・対象となる生徒は介入群か対照群かは所属する学校毎に決められる。
・選択する中学校はハノイ市内の背景が同様の複数の中学校から選別され、無作為に介入群と対照群に割り当てる。
・対象となる生徒は6年生であり、本人と両親の同意を得て研究に参加する。性別で区別はしない。
３）サンプルサイズ
・α10%、1-β90%、P1 0.1、P2 0.05よりサンプルサイズを363名と推定した。従って、介入群、対照群を各400名とした。
・中学校4校を選別し、介入群2校、対照群2校とし、１校あたり200名（１クラス５０名を４クラス）を対象とした。
４）研究実施体制
・バクマイ病院：Anh院長、Lien栄養センター長、Thanh国際部部長、Thanh栄養センター職員
・国立国際医療研究センター：梶尾裕、松下由実（臨床研究センター室長）、岸本美也子（糖尿病・代謝・内分泌科医長）
・都立広尾病院：原光彦（小児科部長）
・対象となる中学校の校長及び職員
・対象となる中学生及びその親
・研究に際し委員会を立ち上げ、その委員会の本に研究を実施する。
５）研究内容
・介入内容
身体活動、食習慣、生活習慣に対して種々のツールを用いて行動変容を図るとともに、体重や歩数のセルフモニタリングや肥満や生活習慣病についての専門家からの講義やクラス単位での自主的なコミュニケーション活動を通じて、自律的な生活改善活動を持続させる。
１）身体活動、食習慣、生活習慣の実態調査として、生徒と親に対して、個別のアンケートを行い、肥満や生活習慣病、運動、食事の実態や知識レベルの確認を行う。（介入前後の２階）
２）介入は２年間で、介入前、１年後、２年後に身体状態を確認するため、身体測定（新調、体重、腹囲）及び、血糖値、HbA1c、総コレステロール、中性脂肪、ＨＤＬコレステロール、アディポネクチンを測定する。
３）研究期間中、３ヶ月おきに身体チェックを実施する。
４）介入対象者に対しての個別指導は、介入前及び介入後は１ヶ月、３ヶ月後に実施し、以後、介入後２年まで、３ヶ月毎に実施する。
（倫理面への配慮）
本研究は国際共同研究であり、関連条項、細則に従い、相手国担当倫理委員会及び担当施設の倫理委員会がともに本計画を認可する場合にのみ実施する。本邦における「臨床研究に関する倫理指針」（厚労省、平成20年7月31日全部改正）を遵守するとともに、ベトナム国における生物医学研究のための関連規則を遵守し、いずれかの国の倫理指針が他方の国の倫理指針よりもより厳しいものである場合には、原則として、研究はより厳しい倫理指針に従って実施する。介入行為は個別の介入が必要であり、その段階では個人は特定できるが、データの解析については、対象者の個人情報の機密保持に関しては情報の保管や伝達に細心の注意を払い、個人が特定できない形で解析を行う。研究結果の発表の時も個人のプライバシーは完全に保護される。個人名と個人のコード番号を結びつける記録簿は厳重に管理される。すべての文書は情報保護の守られた場所に保管する。研究対象者個人を同定するものと関係づけるリストを含むすべてのアンケートや用紙は研究終了時には破棄される。

Ｃ．研究結果
現在、プロトコールを作成し、ベトナム側での倫理員会での承認を得た。現在、研究実施での細部について検討を加勢な手織り、また、対象となる４校が選別された。

Ｄ．考察
本研究は、途上国における生活習慣病対策の重要な研究の一つであり、研究実施にあたって、相手国に則して、充分にコミュニケーションを取りつつ実施していく必要がある。また、本邦の小児生活習慣病の専門家にも参加してもらい、本邦の経験を充分に反映した形で国際協力としてもより充実したやり方が望ましいと思われる。

Ｅ．結論
本研究の、相手国に与える影響は大きく、着実な研究の実施が望まれる。

Ｇ．研究発表
１．論文発表
なし
２．学会発表
なし

Ｈ．知的財産権の出願・登録状況
該当無し

研究報告書

厚生労働科学研究費補助金
((地球規模保健課題推進研究事業（国際医学協力研究事業）

アジアの子供達のおやつと飲料からの糖類摂取量

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研究要旨
糖類の摂取量は肥満やう蝕の原因として見逃せない。一方、糖類は急速な成長期にある子ども達にとって重要なエネルギー源で、子ども達は糖類の入った甘いおやつが好きである。しかしながら、日本食品標準成分表には糖質成分は示されずに炭水化物の合計量が、また2009年公表の日本食品推定糖質成分表掲載の糖質は海外のデータをもとに推計したものであるが、おやつや飲み物に関する掲載数が少なく特に現在多用されている異性化糖を含む飲み物や冷菓類は少ない。このようなことから、子ども達がどのくらい、どのような種類の単糖、二糖類を摂取しているのか未だわかっていない。
研究１では、単糖、二糖類の成分表を作成するために蔗糖、ブドウ糖、果糖、乳糖の4種類について135種類の食品（42種類の飲み物や冷菓、64種類の甘いおやつ、29種類の家庭で食べられる手作りおやつ）の糖類を分析した。分析には2つの方法を用いた。１つは酵素法で、一品につき5サンプルを分析した。2つ目は、1品につき10種類のレシピからの推測で蔗糖を計算した。その結果、和菓子や家庭で作られるおやつには蔗糖のみが使われていた。飲食物には、異性化糖由来と思われるブドウ糖および果糖が使われていた。
研究２では、国内8地域の都道府県から7、10および13歳の児童生徒362人に対して3日間の栄養調査を実施した。給食については秤量法を用い、その他の食事やおやつについては24時間思い出し法を用いた。また、おやつ類と飲料類からの糖類摂取量は、研究1で作成した成分表の数値を用いて計算した。
その結果、おやつからの糖質摂取量は24.7±15.5g/日であった。2009年国民健康栄養調査の結果では、7-14歳の子供の食事からの蔗糖摂取量は5.5g/dayであった。これらを合計すると、子供たちの糖類摂取量は一日に約30gと推測された。この値はFAO/WHOの推奨量（エネルギー摂取量の10%以内、本研究の子供達では49g）の範囲内にあった。摂取量には学年による違いは見られなかった（$p>0.05$）が、高学年では男子よりも女子の摂取量が少なかった($p<0.05$)。食品群別にみた糖類摂取量に対する貢献量は、飲料類25%、ケーキ類19%、アイスクリーム17%で、これらで全体の約60 %を占めていた。果汁を含んでいない食品に単体で果糖が存在する場合、デンプンを加水分解して作られた異性化糖（ブドウ糖と果糖からなる）の利用が考えられ、その使用頻度が多いことがわかった。糖の種類により体内での代謝経路は異なり、血糖値や脂肪の蓄積度合いに影響することが示唆されていることから、糖分の摂取は、甘味度に対する嗜好のみでなく、その種類を把握することが重要であろう。
以上のことは、日本の子供達の糖類摂取量はFAO/WHOの推奨値の範囲内にあるものの、各種の糖類が使われており、それらが健康に及ぼす影響も異なるので今後、各種糖類と健康に関する研究が必要であることを示唆している。

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所属機関における職名：教授

A．研究目的
Objective

Study 1 was aimed to developed a database for mono- and di-saccharides. We have measured concentrations of sugars (sucrose, glucose, fructose and lactose) in 135 sugar rich foods (42 commercial beverages and chilled snacks, 64 commercial cakes and cookies, 29 homemade cookies). We used two methods. One is enzymatic method. We analyzed and calculated the average of mono-and di-saccharides more than 5 samples from different manufacturers of each food. The average values were calculated and published. Second method, we collected 10 recipe books about each food and calculated the average of sucrose about 29 representative home made items.

Study2 was a nutrition survey that conducted for 3 weekdays for about 362 Japanese school children (7, 10 and 13 years old) in 8 prefectures from different areas of Japan and finally the reliable data of 283 were used. In the study of school children, random sampling in the whole country was difficult for us but we did our best to collect the representative samples of the country by selecting school in various areas in Japan. The methods was basically 24 hour recall method, however, weighing method was used for the school meals in order to have the more reliable data. Children's Height and weight were measured when the school overhaul. Results of these data for the participants were similar to Japanese averages. Sugars from beverages and sweet snacks were calculated by the sugar composition table made in Study 1. Sugar eaten outside meals was 24.7±15.5 g /day. We could not estimate the sugar used for meals and used the data from the Japanese National Health and Nutrition Survey conducted in 2009, the mean sucrose intake from meals for 7-14 year old children was 5.5 g /day. Therefore the mean total sugar intake of these children was about 30g/day. The recommendation of sugar by WHO is within the range of 10% energy intake. It is about 48.3g for our subjects. The consumption of the 85% children (mean +1SD) was within the range of WHO recommendation. Mean intakes among age groups were not significantly different ($p>0.05$), but the intakes for girls was lower than boys in the oldest age group ($p<0.05$). Ratios of each sugar to total intake sucrose 64.4±19.1%, fructose 13.2±10.4%, glucose 12.4±8.4%,and lactose8.8±8.2%, respectively. The contributions to sugar intake were 25% from beverages, 19% from cakes and 17 % from cakes and the sum of them was 61% of the total intake. Only sucrose was used in Japanese traditional cakes and homemade cakes and about the equal amount of glucose and fructose was used in the beverages, cakes and ice creams. If the beverages and foods not from fruits contained fructose, usually the isomerized sugar (glucose and sucrose made from starch). Lactose was contained in the milk products. In conclusion, although the average sugar intake of Japanese children met the WHO recommendation, we have to be careful about the kind of sugars and their effects on health.

B．研究方法
Methods

Study 1:

We were selected 106 foods (table1) and analyzed 5 samples of each item by enzymatic method and calculated the average of mono- and di-saccharides these 4 types of sugar (Sucrose, Glucose, Fructose, Lactose). We used F-kit (R-Biopharm AG, Germany) Enzymatic analysis is easy and getting high-precision result and is widely used. Enzymatic analysis has some advantages as shown below;

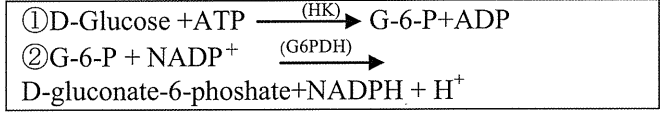
①Clean analysis for environment.
②Nothing high temperature and high pressure
③ small disturb of another matters.
④Before processing is simple method.
⑤ Optical isomers can be quantitative separate.

We obtained the sucrose concentration of 29 representative homemade items cakes from 10 recipe books.

The principles of sugar analyses are shown below.

< Glucose >

For the quantitative, enzymatic determination of glucose in food and other material. Glucose is phosphorylated by ATP using hexokinase. Glucose-6-phosphate is then oxidized to 6-phospho-gluconate in the presence of NAD by glucose-6-phosphate dehydrogenase. During this oxidation, an equimolar amount of NAD is reduced to NADH. The consequent increase in absorbance at 340 nm is directly proportional to glucose concentration. The NADPH formed in this reaction is stoichiometric to the amount of D-glucose and is measured by means of its light absorbance at 340nm.



< Fructose >

For the quantitative, enzymatic determination of fructose in food and other materials. Fructose is phosphorylated by ATP using hexokinase. Fructose 6-phosphate is then converted to glucose 6-phosphate

by phosphoglucose isomerase. Glucose-6-phosphate is then oxidized to 6-phosphogluconate in the presence of NAD by glucose-6-phosphate dehydrogenase. During this oxidation, an equimolar amount of NAD is reduced to NADH. The consequent increase in absorbance at 340 nm is directly proportional to fructose concentration.

G-6-Preacts again with NADPH with formation of D-gluconate-6-phosphate and NADPH ②. The amount of NADPH
formed now is stoichiometric to the amount of D-fructose.

③D-fructose + ATP $\xrightarrow{(HK)}$ F-6-P + ADP
④F-6-P $\xrightarrow{(PGI)}$ G-6-P

＜ **Sucrose** ＞

For the quantitative, enzymatic determination of sucrose in food and other materials. Sucrose is hydrolyzed to glucose and fructose by β-fructosidase. Glucose and fructose are phosphorylated hexokinase. Glucose-6-phosphate is then oxidized to 6-phosphogluconate in the presence of NAD in a reaction catalyzed by glucose-6-phosphate dehydrogenase . The increase in absorbance at 340 nm is directly proportional to sucrose concentration.

The determination of D-glucose after inversion is carried out according to the principle ① ② and the sucrose contain is calculated from the difference of the D-glucose concentrations before and after enzymatic inversion.

⑤ Sucrose+H_2O $\xrightarrow{(\beta\text{-fructosidase})}$ D-glucose+ D-fructose

＜Lactose＞

The amount of NADH formed in reaction ⑦ is stoichiometric to the amount of lactose, and D-galactose ,resp. The increase in NADH is measured by means of its light absorbance at 340nm.

⑥Lactose + H_2O $\xrightarrow{(\beta\text{ - galactOsidas})}$ D-glucose +D-galactose.
⑦D-galactose +NAD^+ $\xrightarrow{\text{galactose dchydrogenuse}}$ D-galactonic acid + $NADH+H^+$

Reagents used in this study are shown below.

＜Sucrose / Glucose / Fructose＞

① Dissolve contents of bottle 1 with 10ml of redist. water.
②Dissolve contents of bottle 2 with 45mlof redist. water.
③ Use contents of bottle 3 undiluted and dilute with the same amount of water of suspension(1.1ml).
④ Use contents of bottle 4 undiluted and dilute with the same amount of water of suspension(0.6ml).

＜ **Lactose** ＞

① Dissolve contents of bottle 1 with 14ml redist. water.
② Use suspension of bottle 2 undiluted and dilute with the same amount of water of suspension (1.7ml).
③ Use solution of bottle 3 undiluted and dilute with the same amount of water of suspension (34ml).
④ Use suspension of bottle 4 undiluted and dilute with the same amount of water of suspension (1.7ml).

Analytical procedures are shown below;

＜Sucrose / Glucose / Fructose＞

	Sucrose		D-glucose and D-fructose	
Test tube	Blank	Sample	Blank	Sample
① Pipette into cuvettes				
・F-kit	0.200ml	0.200ml	—	—
Solution 1	—	0.100ml	—	0.100ml
・Sample solution				
② Mix* incubate for 15min.at 20-25℃				
③ Pipette into cuvettes				
・F-kit	1.000ml	1.000ml	1.000ml	1.000ml
Solution2	1.800ml	1.700ml	2.000ml	1.900ml
・Redist.water				
④ Mix*** read absorbance of the solutions after approx,3min. Start reaction by addition				
⑤ Pipette into cuvettes				
・Suspension3	0.020ml	0.020ml	0.020ml	0.020ml
⑥ Mix***,wait for complete reaction(approx.10-15 min)and read absorbance of the solutions. If the reaction has stopped after 5min,continue to read the absorbance at 2 min intervals until the absorbance onstantly over 2min. Addition				
⑦ Pipette into cuvettes				
・Suspension4	—	—	0.020ml	0.020ml
⑧ Mix***,read absorbance of the solution after 10-15min				

Wavelength: 340nm
Glass cuvette: 1.00cm light path
Temperature: 20-25℃
Final volume: 3.020ml
Sample solution : 5~80μg / cuvette

＜Lactose＞

Test tube	Lactose		D-galactose	
	Blank	Sample	Blank	Sample
①Pipette into cuvettes	0.200ml	0.200ml	0.200ml	0.200ml
Solution 1	0.050ml	0.050ml	—	—
Suspension2	—	0.100ml	—	0.100ml
Sample solution				
② Mix* incubate for 20min.at 20-25℃.Add:				
③Pipette into cuvettes	1.000ml	1.000ml	1.000ml	1.000ml
Solution3	2.000ml	1.900ml	2.050ml	1.950ml
Redist.water				
④ Mix*** after approx.4min. read absorbance of the solutions. Start reaction by addition of:				
⑤Pipette into cuvettes	0.050ml	0.050ml	0.050ml	0.050ml
Suspension4				
Mix***,wait until reaction has stopped and read absorbance of the solutions. If the reaction has stopped after 30min,continue to read the absorbance at 5 min intervals until the absorbance constantly over 5min. Addition of:				

Wavelength: 340nm
Glass cuvette: 1.00cm light path
Temperature: 20-25℃
Final volume: 3.300ml
Blank: water
Sample solution : 5~50μg/cuvette

Sugar concentration was calculated as shown below.

＜Sucrose / Glucose / Fructose＞

ΔEglu＝ (E2－E1) glu/fru sample － (E2－E1) glu/fru blank

ΔE all glu＝ (E2－E1) suc sample－ (E2－E1) suc blank

ΔEsuc＝ΔE all glu － ΔEglu

ΔEfru＝ (E3－E2) glu/fru sample － (E3－E2) glu/fru blank

C (g/ℓ) = V×MW / ε× d × v ×1000 ×ΔE

According to the general equation for calculation the concentration

V (Final volume) ; 3.02ml or 3.04ml

MW (molecular weight of the substance to be assayed [g /mol]) ;

sucrose : 342.30

glucose : 180.16

fructose : 180.16

d (light path) ; 1 cm

ε (extinction coefficient of NADPH) at ; 6.3

v (sample volume) ; 0.1ml

＜ Lactose ＞

ΔE gal＝ (E2－E1) gal ample － (E2－E1) gal blank

ΔE lac＝ (E2－E1) lac sample－ (E2－E1) lac blank

C (g/ℓ) = V×MW / ε× d × v ×1000 ×ΔE

According to the general equation for calculating the concentration

V (Final volume) ; 3.02ml or 3.04ml

MW (molecular weight of the substance to be assayed [g /mol]) ;

lactose : 342.30

d (light path) ; 1 cm

ε (extinction coefficient of NADPH) at ; 6.3

v (sample volume) ; 0.1ml

Samples were prepared as shown below.

①Beverages

Each sample concentration become 0.05～0.8g/l by distilled water. Filter turbid juices (alternative clarify with Carrez reagents) and dilute sufficiently to yield a sucrose +D-glucose+D-fructose concentration of apprpx.0.1-1.5g/L. The diluted sample solution can also be used for the assay if it is colored. Only strongly colored juice which are used undiluted content are to be decolorized. In that case proceed as follows:

②Fruit juice : Mix 10ml of juice and approx.0.1g of polyamide power or PVPP, stir for 1min and filter. Use the clear, slightly colored solution for the assay.

③Carbonic acid beverages

To remove the carbonic acid, stir approx.5-10ml of liquid in beaker for approx.30s with a glass rod or filter through a fluted filter paper. The largely CO_2-free sample can be used undiluted for the assay.

④Sample containing fat

With hot water .Cool to allow the fat to separation, make up to the mark, place the volumetric flask in an ice bath for 15min and filter; alternatively clarify with carrez reagents after the extraction with hot water.

⑤Solid sample containing fat

Homogenize in a mil machine. 1g homogenized sample into a 100ml volumetric flask. Mix with 40~60℃water. Homogenize for 3min in a mil machine again. Put it to Centrifugal tube and centrifuge by the centrifugal separator. For cool to allow the fat to separate, leave in a refrigerated room. Take away upper fat part.

⑥Containing lactic bacteria (Yoghurt and lactic acid drink)

Homogenize in a mil machine. 1g homogenized

sample into a 100ml volumetric flask.mix with 40~60℃water. Mixed and after leave 10minuits. Put it to Centrifugal tube. After top for interception the liquid from outside, and soak 15min in 85℃ water for stop a reaction of enzyme. put it to separater(1000r× 5 min) and use upper part.

⑦Lactose in hard chocolate

Accurately weight approx.2g into a 100ml volumetric flask, add approx.70ml water and incubate for 15min at approx.70℃. Shake from time to time. After cooling to 25℃, fill up to the mark with water and mix. To separate the fat, place in a refrigerator for approx 20min and filter. Discard the first few ml. Use the clear, possibly slightly opalescent solution for the assay.

2) Recipe analysis

Sucrose intake from home made cakes was calculated as the following example.

Example: Pan cake

Sugar in a cake: 30g, Ingested portion: 1/5

Ingested sucrose = 30/5 = 6g

Study 2:

1) Subjects

The survey was conducted in about 350 children of 7, 10 and 13 years old in 8 prefectures from north to south in Japan. The final available number was for 283. We tried random sampling as much as possible in selecting areas, schools and classes so that the subjects would be close to representative for the country as a whole.

Study Subjects : 362 children (n=362, boy =176, girl= 186) (Table6)

Table 6 Study Subjects

	Second grader (7 years)	Fifth grader (10 years)	Eighth grader (13 years)	Total
Boy	45	89	42	176
Girl	59	89	38	186
Total	104	178	80	362

Areas : Hokkaido, Nagano, Nara, Kyoto, Tokushima, Yamaguchi, Miyazaki, Okinawa, (Fig.1)

Table 6 Number of Subjects

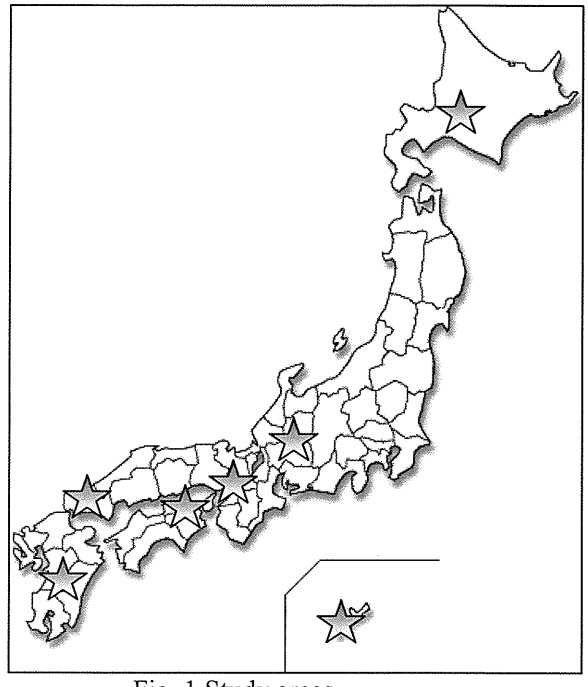


Fig. 1 Study areas

2) Survey

The nutrition survey was conducted for 3 weekdays. An investigation of height and weight was conducted before the commencement of the survey. Regarding the intake of school lunches, researchers measured the actual amount of each student's portion, while that of the other meals, including in-between snacks, was recorded on the investigation form each day with the cooperation of the students' guardians. In the case of incomplete items or unclear descriptions on the form, the researchers confirmed details with the students directly or asked their guardians to fill out the items.

3) Estimation of sugar and energy intakes

Calculations of energy intake were made in accordance with the data listed in "Standard Tables of Food Composition in Japan, the Fifth Revised and Enlarged Edition"(6) and the table of processed foods data (6-9). Sucrose, glucose, fructose and lactose intakes from foods other than meals were calculated by using sugar composition table constructed by us previously . (1,10,11).

4) Ethical considerations

This study was conducted with the approval of the Ethics Committee of Ochanomizu University, and in accordance with the Declaration of Helsinki**:** Ethical principles for research involving human subjects with special attention paid to the following: To prevent the identification of individuals, each subject's personal information was carefully coded and obtained data were strictly managed. We obtained consent that participation in the research was by free will on the

part of the participants and their guardians by providing explanations about the objectives and details of the investigation and the intention to use the results for oral and written presentations. Even after commencement, explanations were provided whenever subjects dropped out of the study, either of their own volition or at the guardian's behest, and no subjects were penalized in any way.

5) Statistical analysis

Analysis of the data was carried out with SPSS (version 17.0) statistical software. Data were assessed by one-way ANOVA and then Tukey's multiple comparison test and p values less than 0.05 were considered statistically significant. Correlation between body weight and sugar intake was investigated by Peason's correlation coefficient test.

C．研究結果

Result

Study 1:

Table shows the result of analysis.

Table shows the result of Recipe analysis.

(See the attached documents)

Study 2:

Table7 shows the height, weight and energy intake of children in this study. All values were similar between our subjects and Japanese average (4,12), indicating that our subjects were similar to the country representative. Energy intakes were higher in boys than in girls in all the age groups and increased by age except for girls of 13.

Table8 shows sugar intakes. Sugar intakes in both sexes in all the age groups were similar except the low intake in 13 year old girls. The average intake for all the children was 24.7±15.5 g/day. When we see the contribution of each sugar, sucrose was the highest at 15.8g and others were similar at about 3g a day. According to the national health and nutrition survey, average sucrose intake from meals is about 5.5g a day. Therefore, the total intake per day is about 30g. WHO recommends less than 10% of energy from sugar. If we calculate 10% of energy and convert this to the sugar by dividing 4 kcal / g, the WHO recommendation for our participants are the figures shown in the right column of Table 2. Average intakes for Japanese children are much lower than the WHO upper limit.

Fig.2 shows the contribution of major foods to sugar intake. Sugars from beverages contributed about 1/4 and baked cakes and ice cream each about 20 and 17%, respectively. These 3 items contributed about 60% of the sugar intake.

The degree of obesity = (actual measured weight – weight for height standards)/ weight for height standards × 100. Weight for height standard was calculated from the School Health Statistics. Children whose values are 20% greater than average are defined as obese, while children whose values are 20% lower than the average are defined as thin. We could not observe the relationship between sugar intake and body shape from (Fig.3-5)

Table 7 Characteristics of the subjects and energy intake

Age (years)	Gender	N	Height(cm)	Weight(kg)	Energy/day (kcal)
7	Boy	33	122.5±5.4[a]	23.6±3.7[a]	1843±310[a]
	Girl	42	120.9±5.2[a]	22.8±3.5[a]	1668±238[a]
10	Boy	64	139.8±6.1[b]	34.8±8.4[b]	2081±385[b]
	Girl	64	140.4±6.9[b]	32.6±6.1[b]	1896±282[a]
13	Boy	42	162.2±8.4[c]	52.5±11.5[c]	2340±446[c]
	Girl	38	156.2±5.3[d]	47.7±7.4[d]	1871±287[a]

Values are mean ± SD.

Data were assessed by one-way ANOVA and then Tukey's multiple comparison test ($p<0.05$).

Table 8 Sugar intakes of Japanese children (g/day)

Age (years)	Gender	n	(A) Glucose	(B) Fructose	(C) Sucrose	(D) Lactose	Total sugar (A)+(B)+(C)+(D)
7	boy	33	3.1±2.6	3.5±3.3	15.9±9.4	2.5±2.3	25.1±14.6
	girl	42	3.5±3.0	3.8±3.6	17.7±11.7	2.4±1.6	27.4±15.9[a]
10	boy	64	3.2±3.4	3.4±3.7	16.8±9.8	2.2±1.9	25.7±14.2
	girl	64	3.4±2.4	3.6±2.8	16.6±9.5	2.4±1.9	26.0±12.7
13	boy	42	4.0±4.2[a]	4.4±4.6[a]	14.6±12.7	2.1±3.1	25.0±20.7
	girl	38	2.0±2.4[b]	2.1±2.7[b]	12.0±11.2	1.4±1.7	17.5±14.3[b]

Values are mean ±SD.

Data were assessed by one-way ANOVA and then Tukey's multiple comparison test ($p<0.05$)

Table 9 Calculate of sample size

X = { SD / (an error ×average) }2

SD ; 15.5

A rate of an error ; 5%

Average ; 24.7

Sample size ={ 15.5 / (0.05×24.7) }2

≒157.5

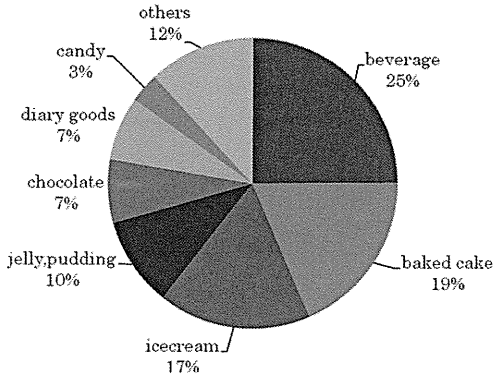


Fig. 2 Contributions of various fo od groups to total sugar in take

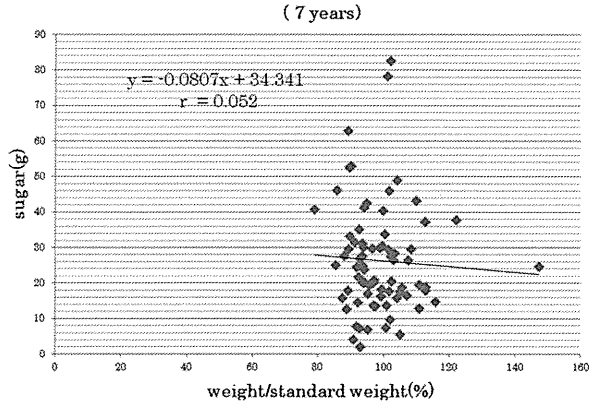


Fig. 3 Relationships between body weight and sugar intakes a t 7 years old.

No relationships were observed in all the 3 age groups.

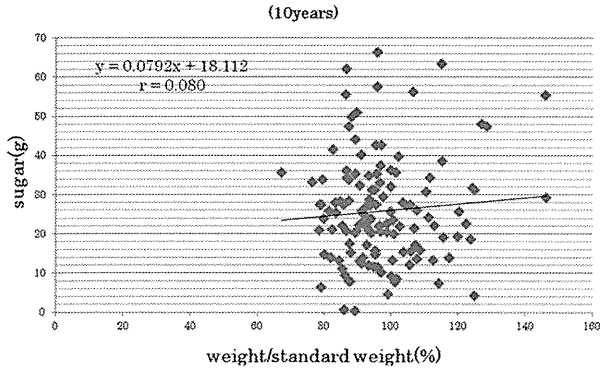


Fig. 4 Relationships between body weight and sugar intakes at 10 years old.

No relationships were observed in all the 3 age groups.

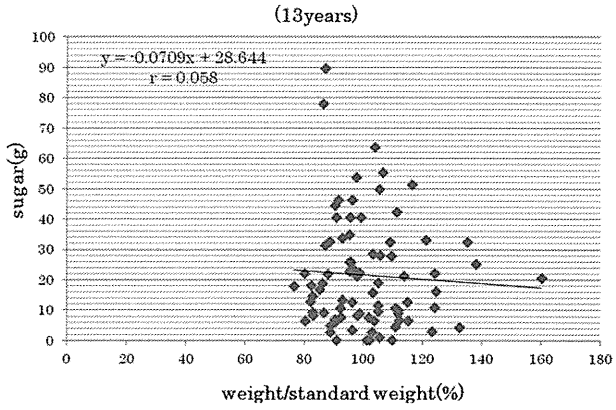


Fig. 5 Relationships between body weight and sugar intakes a t 13 years old.

No relationships were observed in all the 3 age groups.

D. 考察

Discussion

Study 1:

This is the first study in Japan concerning the sugar composition of various snacks, beverages an d other foods. However, we could analyze only 5 samples of 106 commercial products and 10 sa mples of 29 home made cakes. Usually in this t ype of study, as the food composition table, more than 30 samples about the each samples are desir ed. The number of the samples of each food shou ld be increased in the future by many researchers.

The sugar composition table was published in Japan 2009. However, the data were from the fore ign countries. Since the sweetness of American c akes is much stronger than the Japanese ones, we need the sugar composition table of Japanese swee t snacks and home made cookies. Therefore, our study with limited number of the samples must be meaningful.

We found in this study that main sugar of the traditional Japanese cakes and homemade cakes c ontained mainly sucrose but most of the cold beve rages contained higher glucose and fructose than s ucrose. It suggests that producers of cold bevera ges use isomerized sugaras (glucose and fructose) made from starches. It is known that as compare d with glucose , sucrose and lactose, fructose i ncreased blood triglyceride and visceral adiposity, decreased insulin sensitivity, all of which have bee n associated with increased risk for cardiovascular disease and type 2 diabetes, suggesting that we ha ve to realize not only the total amount of sugars but also the type of sugars for our health.

Study 2:

We found in this study that average of sugar intake of Japanese children was about 30g/day and met the WHO recommendation. To our knowledge, this is the first study about the sugar intake of Japanese children. The WHO recommendation is less than 10% of energy (2).

In this study we also measured the energy intake and was 1,960 kcal/day, 10% of it (196 kcal) is equivalent with about 49g of sugar. The energy intake of these children was normal being similar as the Japanese recommendation (6-8). The standard deviation of sugar intake was about 15g. Thus the mean sugar intake + 1SD is about 45g which is smaller than 49g. When the distribution is normal, mean + 1SD covers about 85% of the similar age population. The number of the subjects was 283 and the survey was for 3 days, which suggest the distribution was normal . A sample size meets requirement. (Table9)

There are reports about the sugar intake from various countries, American male children of 6-12 years old consume 124g/day (11), England 84g/day (12)、Holland 135g/day (13), South Africa 42-59g/day (14) and Philippines 60g (15). On the basis of such data, it was easy for us to estimate that Japanese children also consume a considerable amount of sugar, however, it was much less than those of the other countries;

Nutrition surveys often underestimate intakes (16,17). To prevent such problems, in this study we used the weighing method for school lunches and carefully checked other meals and foods. There are seasonal variations in the intakes, however, this study was conducted in summer and in this season sugar intake is usually higher than in other seasons because people drink more cold sweet beverages, which decreases the underestimation problem. To verify the reliability of the present nutrition survey, we compared the energy intakes in the present subjects with those reported by the National Health and Nutrition Survey (6). Intake was 1960±388 kcal in our subjects and 1985kcal in the children reported in the nationwide nutrition survey . Both sets of data were similar, indicating that in our study underestimation was possibly avoided.

Our present result is also supported by the FAO report on sugar intakes by countries estimated from each country's annual supply of sugar (18). From these reports, the sugar intakes per person (g/day) were 48.8g for Japanese, 84.5g for Americans, 139.4g for Cubans, 138.6 for Brazilians, 100.4 g for British, 96.2g for Germans, 47.1g for Koreans, 17.2g for Chinese, 79.6g for Thais, 31.7g for Vietnamese, and 66.0g for Filipinos. From this report, the sugar intake of Japanese is low. The portion size of foods may be one of the major factors for the lower sugar intake by Japanese children than by American children. For example, a single chocolate cookie prepared by the same company contains 35.4 kcal (7g) in Japan, while in USA it contains 53.3 kcal (11.3g) . A beverage from the same company's fast food chain store in Japan is 312 kcal but in USA is 470 kcal.

The contribution of each sugar to the total intake was 64% for sucrose, 13.2% for fructose, 12.4% for glucose and 8.8% for lactose. Major sources of sucrose were traditional cookies cakes as well as Western style ones, chocolate and others. Fructose and glucose were mainly from isomerised sugar (high fructose corn syrup) used in beverages and many other liquid-form sweet foods. This sugar is cheap because it is produced from corn syrup. Major sources of lactose are milk chocolate, ice cream, yogurt and lactic fermented beverages.

From the data shown Fig.5, sugars from beverages was 25% and the highest. These results indicate that fructose and glucose (total 25.6 %) were mainly from beverages. It was also true in our study. Most of the beverages are used isomerized sugar commonly called high fructose corn syrup. They are produced by the hydrolysis of corn starch and other starches and are cheaper than sucrose. However, it is the soluble form and is usually used in the beverages. The different physical effects of these sugars are known. For example, fructose increases the blood triglycerides and obesity more than glucose (21-25). Therefore, we may have to know what kind of sugar we are taking and the effects of them on health.

The lower intake by 13-year-old girls was perhaps due to the concerns about body weight and also to changes in taste. In Japan most adolescent girls think that a slim body is beautiful. Such an image on the part of Japanese girls seems to be more serious than for girls in other countries (26) .

In conclusion, the sugar intake of most Japanese children was within the proper range.

E．結論

Conclusion

The database of sugar rich foods (commercial beverages, chilled snacks, commercial cakes

and cookies, homemade cookies.) usually Japa nese eaten was build up and the sugar content of evidently.

The balance of sugar's types are different fro m kinds of foods, and not only plane sugar b ut also isomerized sugar (high-fructose corn sy rup) dominated in a lot of foods.

This is enough to estimate mono and disaccha rides intakes of Japanese children. More sampl es are required to be analyzed for the establis hment of the reliable data in the future.

Result of this study, Sugar intakes of Japanese children is not too high. That is welcome thi ng for us about obesity and chronic diseases. But we may have to know what kind of sugar we are taking and the effects of them on hea lth.

Japanese children acquire and inherit because of Japanese foods culture has a lot of advantage.

謝辞
Acknowledgement

The authors wish to thank the subjects and their family members for their cooperation in participat ing in this study, as well as everyone in the instit utions for their kind help. The research for this pa per was supported by Grant-in-Aid for Scientific R esearch, as a part of the project in 2008 "Impleme ntation of investigation of eating habits of schoolc hildren at school and at home" (Principal Research er: Shigeru Yamamoto) commissioned by the Mini stry of Education, Culture, Sports, Science and Te chnology.

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「肥満関連疾患のアジアと米国における遺伝疫学的検討とその対策に関する研究」

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研究要旨：耐糖能障害(IGT)診断は、糖尿病への進展と虚血性心疾患発症抑制の観点から重要である。IGT 診断には 75g 経口ブドウ糖負荷試験(OGTT)2 時間後血糖値(2hPG)が重要である。本研究において日本人 OGTT のデータをもとに 2hPG に寄与する因子を検討したところ空腹時血糖(FPG) (r=0.74) と HbA1c (r=0.67) が最も強い相関が得られた。その結果をもとに 2hPG を推定する算出式を作成した。そして推定式の精度を検討したところ、IGT の診断基準である 7.8 mmol/l では、83%の感度が得られた。また推定値のカットオフ値を 7.2 mmol/l に設定すると、感度と陰性的中率は 94%と 5.7%なり、2hPG 推定値 7.2mmol/l 以下で OGTT の施行なく NGT と診断できる可能性が高いことが示唆された。

A. 研究目的

耐糖能障害(IGT)は、糖尿病への進展と虚血性心疾患発症の危険因子であることから、早期診断はその進展、発症抑制の観点から重要である。IGT 診断には 75g 経口ブドウ糖負荷試験(OGTT)を施行し、2 時間後血糖値(2hPG)を評価することが必須である。しかし負荷時間や頻回の採血、費用の点からすべて人を対象として OGTT を施行することは非常に困難である。これまで HbA1c や空腹時血糖などのある特定の因子と 2hPG との関連は検討されてきたが、2hPG に寄与する因子の検討やそれを用いた推定式を開発した報告はない。本研究では OGTT を施行した日本人の結果をもとに 2hPG の寄与因子とそれに基づく 2hPG の推定式を作成し、その有用性について検討する横断研究を行った。

B. 研究方法

2000 年から 2011 年まで OGTT を施行した 380 人の日本人を対象として年齢、性別、BMI、血糖、HbA1c(NGSP 値)、インスリン値、75gOGTT などの身体的・生化学的結果をもとに 2hPG の寄与因子を検討した。次に全症例を無作為に 2 群(Derivation 群(D 群)、Validation 群(V 群))に分け、D 群から 2hPG を推定する算出式を作成し、V 群から receiver operating characteristic (ROC)を用いて推定式の精度を検討した。

統計解析にはSAS ver.9.2を用いた。

C. 研究結果

対象症例の年齢(歳)、BMI、HbA1c(%)は、平均（SD）で58.5 (14.0)、24.6 (4.7)、6.4 (0.7)、57.6%が男性であった。単回帰分析の結果、空腹時血糖(FPG) (r=0.74) とHbA1c (r=0.67) が最も強い2hPGの寄与因子であった。一方で年齢やBMI、空腹時インスリン値、インスリン抵抗性や分泌能の指標であるHOMA-IR、HOMA-β、insulinogenic indexとの強い相関は認めなかった。D群を用いた重回帰分析によって2hPGの推定値は、1.66 ×FPG (mmol/l) + 1.63 × HbA1c (%) - 10.1 (R^2 = 60.2%)で示された。年齢やBMI、空腹時インスリン値を加味しても推定式のR^2は59.0%と上昇を認めなかった。V群でROCを用いた解析の結果、2hPG推定値のカットオフ値をIGTの診断基準である7.8 mmol/lに設定すると、感度と特異度は83.3%、44.1%であった。しかし同設定の陰性的中率は74.3%であるため、2hPG推定値のカットオフ値を7.2 mmol/lに設定すると、感度と特異度および陰性的中率は94%、30.5%、85.7%となり、陰性尤度比は0.2であった。

D. 考察

日本人を対象とした2hPGの寄与する因子は、本研究からFPGとHbA1cでありBMIやインスリン値などには強い相関を示さなかった。その理由として欧米人と比較してインスリン抵抗性が低く、インスリン分泌能が低いという日本人の特性を反映している可能性が考えられる。

E. 結論

2hPGは、FPGとHbA1cに強い相関を認め、その因子から構成される2hPGの推定式はIGTスクリーニングにおいて有用であることが示唆された。特に推定2hPGが7.2 mmol/l以下であれば、陰性尤度比からOGTTの施行なくNGTと診断できる可能性が示唆された。

F. 健康危険情報

該当事項なし。

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H. 知的財産権の出願・登録状況

該当事項なし。

厚生労働科学研究費補助金（国際医学研究調査研究事業）
分担研究報告書

冠動脈疾患既往患者における、高脂血症治療薬（プロブコール）の血管イベント発症の二次予防効果及び抗動脈硬化作用を評価する臨床研究

分担研究者　山下静也 大阪大学医学部附属病院　循環器内科　病院教授、
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研究要旨

脳心血管イベントおよび死亡率の減少を目指して、脂質代謝異常の改善のためスタチン系薬剤が用いられてきたが相対リスク低下度は 30%程度と低い。脂質異常症治療薬プロブコールは LDL 異化亢進・コレステロール胆汁排泄促進・生合成阻害による LDL コレステロール(LDL-C)低下作用のみならず抗酸化作用・コレステロール逆転送促進作用といった動脈硬化プラーク抑制作用により家族性高コレステロール血症(FH)患者の心血管イベント二次予防に有効であった(POSITIVE 試験)。今回、非遺伝性の脂質異常症患者における脳血管疾患の二次予防効果、頸動脈硬化進展への影響につきランダム化非盲検比較試験を日本・韓国・中国国際共同研究として開始した。高 LDL-C 血症(200 mg/dL 以下)により脂質低下剤服用中で冠動脈疾患(心筋梗塞・狭心症、陳旧性心筋梗塞、CABG・PCI 術後)の既往のある患者を継続療法群とプロブコール併用群に割り付け、主要評価項目；脳心血管イベントの発生(心血管死・心臓突然死・非致死性心筋梗塞・非致死性脳卒中・入院を要する不安定狭心症・心不全・冠血行再建術の実施)および副次評価項目；全死亡・全イベント発生の有無及び期間・イベントフリー生存期間・頚動脈硬化の推移及び変化量・重篤な有害事象を追跡期間 3 年で観察する。本邦 860 例(片側 430 例)、中国(300 例)・韓国(300 例)と合わせてアジア全体で 1460 例のメタ解析を行うことによりアジアにおける新たなエビデンスの確立を目指す。

A．研究目的

脂質異常症治療の主目的は脳心血管イベントおよび死亡率の減少にあり、生活習慣の是正に加えて薬物療法が選択される。この目的でLDL-C値を低下させ、脳心血管疾患の新規発症・再発を抑制するスタチン系薬剤が用いられてきたが、相対リスク低下度は30%程度と低く、増量効果もわずかである。プロブコールはLDL-C低下作用（LDLの異化亢進・コレステロール胆汁排泄促進および生合成阻害）のみならず抗酸化作用・コレステロール逆転送促進作用を有し動脈硬化プラーク形成を抑制する。プロブコール（図１）は家族性高コレステロール血症(FH)患者の黄色腫を退縮させ、血管形成術後の再狭窄率減少、冠血管拡張機能改善効果、頸動脈肥厚の退縮効果等の効果を認める。図１にプロブコールの化学構造式とその効果をまとめた。さらに我々はヘテロ接合型FH患者における心血管イベントの二次予防に有効であることを示した(POSITIVE試験)（図２）。しかし、遺伝性でない脂質異常症に対するプロブコールの大規模臨床試験は国内外を問わず未実施であることから、冠動脈疾患の既往があるハイリスクの高LDL-C血症患者を対象として本試験を企画した。プロブコール投与による脳心血管イベントの二次予防効果、頸動脈硬化進展への影響につきランダム化非盲検比較試験を日本・韓国・中国国際共同研究として追跡期間3年で開始

した。

（倫理面への配慮）
本研究の内容は大阪大学医学部附属病院および参加施設の臨床研究倫理審査委員会にて承認され、測定データ及び生体材料は匿名化され研究終了時に破棄された。被験者に不利益が生じた場合には同意撤回及び相談可能とした。

B．研究方法
各施設で臨床研究倫理委員会による承認と施設長による許可、さらに試験参加患者に対する説明文書を用いた十分な説明と文書によるインフォームドコンセントを必須とし、患者の権利を確保する。適格条件は、①脂質低下剤服用中の高LDLコレステロール(LDL-C)血症患者（200 mg/dL以下）、②冠動脈疾患（心筋梗塞・狭心症、陳旧性心筋梗塞、CABG・PCI術後）を有する者である。図３に示したように、得られた情報から適格性を確認し、ランダムにA群(継続療法群)とB群(継続療法＋プロブコール500mg併用)に割り付ける（割付調整因子：高LDL-C血症・糖尿病・高血圧の有無）。我が国の症例数は各群430例の合計860例、スタディ開始時および3か月・1・2・3年後に血液検査（脂質項目及び肝腎機能）（表１）、各年に頸動脈エコー検査を行う。図４に示したように、中国でも同様に300例、韓国でも300例を目標に研究が進行中であり、順調に目標症例数が達成されつつある。我が国では主要評価項目として、脳心血管イベントの発生（心血管死・心臓突然死・非致死性心筋梗塞・非致死性脳卒中・入院を要する不安定狭心症・入院を要する心不全・冠血行再建術；PCIおよびCABG）を検討し、副次評価項目として全死亡・全脳心血管イベント発生の有無及び発生までの期間・ イベントフリー生存期間・超音波による頚動脈硬化の推移及び変化量・重篤な有害事象の発生とその程度を検討する。以上の項目について3年間の追跡調査による一斉転帰を判定する。

C．研究結果
研究は現在進行中である。本研究は既に2009年より開始されており、2012年12月27日現在施設登録数75施設、症例登録数472例で進んでいる。当初の登録終了は2013年２月の予定であったが、症例数のさらなる増加を目指すため、１年間の延長が既に決定し各施設での倫理審査及び試験の継続を開始している。日本動脈硬化学会により本研究に対するサポートをして頂いており、学会員の参加を呼びかけていただいており、学会HPにも掲載されている（http://www.j-athero.org/topics/20111018_1.html）。また、学会評議員の施設でも多くの症例を既に登録して頂いている。さらに、今回の検討は本邦(860例)のみならず中国(300例)・韓国(300例)においても実施され、アジア全体で1460例のメタ解析を行うことによりアジアにおける新たなエビデンスの確立を目指す。

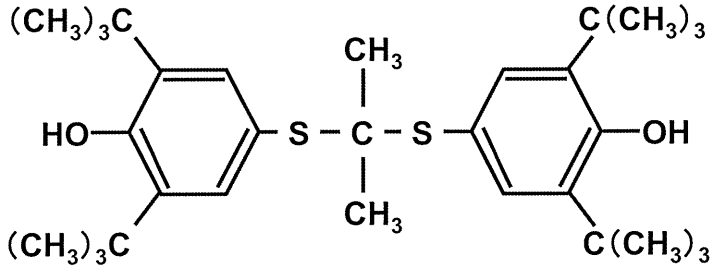
D．考察
この試験は世界初の独創的な試験であり、本邦のみならず中国、韓国においても実施する。この試験の結果、主として従来のスタチンをベースとした治療にプロブコールを併用する療法の心・脳血管イベント抑制効果が明白となれば、冠動脈疾患既往患者の二次的イベント予防を目指した新しい治療となるとともに、3国における結果のメタ解析により、アジア人におけるプロブコールの脳・心血管イベント、頸動脈硬化の抑制作用についてのエビデンスが世界に先駆けて確立されることとなり、本研究の意義は極めて大きいと考えられる。

E．結論
プロブコール投与による脳心血管イベントの二次予防効果、頸動脈硬化進展への影響につきランダム化非盲検比較試験を日本・韓国・中国国際共同研究として追跡期間3年で開始し、現在継続実施中である（施設登録数75施設、症例登録数486例）。

F．健康危険情報
なし

G．研究発表
1.　論文発表
未報告
2.　学会発表
未報告

H．知的財産権の出願・登録状況
（予定を含む。）
1. 特許取得　なし
2. 実用新案登録　なし
3. その他



4,4'-isopropylidenedithio-bis (2,6-di-*tert*-butylphenon)

Probucol

- LDL-C低下作用、HDL-C低下作用、腱黄色種退縮作用
- 抗酸化作用
  - 活性酸素除去作用
  - LDL酸化防止作用
  - 抗酸化酵素（SOD, CAT, GSHPX, NADPH, HO-1, PON-1 etc）の誘導
- コレステロール引き抜き能増強作用
- コレステロール逆転送系賦活化作用

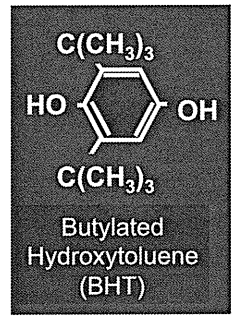


図１．プロブコールの化学構造式と薬理学的効果

POSITIVE study;家族性高コレステロール血症患者に対するprobucol投与の心血管イベント 二次予防効果

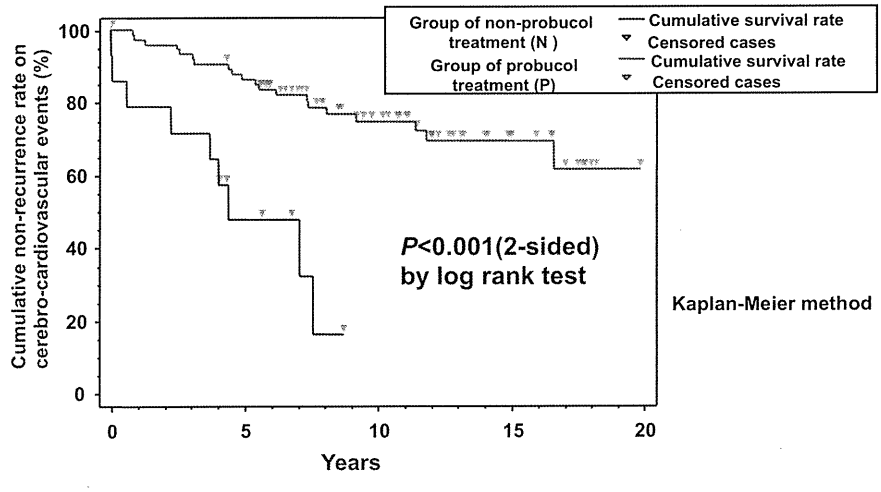


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図２．家族性高コレステロール血症患者に対するプロブコール投与の心血管イベント二次予防効果

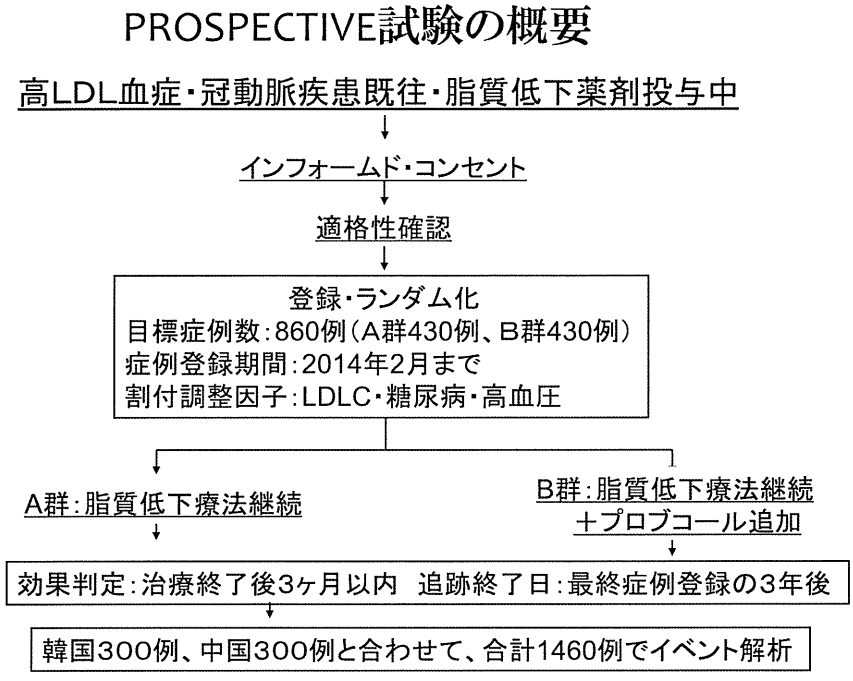

図３．PROSPECTIVE試験の概要

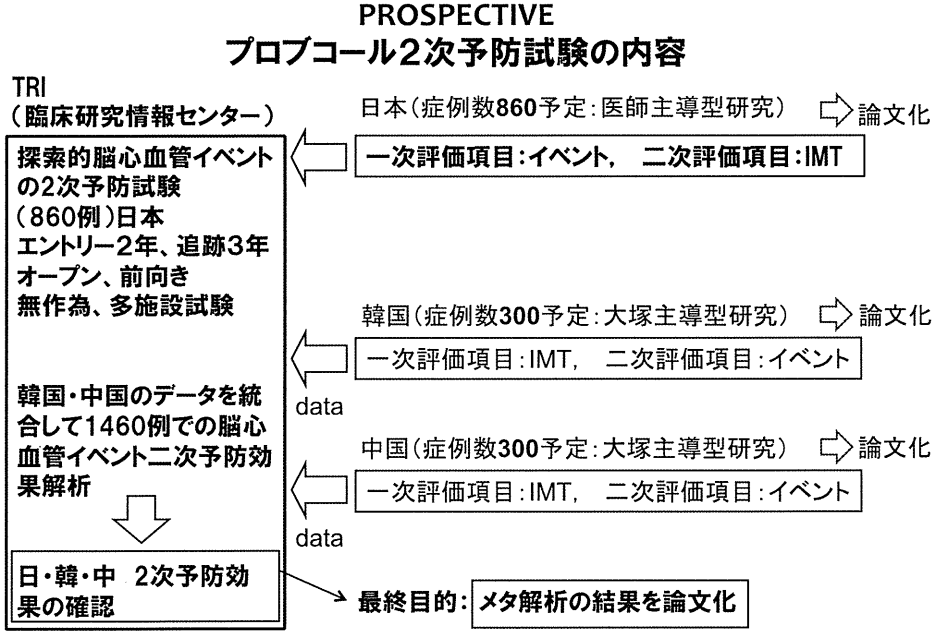

図４．日韓中プロブコール二次予防試験の概要

表１．観察・検査項目スケジュール

＜観察・検査項目：スケジュール＞

	開始前	3ヵ月後	1年後	2年後	3年後	一斉転帰	中止時
同意取得	●						
患者背景	●						
割付	●						
併用治療	●	●	●	●	●	●	●
頚動脈エコー	●		●	●	●		(●)
心血管イベント発生の有無		●	●	●	●	●	●
脂質値、	●	●	●	●	●	●	(●)
hs-CRP，adiponectin	●	●			●		
心電図	●	●	●	●	●		●
有害事象		●	●	●	●	●	●

Ⅲ. 研究成果の刊行に関する一覧表