(tethering height) を測定し，乳頭筋付着レベルの左室短軸像で拡張末期の前後乳頭筋間距離を測定した．

❷ 手術手技

手術は上行大動脈送血，上下大静脈2本脱血で人工心肺を確立し，中等度低体温体外循環下で行い，すべての手技を心停止下に施行した．術中は経食道心エコーで左室壁運動，僧帽弁の形体ならびにMRの評価を行った．

虚血を伴う場合はバイアビリティのある部分への完全血行再建を行い，僧帽弁に対しては，1～2サイズダウンした全周性リングによるMAPを基本術式としたうえで，術前の心エコーでtetheringが著明な場合（tethering height≧7 mm）は，MAPに加えtethering解除のため左室心尖部アプローチでPMAを追加した．左前下行枝に並行して心尖部に小切開を加え，後壁に切開を延長し，前後乳頭筋の基部にプレジェット付き3-0ポリエステル編糸を2～3針かけて両乳頭筋を接合させるようにPMAを行った．

高度な左室拡大（LVEDd≧65 mm，LVEDVI≧90 ml/m^2）を伴う場合，前壁中隔の梗塞・拡大があればseptal anterior ventricular exclusion（SAVE）あるいはオーバーラッピング法により前壁中隔の病変部をカバーするSVRを行い，後下壁部位の線維化・拡大による乳頭筋間距離の開大に対しては，前後乳頭筋間の後壁心筋の切除・縫縮を行うBatista型SVRを行った．前尖の二次腱索がtetheringに関与していると考えられる場合は，腱索切断術を追加した．

❸ 術後検査

術後はすべての患者を当院外来で定期的に診察し，心エコーにより心機能とMRの有無を経過観察した．また術後心不全，遠隔期死亡，死因を調査した．

連続変数は平均±標準偏差で示した．2群間比較にはt検定を行って比較・検討し，$p<0.05$で有意差ありとした．

表1．術前患者背景

	S群($n=22$)	M群($n=17$)
年　齢(歳)	65.7±10.1	63.9±8.0
男[例(%)]	18(82)	14(82)
NYHA分類[例(%)]		
Ⅰ/Ⅱ度	2(9)	9(53)
Ⅲ/Ⅳ度	20(91)	8(47)
原因疾患[例(%)]		
ICM	9(41)	17(100)
DCM	13(59)	0
慢性透析[例(%)]	1(5)	5(29)
高血圧[例(%)]	9(41)	14(88)
糖尿病[例(%)]	10(45)	8(47)
心房細動[例(%)]	5(23)	2(12)

ICM：虚血性心筋症，DCM：拡張型心筋症，NYHA：New York Heart Association

表2．心エコーデータ

	S群($n=22$)		M群($n=17$)	
	術前	術直後	術前	術直後
LVEF(%)	25±6*	27±11	42±11*	45±11
LVEDd(mm)	70±10*	66±8**	59±8*	50±10**
LVEDVI(ml/m^2)	166±55*	135±47**	120±38*	83±38**
MR grade(平均)	3.5±0.5*	0.4±0.9**	2.6±0.7*	0.3±0.6**
0/Ⅰ/Ⅱ[例(度)]	0/0/0	16/3/0	0/0/9	13/3/1
Ⅲ/Ⅳ[例(度)]	11/11	1/0	6/2	0/0
ERO(cm^2)	0.4±0.1	−	0.3±0.2	−
RV(ml)	52±13	−	46±23	−
tethering height(mm)	9±3*	4±2**	5±2*	−
両乳頭筋間距離(拡張期)[mm]	34±6	19±8**	−	−
LAD(mm)	52±11*	51±9	45±8*	41±8
TR grade(平均)	1.4±1.0	1.2±1.1	0.9±1.0	0.3±0.6

LVEF：左室駆出率，LVEDd：左室拡張末期径，LVEDVI：左室拡張末期容量係数，MR：僧帽弁閉鎖不全，ERO：有効逆流面積，RV：逆流量，LAD：左房径，TR：三尖弁閉鎖不全，*両群間で有意差あり，**術前後で有意差あり

表3. 手術術式詳細

	S群(n=22)	M群(n=17)
緊急手術[例(%)]	4(18)	2(12)
術前IABP[例(%)]	4(18)	2(12)
術前カテコラミン依存[例(%)]	6(27)	2(12)
人工心肺時間(分)	206±56	191±42
大動脈遮断時間(分)	136±42	138±34
僧帽弁手術 MAP[例(%)]	21(95)	17(100)
リングサイズ[平均(mm)]	27.6	27.6
26～27(例)	4	8
28(例)	17	7
30(例)	0	2
乳頭筋間縫縮術[例(%)]	20(91)	0
二次腱索切断[例(%)]	6(27)	0
左室形成術[例(%)]	22(100)	0
Batista	10(45)	
SAVE	8(36)	
オーバーラッピング	2(9)	
心尖部切開のみ	2(9)	
CABG[例(%)]	8(36)	15(88)
TAP[例(%)]	8(36)	2(12)
maze手術[例(%)]	5(23)	1(6)

IABP：大動脈内バルーンパンピング，MAP：僧帽弁輪形成術，SAVE：septal anterior ventricular exclusion，CABG：冠状動脈バイパス術，TAP：三尖弁輪形成術

表4. 術後中期成績

	S群(n=22)	M群(n=17)
平均追跡期間(月)	14±12	26±11
再手術[例(%)]	1(5)	1(6)
30日死亡[例(%)]	2(9)	0
入院死亡[例(%)]	4(18)	0
遠隔期死亡(例)	5	1
NYHA分類[例(度)]		
Ⅰ	0	4
Ⅱ	8	12
Ⅲ	5	0
Ⅳ	0	0

Ⅱ. 結　　果

❶ 患者背景

術前の患者背景を表1に示す．平均年齢はS群65.7±10.1歳，M群63.9±8.0歳で，術前心不全はNew York Heart Association（NYHA）分類Ⅲ/Ⅳ度はS群で91%，M群で47%とS群がより重症であった（p<0.01）．原因疾患としてS群ではICM 41%，DCM 59%で，M群では全例がICMであった．心エコーの結果を表2に示す．術前LVEFはS群が25±6%，M群が42±11%（p<0.001）で，術前LVEDdはS群が70±10 mm，M群が59±8 mm（p<0.01）で，S群でより低心機能かつ左室高度拡大例が多かった．同様に術前MR gradeでもS群は3.5±0.5度，M群は2.6±0.7度と有意にS群で高度であった（p<0.001）．

❷ 手　　術

手術術式・合併手術の詳細を表3に示す．S群の4例，M群の2例が，術前より大動脈内バルーンパンピング（IABP）が挿入された状態の緊急・準緊急手術であった．僧帽弁に対して，S群の1例（MAP後MR再発に対してSVRのみを施行）を除きすべてMAPを施行し，使用リングサイズの平均は両群とも27.6 mmであった．冠血行再建を行った症例はS群が8例（36%）に対し，M群は15例（88%）であった．S群では20例（91%）に左室心尖部切開からPMAを行ったが，SVRの手技としては後下壁拡大の10例にBatista型の後下壁切除術を行った．また前壁中隔拡大が中心の8例にSAVE手術を，2例にオーバーラッピング手術を行った．人工心肺時間，大動脈遮断時間は両群間に差はなかった．M群では術中・術後に新たにIABPなどの循環補助を要した症例はなかったが，S群では術前からの4例に加えて9例で術中にIABPを挿入し，循環補助を行った．

❸ 術後評価および初期成績

術前後の心エコーデータを表2に示す．術後心エコーでは，両群ともにLVEFの改善はわずかで，有意差はなかった．しかしLVEDdならびにLVEDVIは，両群ともに有意に減少していた［LVEDd：S群 70 → 66 mm（p<0.01），M群 59 → 50 mm（p<0.001），LVEDVI：S群 166 → 135 ml/m^2（p<0.0001），M群 120 → 83 ml/m^2（p<0.001）］．また，両群ともにMRの制御は良好であった［S群 3.5 → 0.4度（p<0.0001），M群 2.6 → 0.3度（p<0.0001）］．特にS群ではtetheringが良好に改善し，両乳頭筋間距離が縮小していた．S群では4例の入院死亡があり，うち2例が心不全・低心拍出量症候群（LOS）によるもので，2例が重症感染症・敗血症によるものであった．M群では入院死亡はなかった．

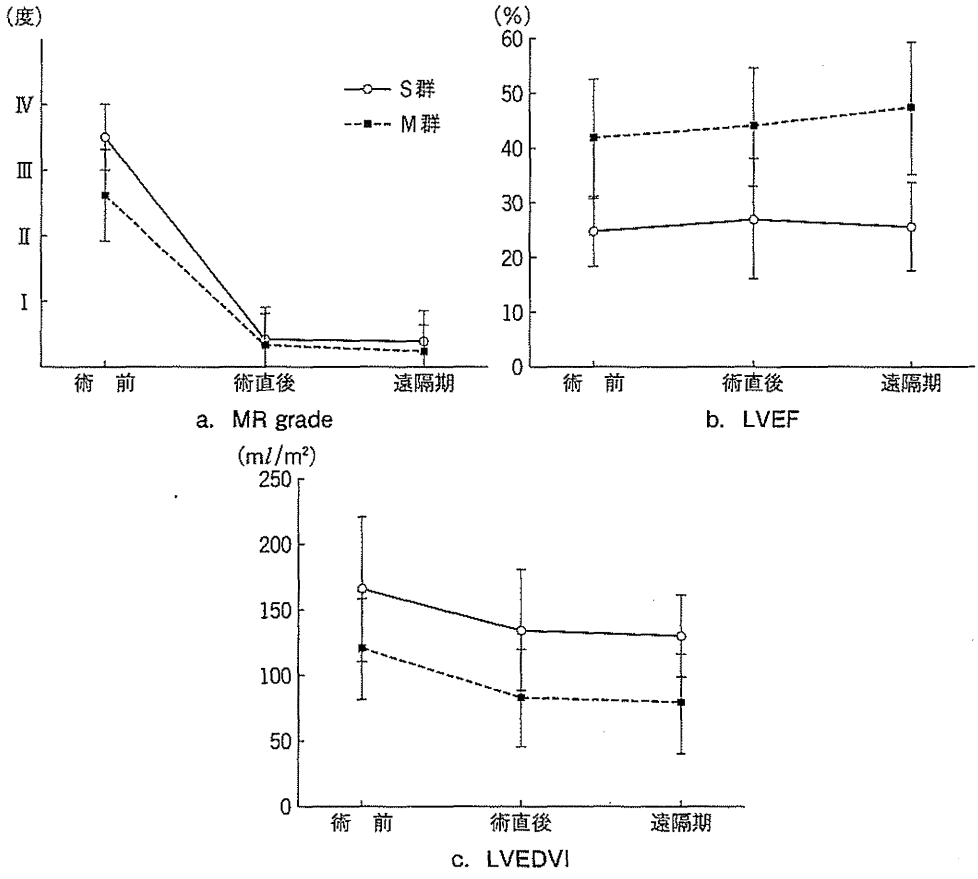

図1. 心エコーデータの経時的変化

㊹ 中期成績

対象例全例について，平均観察期間19±13ヵ月における中期成績を調べた．その結果を表4に示す．遠隔期に再手術を要した症例をS群，M群ともに1例ずつ認めた．S群ではMR再発（SVR時にPMA未施行の症例で後に乳頭筋間の再開大を認め，これがMR再発の原因と考えられた）に対して，M群では僧帽弁感染性心内膜炎に対してそれぞれ僧帽弁置換術を行った．再手術の病院死亡はなかった．

M群に突然死による術後遠隔期死亡1例を認めたが，生存例はすべてNYHA分類Ⅱ度以下で心不全は良好に制御されており，心不全による再入院もなかった．一方，S群では生存退院18例中5例の遠隔期死亡を認め，うち4例が心不全によるもので，経過観察中の死亡例を含め，13例でNYHA分類Ⅲ度以上の心不全を認めた．また遠隔期生存13例中5例が，心不全再発による再入院を経験していた．ただし再手術となった症例を除き死亡例，生存例いずれの症例においても心エコーでⅡ度以上のMRは認めず，心不全の主因は弁膜症ではなくポンプ失調によるものと考えられた．

心エコーの経時的変化を図1に示す．S群，M群ともに経過観察中にMRの増悪とLVEFの悪化はなく，FMRについては両群ともに良好に制御されていた．

Ⅲ. 考　　察

心筋梗塞後のMR合併により心不全発症率，心臓関連死が増加することは以前より知られていたが[3]，近年，非虚血性心筋症に関しても，中等度以上のMRが心不全および心臓関連死の独立した予測因子であることが示され[4]，FMRは虚血の有無によらず心不全発症や生命予後を決定する重要な因子といえる．

FMRの発症には左室のリモデリングが関与し，弁輪拡大に加えて，左室拡大に伴う乳頭筋の心尖部および後外側方向への偏位により僧帽弁尖の心尖部方向へのtetheringが生じ，弁尖接合不全により逆流が生じる[2]．これは多くの場合，前後乳頭筋付着部間距離の拡大を伴う．さらに前尖の二次腱索による局所的な僧帽弁の変形も，tethering増悪の一因となる[5]．

FMRの原因が持続する心筋虚血の場合，血行再建による左室収縮力の改善と左室形体の正常化によりMRが改善することがあるが，中程度のMRは冠状動脈バイパス術（CABG）施行時に放置すると，遠隔期に再発・増悪し心不全の発症につながることが多く，MAPを同時施行すべきである[6]．

FMRに対して，両弁尖のより広い接合範囲を得るため通常より1～2サイズ小さい人工弁輪を用いたサイズダウンしたMAP（undersized MAP）が提唱され[7]，MR制御によるリモデリング改善効果が期待されたが，その後の研究でMRの術後高頻度再発が指摘されるようになった[8]．Undersized MAPは後尖弁輪の中隔方向への偏位により弁輪の前後径を縮小させ，逆流を制御するが，後尖のtetheringはむしろ増悪する．人工弁輪による前後径の縮小効果と後尖のtethering増悪のバランスによりMRが制御できるかどうかが決まり，弁輪前後径の縮小が不十分な場合や，術後の左室拡大で前尖のtetheringが増強する場合には，MRが残存・再発する原因となる[9]．また逆流制御のためサイズダウンしすぎると，狭小化した弁輪・弁下レベルで狭窄が生じる可能性があり，心不全悪化の原因となる[10]．Tetheringが強く関与する症例は，MAPのみではFMRの制御はむずかしい．

FMRは弁膜疾患というより，左室拡大とそれに伴う弁尖のtetheringが原因の心室疾患であるという考え方から，弁尖より下部の構造物，つまり腱索，乳頭筋，左室心筋に対して手を加える必要性が提唱された．弁下部追加手技としては二次腱索切断[11]，乳頭筋の右線維三角方向への移動・吊り上げ[12]，両乳頭筋間縫縮（PMA[13]あるいはpapillary muscle sling[14]）などが報告されている．

またFMRに対する治療として，前後乳頭筋を直接縫縮するPMAも，前後乳頭筋間の左室後壁を切除・縫縮するBatista型手術も，左室拡大に伴う乳頭筋の偏位を矯正してtetheringを解除するという意味で，まったく同じ効果をもつと考えられた．当科におけるこれまでの経験では虚血の有無を問わず，拡大した心臓でtetheringが高度なMR例ではほとんど例外なく後下壁部位の線維化・拡大に伴い乳頭筋間距離が開大しており，PMAを中心に個々の症例に応じたSVRを加えることで，左室径の縮小に伴ってtetheringも改善し，FMRの制御が可能であった．乳頭筋間縫縮を行った症例では，その後の経過中にMRの再発・増悪は認めていない．しかし，左室のポンプ失調が原因で心不全が遷延・増悪する症例も少なくなかった．

元来，左室瘤や左室無収縮部の治療目的で発展してきたSVRであるが，現在行われている心不全治療としてのSVRは主に，①左室容量縮小，②左室形体改善[15]，③FMR制御のためのtethering軽減の三つの役割があると考えられた．いずれも駆出効率改善に加えて，左室容量および圧負荷による左室リモデリングの負の連鎖を防止する手段として重要な意味をもち，この負の連鎖を防止できるかどうかが中期・遠隔期予後に大きな影響を与えると考えられた．

現在のところ，重症心不全に対するSVR自体に心機能や生命予後を改善させるというデータは得られておらず，明らかに生命予後・生活の質（QOL）を改善しうる心臓移植や植込み型左心補助装置（LVAD）に比べてその効果には疑問点も多く存在する．しかし本報告の対象例の中には心臓移植やLVADの適応外症例が多く，FMRを改善する術式として依然としてSVRは一定の意義があると考えられた．将来的には再生医療の応用なども含めた新しい治療手段の開発が必要であると考えられた．

おわりに

1）高度の左室拡大およびtetheringを有する重度のFMR例に対して，MAPに加えて積極的にSVRを施行し，良好な左室縮小効果ならびにMR改善効果を得ることができた．

2）中期的にもMRの再発はまれであったが，SVRを要するような重症心筋症患者ではポンプ

失調による心不全の再発が多く，予後は不良であった．

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SUMMARY

Surgical Ventricular Restoration for Functional Mitral Regurgitation

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Background : This study evaluated the effectiveness and limitations of the surgical ventricular restoration (SVR) procedure in patients with functional mitral regurgitation (FMR) due to severe leaflet tethering.

Methods : From 2008 to 2012, FMR was treated in 39 patients by either mitral annuloplasty (MAP) alone (group M : $n=17$) or MAP combined with SVR (group S : $n=22$). Preoperatively, patients in group

S had lower ejection fraction (EF), larger left ventricle, and more severe mitral regurgiation (MR) comparing to group M.

Results : The SVR performed in group S included posterior wall exclusion (Batista) in 10, septal-anterior ventricular exclusion in 8, overlapping ventriculoplasty in 2, and others in addition to papillary muscle approximation (PMA). Coronary revascularization was more common in the group M. Hospital mortality were 18% in group S and 0 in group M. There were no significant improvement on EF in both group, but left ventricular (LV) dimensions decreased significantly in both groups. Also, MR grade decreased significantly in both groups. Leaflet tethering was improved significantly in group S. There were 5 and 1 late deaths in group S and M, respectively.

Conclusion : SVR in addition to MAP yielded excellent reduction of leaflet tethering and MR in patients with severe LV dilatation. However, long-term outcomes were poor in those requiring SVR.

KEY WORDS

functional mitral regurgitation/surgical ventricular restoration/papillary muscle approximation/mitral annuloplasty

「胸部外科」特集原稿募集

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テーマ

弓部大動脈瘤
——こだわりの術式と遠隔期成績

術式の定型化，脳保護法の進歩，人工血管の改良などによって，弓部置換の手術成績は大きく改善してきた．しかし瘤腫とそれに伴う高度動脈硬化例，併発症を有する高齢者，合併手術（冠状動脈バイパス術，弁膜症手術）の必要性など，ハイリスクとなる場合が少なからず経験される．脳保護法は，順行性脳灌流法の優位性が多く報告されてきたが，最近では最低深部温（あるいは鼓膜温）をあまり低下させる必要がないという報告も増えている．弓部大動脈瘤の脳保護はどうすべきか，どこまで進歩するのか，各施設のこだわりを報告していただきたい．Debranching TEVARが普及し，zone 1，2のみならず，zone 0に及ぶ大動脈瘤をTEVARで治療できる時代になってきた．TEVARの適応をどこまで拡大できるのか，zone 0にどこまで挑戦するのか，そのこだわりを報告していただきたい．その一方で，オープンステントやfrozen elephant trunkのような，通常の弓部置換にステントグラフトを併用する方法を採用する施設もある．その最大のメリットは何か，オープンステント併用による分割手術の成績は向上してきたのか，ぜひともたくさんのご報告をいただければと思う．

『胸部外科』編集主幹　近藤　丘，小野　稔

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○内　　容：臨床と研究，臨床経験などテーマに沿ったもの
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なお採用論文は下記のとおりご執筆をお願いいたします．
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Committee Report 4

Absolute Risk of Cardiovascular Disease and Lipid Management Targets

Executive Summary of the Japan Atherosclerosis Society (JAS) Guidelines for the Diagnosis and Prevention of Atherosclerotic Cardiovascular Diseases in Japan—2012 Version

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Committee for Epidemiology and Clinical Management of Atherosclerosis

Traditionally, the relative risk has been primarily used to evaluate the strength of the associations between risk factors and cardiovascular disease (CVD) and the effects of treatment. In Western countries, scoring tables consisting of scores for each risk factor weighted according to their absolute risk and risk assessment charts in which squares at the points of intersection of the vertical and horizontal axes, each of which has a different risk factor at a different level, are expressed in different colors to represent the absolute risk have been developed to predict an individual's absolute risk in several guidelines. Typical examples are the U.S. Framingham risk score[1] and the European SCORE risk chart[2]. As the name implies, the Framingham risk score is a method for scoring sex (the weighting of each risk factor differs between men and women), age, total cholesterol (TC), the smoking status, high density lipoprotein cholesterol (HDL-C) and systolic blood pressure. The probability of developing coronary artery disease (CAD), coronary death and nonfatal myocardial infarction within 10 years is calculated from the sum of the scores. The SCORE is a risk assessment chart method used to calculate the probability of death due to all CVD, including stroke, within 10 years based on sex, age, TC, the smoking status and systolic blood pressure. Because the mortality of CVD differs between countries even at the same level of risk factors, the SCORE risk chart is classified into two types: one used in countries with low cardiovascular mortality (e.g., France and Italy) and the other used in countries with high mortality (e.g., the U.K. and Germany).

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In Japan, where the size of the aging population is increasing, the concept of absolute risk is important for the management of risk factors for CVD in terms of determining the priority of treatment options and promoting efficient preventive strategies. In addition to the J-LIT chart for dyslipidemia[3], many risk assessment tools for predicting CVD based on cohort studies in the general population have recently been published in Japan[4-9]. This chapter explains the background and rationale of classifying patients according to absolute risk and the management targets for dyslipidemia in each category.

1. Establishing the Absolute Risk

In this guideline, the NIPPON DATA80 risk chart[5] was used as source data to establish the absolute risk for the following reasons:

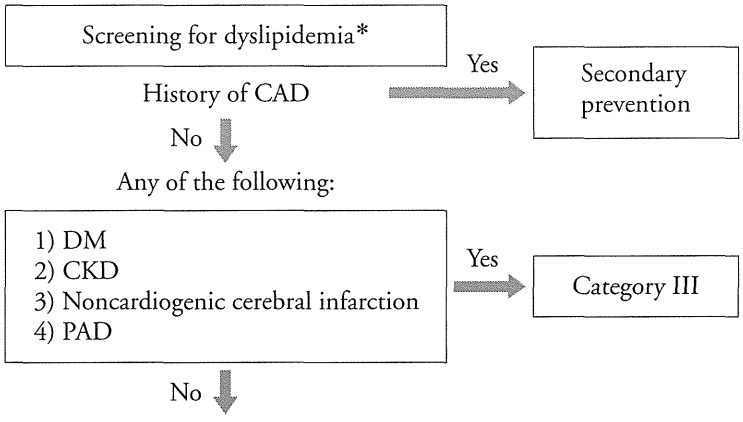
1) There was no regional bias, as approximately 10 thousand people living in 300 districts were randomly selected throughout Japan for the evaluation;

2) At the time of TC measurement (1980), the administration of medications to treat hyperlipidemia was uncommon, and statins, in particular, which strongly affect the prognosis, had not been launched;

3) The health examinations for community residents (health checkups based on the Health and Medical Service Act for the Aged) first introduced the measurement of TC in 1986, hence the TC levels were measured with almost no interventions, including lifestyle modification, suggesting that these levels reflected the natural conditions of Japanese individuals;

4) The participation rate observed in the baseline survey when the Basic Resident Register was used as the denominator was high, at approximately 75%;

5) The follow-up rate was >90%; and



Management categories based on absolute risk for the primary prevention of CAD

10-year probability (absolute risk) of CAD death derived from NIPPON DATA80	Additional risk factors	
	No additional risk factors	One or more of the following: (1) Hypo-HDL cholesterolemia (HDL-C <40 mg/dL) (2) Family history of premature CAD in first-degree relatives (a man aged <55 years or a women aged <65 years) (3) Impaired glucose tolerance
< 0.5%	Category I	Category II
≥0.5% < 2.0%	Category II	Category III
≥2.0%	Category III	Category III

*This flow chart is not applicable to patients with FH.

Fig. 1. Flow Chart for Establishing the Management Targets for LDL-C.

6) The measurement of TC was internationally standardized.

The limitations of the chart include:

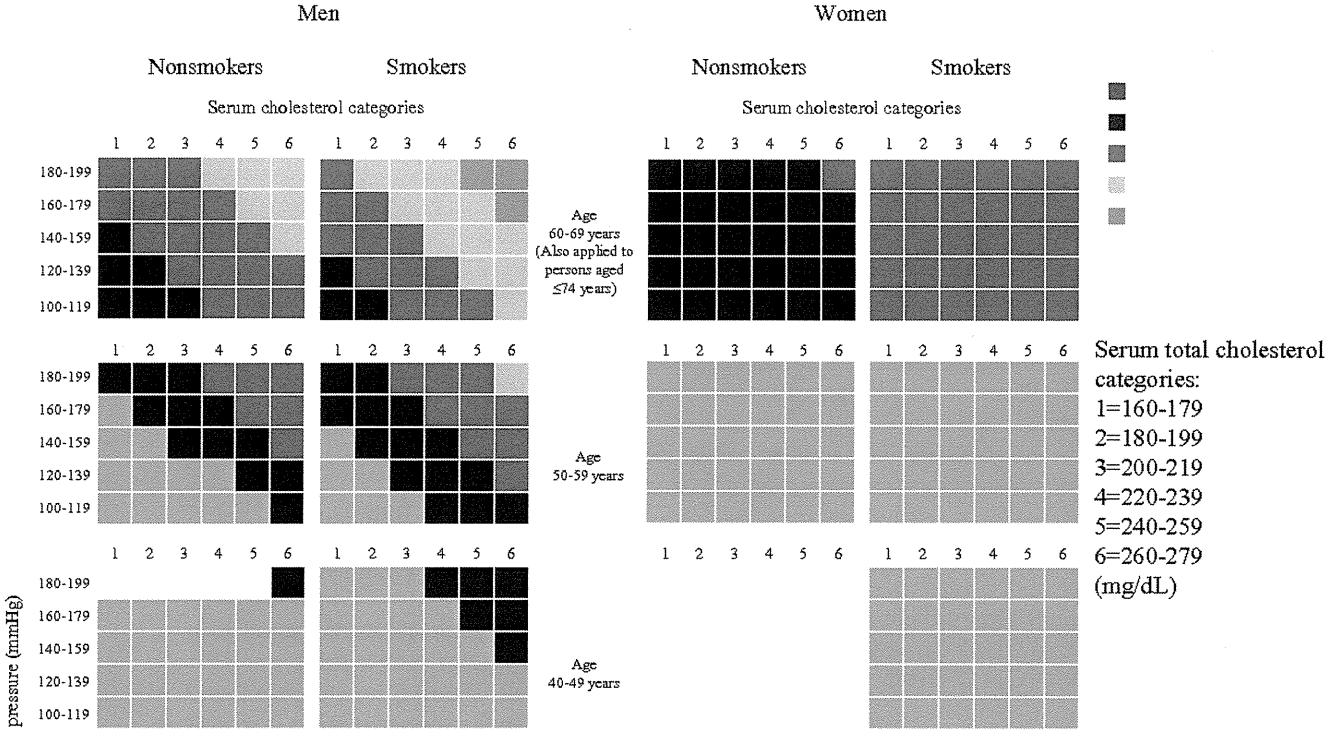
1) The end point was death, although incidence was preferable if possible;

2) Information on low-density lipoprotein cholesterol (LDL-C) and HDL-C is lacking; and

3) Blood was collected in a non-fasting state.

The advantages and disadvantages may be paradoxical. At present, there are no risk assessment tools that meet all ideal conditions required to establish guidelines.

With regard to the guidelines for primary prevention, it is difficult to perform a cohort study in a large population or urban area if accuracy of the end point is pursued. In particular, the majority of epidemiological studies in which the end point is the incidence of CVD have been conducted in non-urban areas. For example, the pooled analysis of a cohort study called the JALS-ECC, in which the end point was myocardial infarction morbidity and information on the HDL-C levels was provided[4], included almost no urban areas. The crude incidence of myocardial infarction in the JALS-ECC was approximately 0.6 per 1,000 person-years, whereas that observed in the Suita study of a cohort of only urban dwellers was 1.4 per 1,000 person-years, a rate that is two-fold or more higher (no significant differences were observed in sex, age composition or the initial year of follow-up)[10]. In this case, it cannot be determined which study is more representative of the Japanese population, and estimating the absolute risk based on the data obtained for only one area is not recommended.



The section of hyperglycemia from the NIPPON DATA80 risk assessment chart is omitted here. These charts cannot be applied to high-risk patients, such as those with DM or CKD.

Fig. 2. Absolute risk assessment charts for death from coronary artery disease (primary prevention).

Absolute risk should be reassessed at least once a year since it may be affected by either risk factors or aging.

Step 1: The applicable portion of the above figures should be used based on gender, age, the present smoking status, systolic blood pressure (mmHg) and the TC level (mg/dL).
Absolute risk ≥ 2% → Category Ⅲ
Absolute risk < 2% → To Step 2
Step 2: The presence of any of the following conditions: Hypo-HDL cholesterolemia (< 40 mg/dL), a family history of CAD and/or impaired glucose tolerance
Absolute risk ≥ 0.5% < 2% + Yes → Category Ⅲ
Absolute risk ≥ 0.5% < 2% + No → Category Ⅱ
Absolute risk < 0.5% + Yes → Category Ⅱ
Absolute risk < 0.5% + No → Category Ⅰ
Supplementary notes
(1) The TC category 160-179 mg/dL should be used in patients with a TC level of < 160 mg/dL.
(2) The TC category 260-279 mg/dL should be used in patients with a TC level of ≥ 280 mg/dL.
(3) The systolic blood pressure category of 100-119 mmHg should be used in patients with a systolic blood pressure of < 100 mmHg, while the systolic blood pressure category of 180-199 mmHg should be used in patients with a systolic blood pressure of ≥ 200 mmHg.
(4) These guidelines cannot be applied to persons 75 years of age or older. For patients < 40 years of age, the relative risk charts (Supplementary Table 1) should be used.
(5) Blood pressure should be managed according to the guidelines established by the Japanese Society of Hypertension, and diabetes mellitus should be managed according to the guidelines established by the Japan Diabetes Society.
(6) It is desirable to encourage smokers to stop smoking, irrespective of the level of absolute risk.

2. Categorical Classification Based on Absolute Risk

It is impossible to statistically determine the cut-off point for the absolute risk at which patients are at a high risk; the criteria must be determined based on clinical consensus or socially accepted ideas. The U.S. NCEP ATP Ⅲ [11] defines a high risk as a ≥ 20% risk of developing fatal CAD or nonfatal myocardial infarction within 10 years based on the Framingham risk score. However, because the incidence of CAD greatly differs between Japan and the U.S., it is not appropri-

ate to use this absolute risk criterion as a reference.

Meanwhile, the European guidelines using the SCORE risk chart[12] are similar to the NIPPON DATA in that they both use the end point of death. The European guidelines that are based on the SCORE risk chart define a high risk as a ≥5% risk of cardiovascular disease death within 10 years. The chart for all CVD deaths in the NIPPON DATA80 employs almost the same end point as that used in the SCORE risk chart. However, strokes account for a high proportion of CVD in Japan, and similar to most cohort studies conducted in Japan, the NIPPON DATA80 shows no relationship between the TC level and stroke mortality. The ratio of stroke death to CAD death in Japan is approximately 2:1. The purpose of these guidelines is to promote the comprehensive prevention of CAD and provide lipid management goals for Japanese individuals. Therefore, in reference to these categories, these guidelines define Category I (low risk) as a <0.5% risk of CAD mortality, Category II (intermediate risk) as a ≥0.5% to <2% risk of CAD mortality and Category III (high risk) as a ≥2% risk of CAD mortality.

A flow chart for establishing management targets for LDL-C based on the absolute risk is shown in **Fig. 1**. First, after screening for dyslipidemia, a check is performed to determine whether the patient is a candidate for secondary prevention. Next, it is necessary to determine whether the patient has a condition that by itself classifies the patient into Category III, such as diabetes mellitus (DM, excluding impaired glucose tolerance), chronic kidney disease (CKD), noncardiogenic cerebral infarction and peripheral arterial disease (PAD). If no such conditions are observed, then the clinician can proceed to using the absolute risk assessment chart for the primary prevention of CAD. Referring to **Fig. 2**, it is possible to classify patients into the respective management categories, i.e., Categories I to III, according to the magnitude of the absolute risk based on the patient's laboratory findings. Regarding these categories, if at least one of the following conditions (hypo-HDL cholesterolemia, a family history of premature CAD or impaired glucose tolerance (excluding DM)) is observed, the category moves up one level (however, if the patient is classified into Category III, the category does not change). Because the absolute risk changes depending on age and the risk factor level, the absolute risk should be reassessed and the management categories should be reviewed on an annual basis, at minimum.

In the NIPPON DATA80 chart used in the assessment of absolute risk, sex, age, hypertension[13], smoking[14], DM (a random glucose level)[15] and TC[16] are included in the criteria for absolute risk. With respect to DM, because the absolute risk greatly depends on the presence or absence of complications and severe patients tend to be managed at medical institutions and are less likely to participate in community-based cohort studies, this guideline considers DM separately and does not use the DM category (a random glucose level ≥200 mg/dL) included in the original NIPPON DATA80 chart. Although the guidelines used in Western countries define patients with DM as high-risk as secondary prevention patients (patients with a history of CAD), at present there is no clear evidence suggesting that patients with DM correspond to secondary prevention patients in Japan. Therefore, in the same way as patients with noncardiogenic cerebral infarction or PAD, those with DM (excluding impaired glucose tolerance) are assigned to Category III, regardless of other factors, in this guideline. Recently, evidence that CKD is an important risk factor for CVD among Japanese has been reported[17-21], and patients with CKD are also considered as being at high risk according to the SCORE chart. Therefore, these guidelines classify patients with CKD into Category III, regardless of other factors.

As described above, a history of premature CAD in a first-degree relative is not included in the NIPPON DATA80 chart; thus, if this factor exists, the management category should be moved up to the next level. However, age (the age of the family member at the onset of disease) is important when recording the family history. Accordingly, this guideline defines a family history of premature CAD as <55 years of age for men and <65 years of age for women. Note that because patients or their family members may have vague memories, the patient should be carefully monitored if they have a family history of CAD, even if the CAD is not known to be premature.

3. Patient Management Based on the Relative Risk

Some women and young people exhibit a remarkably higher relative risk depending on the number or level of their risk factors compared with people of the same generation or same sex, even when they are classified into Category I. In principle, the lifestyles of such subjects should be modified immediately, even if the absolute risk is low. Because the absolute risk rapidly increases with age, careful monitoring is required. In order to motivate such subjects, relative risk charts are prepared using the NIPPON DATA80 risk chart (**Supplementary Table 1**). We recommend using this chart for patient instruction as needed.

Table 1. Lipid Management Targets for Patients with Different Risk Levels

Therapeutic principle	Management category	Lipid management target (mg/dL)			
		LDL-C	HDL-C	TG	Non HDL-C
Primary prevention Drug therapy should be considered after lifestyle modification	Category I	<160	≥40	<150	<190
	Category II	<140			<170
	Category III	<120			<150
Secondary prevention Drug therapy should be considered, together with lifestyle modification	History of CAD	<100			<130

- For patients at low absolute risk, such as the young, the relative risk charts (Supplementary Table 1) should be used and changes in the absolute risk should be monitored carefully while encouraging the patient to modify their lifestyle.
- These values should be considered as general goals, not mandatory goals.
- A 20%-30% reduction in the level of LDL-C is considered to be a prime target for pharmacological intervention.
- The management target for non HDL-C is the secondary target to be used after a patient with hypertriglyceridemia has achieved the management target for LDL-C. The non HDL-C level should be used if blood is collected after meals or if the TG level is ≥400 mg/dL.
- For patients in any category, the management goals should generally be achieved through lifestyle modification.
- For patients in category I, drug therapy should be considered if the LDL-C level is ≥180 mg/dL.

4. Management Targets for Dyslipidemia

The management targets for dyslipidemia for each category are shown in **Table 1**. For primary prevention, in principle, lifestyle factors should be modified for three to six months in order to assess the effects, then the administration of medications should be considered. However, if the LDL-C level continues to be ≥180 mg/dL in a patient in Category I, medication administration may be considered together with lifestyle modification. The management targets for Category I (low absolute risk) is an LDL-C level <160 mg/dL, that for Category II in an LDL-C level <140 mg/dL and that for Category III (high absolute risk) is an LDL-C level of <120 mg/dL. These targets are the same as the management targets for each category in the previous guidelines; however, the previous guidelines defined the categories simply based on the number of risk factors, while these guidelines define the categories based on the absolute risk. These management targets reflect the typical goals; in some cases, such as patients with very high LDL-C levels, it is difficult to achieve these management goals[22, 23]. A meta-analysis of randomized controlled trials of statins showed that a 20% to 30% reduction in the LDL-C level results in approximately a 30% reduction in the incidence of CAD[22, 23]. Therefore, considering the long-term efficacy and safety, a 20% to 30% reduction in the LDL-C level can be used as the management target. Note that this guideline cannot be applied to patients with familial hypercholesterolemia (FH). It is recommended that FH patients be referred to specialists because treating FH is difficult, and such patients are at very high risk for CAD.

Although we assume that these guidelines will generally be applied to adults <65 years of age, they can also be applied to the young old <75 years of age (the absolute risk should be calculated according to the category of 60 to 69 years of age). For patients <40 years of age, the need for lipid management is left to the discretion of the attending physician; if management is judged to be necessary, the absolute risk should be calculated according to the category of 40 to 49 years of age.

Because a substantial portion of the absolute risk is determined based on sex, age and other factors, achieving the management goals may not result in sufficient decreases in the risk of CAD leading to changes in the category of absolute risk; however, the absolute risk itself will certainly decrease.

In contrast, secondary prevention patients with a history of CAD, who likely require treatment for CVD, should be managed completely separately from primary prevention patients. The management targets for LDL-C for secondary prevention should be established at lower levels than those for primary prevention. Large-scale clinical studies conducted in Western countries have shown that reducing the level of LDL-C, even in subjects with average LDL-C levels, is effective in preventing the recurrence of CAD and the development of strokes and reducing total mortality. Subsequent observational and clinical studies conducted in Japan have shown that the likelihood of recurrence of CAD decreases in association with a decrease in the LDL-C level to 100 mg/dL[24, 25]. The

administration of drug therapy together with lifestyle modification is desirable in secondary prevention patients. In Japan, there is little evidence regarding whether the management target for LDL-C should be set at a lower level than < 100 mg/dL. Therefore, for secondary prevention, these guidelines define the management target as an LDL-C level of < 100 mg/dL, which is the same as that used in the previous guidelines.

Similar to the previous guidelines, it is recommended that the management target for TG and HDL-C be defined as < 150 mg/dL and ≥ 40 mg/dL, respectively, for both primary and secondary prevention patients. Although these guidelines use the LDL-C level as an index for the management goals, the non HDL-C level, which is calculated by subtracting HDL-C from TC, rather than LDL-C, is useful for managing lipid abnormalities in which hypertriglyceridemia is predominant, and the accumulation of such evidence has also occurred in Japan[10, 26-29]. The NCEP-ATP III defines the cutoff for the non HDL-C level as 30 mg/dL higher than the LDL-C level, and the findings in Japan are similar[10, 30, 31]. Accordingly, these guidelines define the management targets for the non HDL-C level to be 30 mg/dL higher than those for the LDL-C level. The management targets for non HDL-C are secondary targets applicable to patients with hypertriglyceridemia who have achieved the management targets for LDL-C. If the TG level is ≥ 400 mg/dL or blood is collected after meals, the non HDL-C target should be used initially.

These guidelines have been used to determine the categories for lipid management targets based on absolute risk. Absolute risk can be also estimated to some extent by counting the number of risk factors and considering the sex and age of the patient. Please refer to the illustration presented (**Supplementary Table 2**). If an absolute risk chart is not readily available, the management targets can be expediently established using this illustration.

Footnotes

This is an English version of the guideline from the Japan Atherosclerosis Society (chapter 4) published in Japanese in June, 2012.

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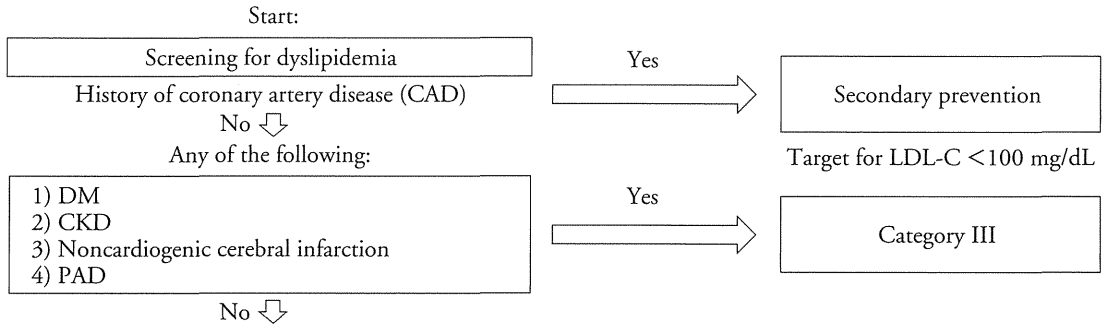
Supplementary Table 1. Relative Risk Charts for Patients with a Low Absolute Risk (based on the risk charts of the NIPPON DATA80)

			Nonsmokers			
Systolic blood pressure						
Second-degree or higher hypertension (≥160 mmHg)	2.2	2.8	3.6	4.6	5.8	7.4
First-degree hypertension (140-159 mmHg)	1.7	2.2	2.8	3.5	4.5	5.7
Normal (≤140 mmHg)	1.0*	1.3	1.6	2.1	2.6	3.4
TC category (mg/dL)	160-179	180-199	200-219	220-239	240-259	260+
			Smokers			
Systolic blood pressure						
Second-degree or higher hypertension (≥160 mmHg)	3.2	4.1	5.2	6.6	8.4	10.7
First-degree hypertension (140-159 mmHg)	2.5	3.1	4.0	5.1	6.5	8.2
Normal (≤140 mmHg)	1.4	1.8	2.3	3.0	3.8	4.8
TC category (mg/dL)	160-179	180-199	200-219	220-239	240-259	260+

*Reference group
To calculate the relative risks used in this table, the representative values in each risk factor category were used. The representative values in each TC category were set at 160, 190, 210, 230, 250 and 270, the representative values in each systolic blood pressure category were set at 110 (normal), 150 (degree I) and 170 (degree II) and the patients were assumed to not have DM. The relative risk for patients who are nonsmokers with a TC level of 160 to 179 and a normal blood pressure was used as the reference value (i.e., relative risk: 1.0). For the sake of convenience, the relative risks were calculated assuming that the patients were men 40 years of age because the values cannot be calculated if the sex and age are not fixed. If the TC level cannot be used, the LDL-C + 80 value should be used.

Supplementary Table 2. Simple Chart Based on Sex, Age and the Number of Risk Factors for Predicting the Absolute Risk of CAD



Sex	Baseline risk: Age	Determined based on the number of risk factors: (1) Hypertension, (2) Smoking, (3) Hypo-HDL cholesterolemia (HDL-C <40 mg/dL), (4) Family history of premature CAD (first-degree male relatives aged <55 years or female relatives aged <65 years), (5) Impaired glucose tolerance (excluding DM)	Absolute risk of CAD (%)	Category*
Men	40-49 years (Also applied to persons aged 30-39 years)	0	0.23	Category I
		1-2	0.32-0.55	Category II
		≥3	0.48-0.83	Category III
	50-59 years	0	0.63	Category II
		1	0.91-1.08	Category II
		≥2	1.55	Category III
	60-69 years (Also applied to persons aged ≤74 years)	0	1.78	Category II
		≥1	2.55-4.31	Category III
Women	40-59 years	0-1	0.10-0.20	Category I
		≥2	0.24	Category II
	60-69 years (Also applied to persons aged ≤74 years)	0-1	0.87-1.83	
		≥2	2.19	Category III

In this simple chart, the serum level of LDL-C was set at 170 mg/dL (TC=250 mg/dL), which exceeded the upper limit of the least strict management target (LDL-C=160 mg/dL). Then, the absolute risk of CAD death was calculated using the NIPPON DATA risk chart as follows:

1) For age, the median (men: 45, 55 and 65 years; women: 50 and 65 years) was used.
2) The number of risk factors was calculated according to the presence or absence of hypertension (presence: SBP=160 mmHg; absence: SBP=120 mmHg) and the presence or absence of smoking, of which the maximum number was 2.
3) In cases in which the number of risk factors was ≥3, the absolute risk was estimated based on the assumption that the third risk factor (other than hypertension and smoking) increases the risk 1.5-fold.

*Depending on the level of additional risk factors, the absolute risk may not always be within the same range as in Fig. 1. Furthermore, because the relative risk for patients in the same sex and age group is also taken into consideration, it should be noted that the category may not always be consistent with the range of the estimated absolute risk determined using the NIPPON DATA risk charts. This chart may be used as a convenient method if the NIPPON DATA risk chart is not readily available.

Management Category Target for the LDL-C level:

Category I <160 mg/dL, Category II <140 mg/dL, Category III <120 mg/dL, Secondary prevention <100 mg/dL

Committee Report 2

Comprehensive Risk Management for the Prevention of Cardiovascular Disease

Executive Summary of the Japan Atherosclerosis Society (JAS) Guidelines for the Diagnosis and Prevention of Atherosclerotic Cardiovascular Diseases in Japan—2012 Version

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Dyslipidemia is one of the most important risk factors for cardiovascular disease (CVD), and managing dyslipidemia is extremely important for preventing CVD. Appropriately managing other major risk factors for which intervention is possible, including smoking, hypertension and diabetes mellitus (DM), is also important for treating dyslipidemia.

A "Comprehensive Risk Management Chart for the Prevention of Cardiovascular Disease" is shown in **Fig. 1**. This chapter describes the procedures for diagnosis, assessment and intervention that are required for the comprehensive management of risk factors to prevent CVD, particularly coronary artery disease (CAD).

Special attention should therefore be paid to cerebrovascular disease as well as CAD in Japan. Correcting dyslipidemia, along with hypertension, smoking and DM, plays an important role in preventing cerebrovascular disease, particularly noncardiogenic cerebral infarction.

1. Screening

Step 1: Screening for the Assessment of Risk Factors for Cardiovascular Disease

- *A thorough assessment of the major risk factors for CVD, all of which must be considered, careful recording of medical/family history and examinations, including blood chemistry tests, are important.*
- *Regarding laboratory tests, fasting venous blood* should be collected, in principle.*

*) *A "fasting state" is defined as fasting for ≥ 10 to 12 hours. Liquids with no calories, such as water and tea, can be consumed.*

The subjects described in this section are primarily those who are initially diagnosed as "requiring further investigation" of risk factors for atherosclerosis. In addition, subjects with a history of CVD, such as CAD, as well as patients who have already been treated or followed up for dyslipidemia, DM or hypertension, should periodically undergo screening tests according to the methods described in this section, and their risk factors and management should be reassessed over time.

The interview items, important physical findings and screening test results required to assess the risk of CVD among individual patients are shown in **Table 1**. For patients with a history of CVD or symptoms or those who are expected to have a higher risk because they are being treated for dyslipidemia, hypertension or DM or because they have remained untreated for a long period, the tests (including diagnostic imaging) shown in **Table 2** should be considered.

If familial hypercholesterolemia (FH) is suspected based on an LDL-C level of ≥180 mg/dL or the patient's medical history, obtaining a soft tissue X-ray film of the Achilles tendon is recommended. Detecting small dense LDL on polyacrylamide gel electrophoresis (PAGE) of plasma lipoproteins and/or measuring the apo B/LDL-C ratio is useful for making a diagnosis of familial combined hyperlipidemia, while detecting broad β, measuring the level of apo E and/or analyzing isoforms of apo E is useful for diagnosing familial type Ⅲ hyperlipidemia. Primary hyperlipidemia, including FH, requires strict management from the early stage of the disease, and screening family members (relatives) of the patient is essential.

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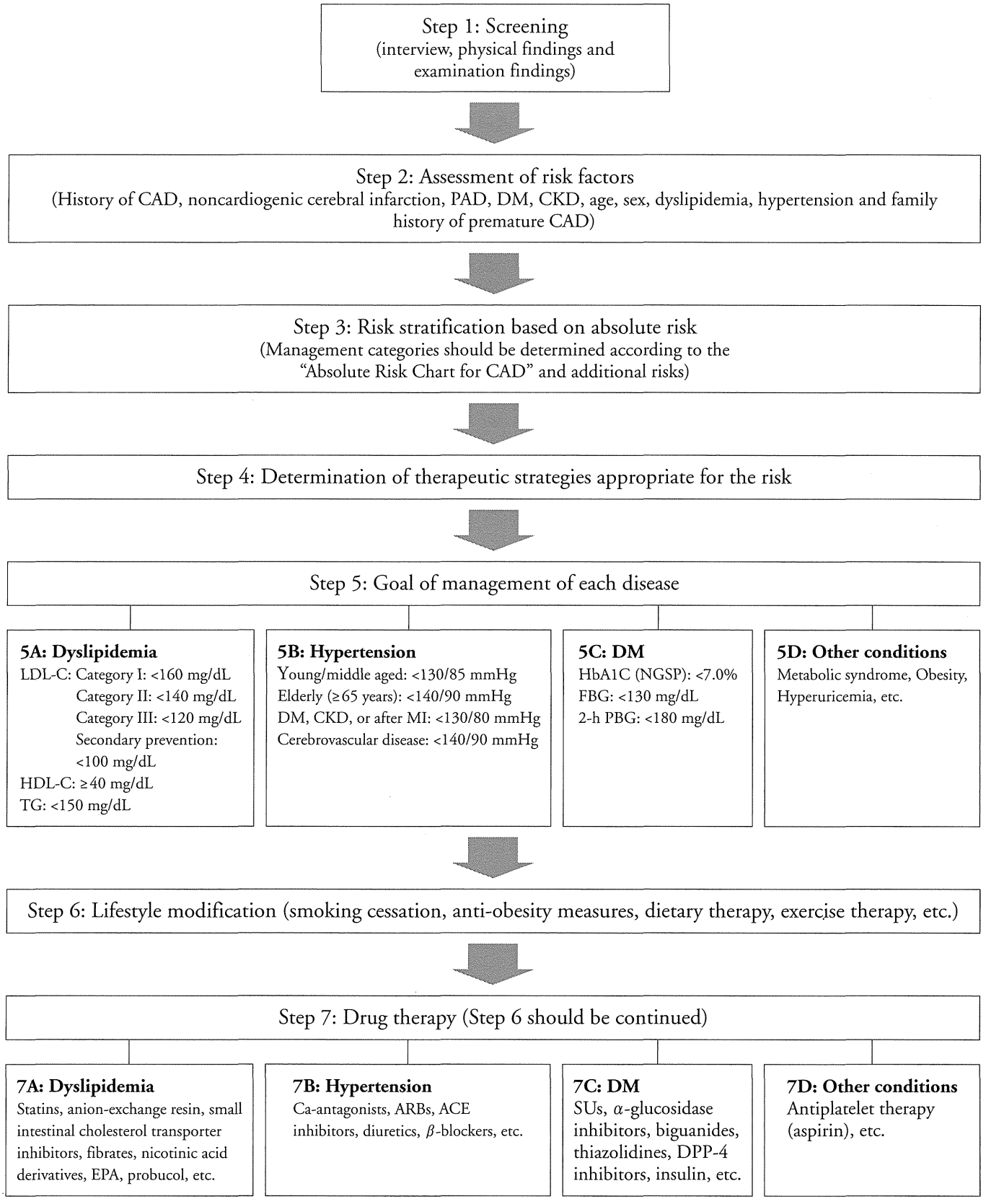

Fig. 1. Comprehensive Risk Management Chart for the Prevention of Cardiovascular Disease.

Table 1. Screening Tests (Basic Tests)

Step 1a: Screening Tests (Basic Tests)	
Medical history	• Type(s), time of onset and time-course of changes of symptoms (anginal pain, intermittent claudication, amaurosis, aphasia, transient quadriplegia, abdominal pain, etc.) • Lifestyle (smoking, drinking, dietary habits, regular exercise, etc.) and regular medication • Medical history (particularly CVD) and weight change • Family history (CVD, lifestyle-related diseases, sudden death, premature death, etc.) and consanguineous marriage or not
Physical findings	• Height, body weight, BMI and waist circumference • Pulse rate and blood pressure[†] (presence or absence of asymmetry) • Arcus corneae, Achilles tendon hypertrophy, cutaneous or tendon xanthoma (extensor surfaces of joints, wrist, buttocks, etc.), goiter, carotid bruits, heart sound, abdomen (pulsatile mass and arterial bruits) and limbs (arterial palpation, edema and motor or sensory disturbance)
Laboratory tests[‡]	• Peripheral blood count and routine urinalysis • Serum lipids (TC, LDL-C,[#] HDL-C and TG) • Blood chemistry tests: AST, ALT, LDH, γ-GTP, ALP, cholinesterase, CK, BUN, CRE, eGFR,[*] Na, K, UA, FBS and HbA1c • Thyroid function tests (TSH, free T3 and free T4)
Physiological tests	• ECG
Imaging	• Chest radiography (cardiothoracic ratio and aortic calcification)

[†] Office blood pressure measurement should follow the "Guidelines for the Management of Hypertension JSH 2009" issued by the Japanese Society of Hypertension.
[‡] Fasting blood should be collected, in principle. Appropriate tests should be performed in each patient.
[#] Calculated with the Friedewald formula: LDL-C = TC − HDL-C − TG/5 (in cases of fasting blood collection and TG < 400 mg/dL).
[*] Men: eGFR (mL/min/1.73m^2) = $194 \times Cre^{-1.094} \times age^{-0.287}$
Women: eGFR (mL/min/1.73m^2) = $194 \times Cre^{-1.094} \times age^{-0.287} \times 0.739$ ("Clinical Practice Guidebook for the Diagnosis and Treatment of Chronic Kidney Disease 2009" issued by the Japanese Society of Nephrology)

Table 2. Screening Tests (Selective/Additional Tests)

Step 1b: Screening Tests (Selective/Additional Tests)	
Diagnostic imaging	• Soft X-ray imaging (Achilles tendon) • Carotid ultrasonography • Echocardiography • Vascular ultrasonography (limbs) • Coronary CT and chest and abdominal CT • Magnetic resonance imaging (MRI) and magnetic resonance (MR) angiography
Physiological tests	• Ankle-brachial index (ABI), brachial-ankle pulse wave velocity (baPWV) and cardio-ankle vascular stiffness index (CAVI)
Laboratory tests	• Agarose gel electrophoresis of lipoproteins and polyacrylamide gel electrophoresis (PAGE) • Apolipoproteins (AI, AII, B, CII, CIII and E) • Small dense LDL, lipoprotein (a) (Lp [a]), remnant lipoprotein cholesterol (remnant-like particle-cholesterol [RLP-C] and remnant lipoprotein cholesterol [RemL-C]), lipoprotein lipase (LPL), hepatic lipase (HL) and lecithin cholesterol acyltransferase (LCAT) • Urine microalbumin • Pituitary/adrenal hormones • Other tests (MDA-LDL, etc.)

Table 3. Major Secondary Hyperlipidemia

- Hypothyroidism
- Nephrotic syndrome
- Renal failure/uremia
- Primary biliary cirrhosis
- Obstructive jaundice
- DM
- Cushing's syndrome
- Obesity
- Alcohol
- Autoimmune diseases (systemic lupus erythematosus, etc.)
- Drug-induced (diuretics, β-blockers, corticosteroids, estrogen, retinoic acid, cyclosporin, etc.)
- Pregnancy

Screening for primary hyperlipidemia is extremely important; therefore, referring the patient to a specialist is desirable if primary hyperlipidemia is suspected.

If secondary hyperlipidemia is suspected (the major causes of this disease are shown in **Table 3**), tests required to make a diagnosis of this condition should be added. In patients with goiters or the elderly, attention should be paid to the possibility of hypothyroidism.

2. Assessment of Risk Factors

Step 2: Risk Factors Requiring Consideration

- *CAD*
- *DM/impaired glucose tolerance*
- *CKD*
- *Noncardiogenic cerebral infarction/PAD*
- *Age and sex*
- *Dyslipidemia*
- *Hypertension*
- *Smoking*
- *Family history of premature CAD in a first-degree relative*

Significant risk factors for absolute risk assessment and risk stratification of cardiovascular disease include a history of CAD, DM/impaired glucose tolerance, chronic kidney disease (CKD), the presence or history of other types of CVD, such as noncardiogenic cerebral infarction or peripheral arterial disease (PAD), age, sex, dyslipidemia, hypertension, smoking and a family history of premature CAD in a first-degree relative (men <55 years of age or women <65 years of age). Regarding a family history of CAD, it is often unclear whether CAD is premature. If a first-degree relative has a history of CAD or sudden death, further consideration is therefore required regarding risk stratification and management.

The diagnostic criteria for hypertension[1], DM[2] and CKD[3] should conform to the clinical practice guidelines released by relevant societies.

3. Risk Stratification Based on Absolute Risk

Step 3: Risk Stratification

- *First, it should be determined whether a patient requires secondary prevention or primary prevention according to the presence or absence of a history of CAD.*
- *For primary prevention, a patient is classified as belonging to category III if he/she has any of the following: (1) DM, (2) CKD, (3) noncardiogenic cerebral infarction or (4) PAD.*
- *If a patient does not have any of the above-mentioned conditions (1) to (4), the absolute risk (10-year risk of CAD death) should be determined based on the patient's age, sex, TC level, systolic blood pressure and smoking status according to the "Absolute Risk Charts for CAD (Primary Prevention)" section. Subsequently, the presence or absence of any of the following additional risks should be assessed to determine each patient's risk management category: (1) hypo-HDL cholesterolemia (HDL-C <40 mg/dL), (2) family history of premature CAD and (3) impaired glucose tolerance (excluding DM).*
- *For low-risk patients, such as young individuals and premenopausal women, the relative risk chart should be applied to predict the future risk.*

Based on the information obtained in Steps 1 and 2, it should first be determined whether a patient requires secondary prevention. If a patient requires primary prevention, the risk management category should be determined according to the presence of additional risk factors, and the "Absolute Risk Charts for CAD (Primary Prevention)" (10-year risk of CAD death) should be used to stratify the risk for each patient (**Fig. 2**).

The absolute risk and management category will vary depending on the age and risk factors of the patient. Therefore, the progression of organ damage due to atherosclerosis and/or each individual risk factor should be periodically and objectively reassessed at least annually (refer to section "1. Screening" in this report) to review the absolute risk and management categories.

Patients with a history of CAD require strict risk management as "secondary prevention patients."

Along with a history of CAD, smoking, a history of DM (including impaired glucose tolerance) or CKD, a history of or complications associated with noncardiogenic cerebral infarction or PAD, metabolic syndrome and the presence of more than one major risk factor places the patient at a higher risk and

Table 4. Patient Conditions Requiring Stricter Management in Secondary Prevention

- Acute coronary syndrome
- Smoking
- DM
- CKD
- Noncardiogenic cerebral infarction/PAD
- Metabolic syndrome
- More than one major risk factor

Table 5. Diabetic Patients at Higher Risk of Developing CAD

- Microangiopathy (retinopathy, nephropathy, etc.)
- Persistent poor glycemic control*
- Smoking
- Noncardiogenic cerebral infarction/PAD
- Metabolic syndrome
- More than one major risk factor

*HbA1c (NGSP) ≥8.4%

requires stricter management (**Table 4**).

For primary prevention, a patient is classified into "category Ⅲ" if the absolute risk is ≥2% or, regardless of the absolute risk, he/she has any of the following: DM (excluding impaired glucose tolerance), CKD, noncardiogenic cerebral infarction or PAD.

If patients with DM have microangiopathy, such as retinopathy or nephropathy, persistent poor glycemic control, such as an HbA1c (NGSP) level of ≥8.4%, a current history of smoking, a history of or current noncardiogenic cerebral infarction or PAD, metabolic syndrome or more than one major risk factor, they are at higher risk of developing CAD or death, and comprehensive strict management of each risk factor, including dyslipidemia, should be performed starting from an early stage (**Table 5**).

Even if the absolute risk is <2%, if a patient has at least one of the following additional risk factors, hypo-HDL cholesterolemia, a family history of premature CAD (a first-degree male relative <55 years of age or a female relative <65 years of age) or impaired glucose tolerance (excluding DM), the risk management category increases to the next higher category.

4. Determination of Appropriate Therapeutic Strategies for Each Risk Category

Step 4: Therapeutic Strategies Appropriate for the Risk

- *Lifestyle modification, including dietary therapy, exercise and smoking cessation, forms the basis for the prevention of CVD. All patients should be provided adequate guidance regarding lifestyle modification.*
- *A management/treatment goal should be determined for each disease, such as dyslipidemia, hypertension and DM, according to each patient's risk.*
- *Even if a patient has a low risk, intervention for or adequate management of each risk factor should be considered early in anticipation of a future increase in risk.*

Lifestyle modification provides the basis for the prevention of cardiovascular disease. Regardless of the patient's risk category, all patients should be provided adequate guidance regarding lifestyle modification.

Although younger patients and some women may have a lower absolute risk in their current state, atherosclerosis can advance asymptomatically, and both CAD and cerebrovascular disease occur more frequently with age. Therefore, a management goal should be determined for each risk factor in anticipation of a future increase in risk. It is desirable to utilize "the relative risk chart" in order to anticipate future risks and provide continuous observation and patient guidance (**Supplementary Table 1** "Relative Risk Charts for Patients with a Low Absolute Risk"). The absolute risk can also be estimated to some extent according to the "Simple Chart Based on Sex, Age and Number of Risk Factors and Predicted Absolute Risk of CAD," which is shown in **Supplementary Table 2**. Lifestyle modification is an effective tool that can be used for intervention, even in low-risk patients.

5. Goals of Management

Step 5A: Management Targets for Dyslipidemia (Fasting Venous Blood)

- *Management of lipids should be performed as described in **Fig. 2** and **Table 6**.*

The LDL-C level should be calculated using the Friedewald formula, in principle. However, if the TG level is high (≥400 mg/dL) or if collecting a fasting blood sample is difficult, the non HDL-C level should be used as the target, instead of the LDL-C level. The targets for LDL-C and non HDL-C are shown in **Table 6**.

The target LDL-C level for each patient should be determined by comprehensively considering the duration of exposure to risk factors, including dyslipidemia (duration of the disease), and the clustering of risks.

These targets can be considered general goals for the long term. The immediate target should be at least a 20% to 30% reduction in the level of LDL-C. In