	4.3	4.3
● 入院中の生活の説明に不満	4.5	4.5	4.3
① 食事が選択できることを教えてくれなかった	4.3	4.2	4.2
② 入浴、食事、消灯時間の説明なし	4.2	4.0	4.3
③ 非常口、トイレ、浴室などの場所の説明なし	4.3	4.2	4.3
④ 売店、洗濯、テレビ等のサービスの説明なし	4.3	4.2	4.2
⑤ 入院生活がどうなるのか分からないまま入院	4.2	4.1	4.0
2. 入院中の診療	3.9	4.0	4.5
● 医師の態度や言葉使いが悪い	4.6	4.6	4.7
① 症状や治療の質問ができなかった	4.5	4.5	4.6
② 声が小さく聞き取りづらい	4.6	4.6	4.6
③ プライバシーに配慮しない	4.6	4.6	4.6
④ 自分の為に、十分な時間を取ってくれなかった	4.5	4.5	4.5
⑤ 顔を向けずに説明、嫌な顔をする	4.7	4.7	4.7
● 医師の技術や知識に不安を感じた	4.6	4.5	4.6
① 説明がわかりにくい	4.6	4.5	4.6
② 検査数値や画像を用いて説明してくれない	4.4	4.4	4.4
③ 処置が下手	4.5	4.4	4.5
④ 複数の治療法がありうることの説明なし	4.5	4.4	4.4
⑤ 自分が良くなっている実感が持てない	4.4	4.4	4.4
● 看護師の態度、言葉使い、処置の仕方に不満	4.5	4.4	4.5
① 説明が分かりにくい	4.5	4.4	4.5
② 医師の指示や処置を間違える	4.5	4.5	4.5
③ 質問や相談の対応がない	4.5	4.5	4.5
④ プライバシーに配慮しない	4.6	4.6	4.6
⑤ 話をしている、嫌な気持ちになった	4.5	4.4	4.4
● 入院中に受けた日常生活の介助について不満	4.5	4.5	4.6
① ナースコールしても長く待たされ、対応してもらえない	4.5	4.4	4.5
② 身体を拭くなど清潔に関する介助が不十分	4.5	4.4	4.5
③ 身体の向きを変える、食事などの介助が不十分	4.5	4.5	4.5
④ 日常生活の手助けを必要な時に頼めなかった	4.5	4.5	4.5
⑤ 病室の変更にならないうる	4.4	4.4	4.4
● 医師や看護師など医療スタッフのチームワークが悪い	4.4	4.4	4.5
① 同じ事を別の職員から何度も聞かれた	4.4	4.3	4.5
② 氏名、病名、薬などを間違えられた	4.6	4.6	4.7
③ 受け持ちの医師や看護師が代わって不安だった	4.4	4.4	4.4
④ スタッフの人間関係が悪く不安	4.6	4.6	4.6
⑤ 職員同士の私語が多く不快	4.5	4.5	4.6
3. 入院中の検査・手術・その他の治療	4.6	4.6	4.6
● 受けた検査について納得できない	4.6	4.6	4.6
① 検査の待ち時間が長すぎる	4.5	4.4	4.5
② 検査前、本人確認されなかった	4.7	4.7	4.7
③ 恥ずかしい思いに十分な気配りが無い	4.6	4.6	4.6
④ 検査室が不潔だった	4.6	4.7	4.7
⑤ 説明が分かりにくい検査技師がいた	4.6	4.6	4.6
● 受けた手術について納得できない	4.7	4.7	4.8
① どのような手術なのか十分に理解できなかった	4.7	4.7	4.7
② 思っていたような手術でなかった	4.7	4.7	4.7
③ 麻酔についての説明なし	4.7	4.7	4.7
④ 手術後の痛みや不快感に対応なし	4.7	4.7	4.7
⑤ 手術結果について十分に理解できなかった	4.6	4.6	4.7
● 受けた治療・処置について納得できない	4.7	4.7	4.6
① 治療・処置の前に本人確認されなかった	4.7	4.7	4.7
② 何をされるのかわからず、不安に思った	4.5	4.5	4.5