

吸不全の発生頻度が低く、入院期間も短かったとされ、高齢者ほど上行大動脈の動脈硬化性病変が強く、上行大動脈への手術操作によるアテローム脳塞栓のリスクも軽減する効果も期待できる。

e. 糖尿病

糖尿病例は、硬化変性の著明な冠動脈や縦隔炎など周術期合併症の懸念や遠隔期の心事故の危険因子である。これまでの大規模 study の結果から、遠隔成績の観点からカテーテル治療に対する CABG の優位性が大きいとされ、より外科的な血行再建を選択する根拠となっている。糖尿病には、び慢性に血管径が狭小化した冠動脈枝がしばしば見られる。国立循環器病センターでは、off-pump CABG においても、積極的に狭小冠動脈に対して吻合を行っており、全バイパス吻合箇所のうち、約 1/3 は内径 1.5mm 未満の狭小冠動脈枝である。術後のカテーテル検査では、血管径 1.5mm 以上と以下とでグラフト開存率に差はなく、良好な開存が得られた。

罹患枝数による適応については、本邦での報告も欧米の成績と現時点では明らかな差はなく、ガイドラインに沿った判断が妥当と思われる。CABG の適応には、全身状態の評価が不可欠であるが、手術成績のさらなる向上のためには、個々の症例についてこれらリスク要因を評価し、各患者の特徴に合わせた治療方針の選択が重要と考えられる。

(中嶋博之)

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心筋疾患

心筋症の外科治療

心筋症は、主として肥大型心筋症と拡張型心筋症に分けられる。肥大型心筋症の約 1/4 の症例に左室流出路狭窄を認め、肥大型閉塞性心筋症 (HOCM) として外科的治療の対象となる。本稿では HOCM の外科治療について述べる。

1. HOCM の概念

HOCM は、特発性肥大性大動脈弁下狭窄とほぼ同義語である。流出路圧較差上昇による左室圧上昇と左室肥大が、心筋の壁応力の上昇・酸素消費量増加・相対的虚血を引き起こし、胸痛・動悸・息切れ・失神などの臨床症状を生じる。また HOCM には、しばしば僧帽弁閉鎖不全を合併する。これは、僧帽弁前尖が Venturi 効果により収縮期に流出路に引き込まれる前方運動 (systolic anterior motion : SAM) により起こるとされており、流出路狭窄を増強させる因子となっている。

2. 手術適応

最大限の薬物治療 (β 遮断薬・Ca 拮抗薬・抗不整脈薬) によっても、なお症状のコントロールが困難で、QOL が著しく障害される患者においては外科的治療が検討されるべきである。近年報告された ACC/ESC による HOCM ガイドラインにおいても、手術の適応となるのは、最大限の薬物治療に抵抗性であり、安静時の左室流出路最大圧較差が 50 mmHg 以上、労作時の呼吸困難や胸痛により NYHA 分類のⅢ～Ⅳ度に相当する症例であるとしている。二腔ペーシング (DDD) によるペースメーカー植込み術、あるいは、カテーテルにより左冠動脈の中隔枝に無水アルコールを注入して、流出路中隔の肥大心筋を梗塞に陥らせる経皮的な心筋中隔アブレーション法 (PTSMA) も考慮する必要がある。

外科治療が、生命予後を改善するという報告がないため、手術は重篤な症状

の改善による QOL の向上を目的とすることとなる。また症状が軽度であっても、心肺蘇生を受けた患者は適応となる。

3. 手術術式とその選択

Morrow らが報告した Myotomy-Myectomy 法が確立された手術術式である^{1,2)} 上行大動脈を切開し、大動脈弁を介して肥大した左室側の中隔心筋にアプローチする。約 1 cm 離れた 2 本の平行する中隔基部に垂直な切開を 1.0~1.5 cm の深さに入れて、これを心尖に向けて約 4 cm 進める。中隔に平行した第 3 の切開を加えて、心筋を切除する。この際に刺激伝導系と膜様部中隔を傷つけないように注意を要する。また大動脈弁を損傷しないように心筋切除は弁下の 5 mm から開始する (図 1)。肥大領域によっては、積極的に切除範囲を拡大し乳頭筋基部の部分切除にまで至る extended myectomy の報告もみられる。

僧帽弁置換術 (MVR) も HOCM に対する手術法の一つである。現在では血行動態の優れた機械弁が使用可能となっているが、ワルファリンを永続的に服用しなければならず、機械弁にともなう合併症も起こりうる。適応として、1) 非対称性心室中隔肥大 (atypical septal hypertrophy : ASH) が著明でなく、流出路中隔の壁厚が 18 mm 以下の症例、2) 心基部の中隔が比較的薄く、僧帽弁と接する中隔が肥厚しているもの、肥大が広範囲にわたり存在し、すべての中隔が一様に肥厚している非定型的な中隔の解剖、3) HOCM に対して Morrow 法が施行されたが、圧較差が残存して症状のある再手術症例、4) 器

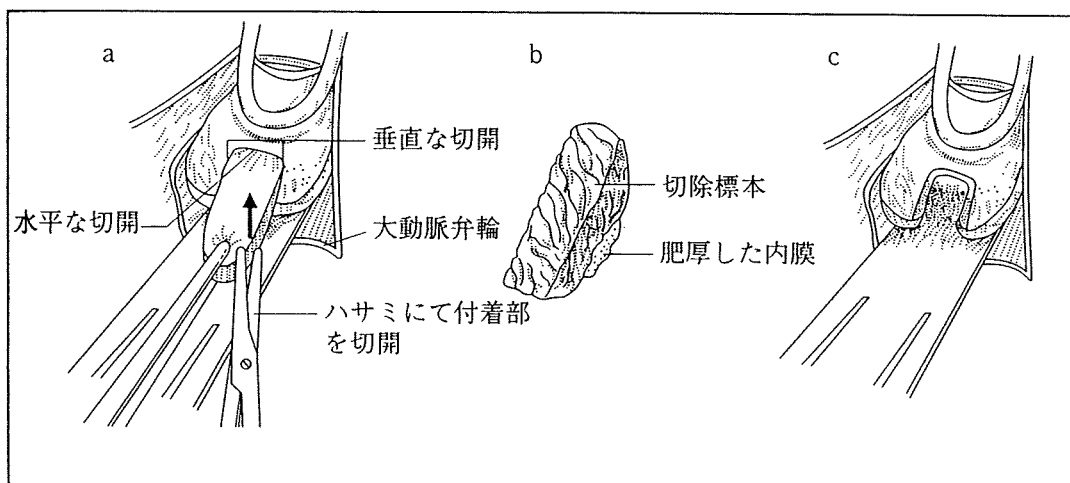


図 1 中隔心筋の標準的な Myectomy 法

(McIntosh CL, et al. Ann Thorac Surg 1989²⁾ より)

質的な僧帽弁異常のある症例が適応とされている。非定型的な中隔の解剖とは、心基部の中隔が比較的薄く、僧帽弁と接する中隔が肥厚しているもの、肥大が広範囲にわたり存在し、すべての中隔が一様に肥厚しているものと考えられる。

MVR は手技的に容易で、術者の技術に左右されない成績が得られ、中隔肥厚の形態によっては HOCM に対する有用な術式と考えられる。MVR では左室拡張能が Morrow 法より改善するとされるが、そのためには僧帽弁は、乳頭筋の基部まで切除し、異常な筋束を切除して、左室内腔を球形に拡大させることが重要である。機械弁は、St. Jude Medical 弁などの左室に突出しないプロフィールの低いものを選択すべきであり、高齢者でも生体弁は不適である。

4. 術後管理

Morrow 法では術直後も、流出路に dynamic な狭窄が残存すると考えて、カテコラミン・ジギタリスの使用を控える。血圧維持の目的であればノルアドレナリンを使用し、原則として血管拡張薬は禁忌である。左室拡張能は低下しており、また内腔も小さいことから、適正な前負荷の管理が重要である。左室肥大のため、術後洞調律の維持は重要であり、頻脈に対しては β 遮断薬が有効である。術前使用している β 遮断薬・Ca 拮抗薬・抗不整脈薬は続けておく。

5. 手術成績及び遠隔成績

HOCM に対する手術及び遠隔成績を表 1 に示す²⁻⁸⁾。Morrow 法単独の場合、手術リスクは 1～3% と低い報告が多い。しかし、高齢者や再心筋切除症例、あるいは他の心臓手術の併施例では高くなる傾向にあるといわれている。Morrow 法の合併症としては、完全房室ブロックや心室中隔穿孔などの重篤なものもあるが、頻度は 1～2% 以下であると報告されている。これに対し、完全左脚ブロックは術式上避けがたい合併症であるが、遠隔期に及ぼす影響は少ないと思われる。

本邦における HOCM に対する外科治療の現況を、2000～2004 年度の日本胸部外科学会 Annual report でみると Morrow 法は後天性心疾患に対する開心術全 168,666 例中 202 例 (0.12%) とまれであり、同時に MVR が 71 例に、MVP が 27 例に行われている。死亡率は 10.4% と欧米の報告に比し高い。

遠隔成績については、左室内圧を収縮期および拡張末期において減少させることから、臨床症状を術後 5 年以上にわたり軽減、消失させることが報告され

表1 閉塞性肥大型心筋症の外科治療成績

報告者	施設	発表年度	症例数	手術術式	手術死亡率	遠隔生存率
McIntosh ²⁾	NIH	1988	156	M法 108例 MVR 48例	全体 3.8% M法 2.7% MVR 6.2%	
McCully ³⁾	Mayo Clinic	1996	65	M法 45例	全体 4.6% M法 0%	5年 92%
Schulte ⁴⁾	Heine University	1999	519		4.4%	10年 88% 20年 72%
Scoendube ⁵⁾	Aachen	2004	82	M法 82例	1.2%	5年 94% 10年 86%
Minami ⁶⁾	Bad Oeynhansen	2002	125	M法 125例	1.6%	5年 90% 10年 83%
Omman ⁷⁾	Mayo Clinic 他	2005	289	M法 289例	0.8%	5年 96% 10年 88%
Smedira ⁸⁾	Cleveland Clinic	2008	323	M法 323例	0%	5年 95% 8年 90%

M法：Morrow法，MVR：僧帽弁置換

ている。5年生存率は90～96%，10年生存率は83～86%と良好であり（表1）臨床症状がNYHAのI，IIとなる症例が70～94%である。

術後フォロー中の年間死亡率は0.6～1.8%と報告されている。術後の血行動態の変化として、左室流出路圧較差はMVRもMorrow法も、ともに平均20mmHg以下に減少するが、左室拡張末期圧はMVRでMorrow法に比べてより低下する。遠隔期の問題として、大動脈弁閉鎖不全がある。大動脈弁輪の小さな症例、中隔の肥厚が基部より心尖にあり、僧帽弁前尖との接触部あるいは、さらに心尖部にあった症例が、大動脈弁閉鎖不全を起こしやすいとされる。

6. ほかの非薬物治療と外科治療の位置づけ

近年外科治療にかわる治療法として、ペーシング治療やPTSMAが積極的に行われるようになってきているが、合併症の危険もあり、また大動脈弁直下に限局したASHによる狭窄以外では理論的に無効である。したがって、広範な流出路狭窄に対しては、今後も外科治療が選択されるべきであると考えられる。

（小林順二郎）

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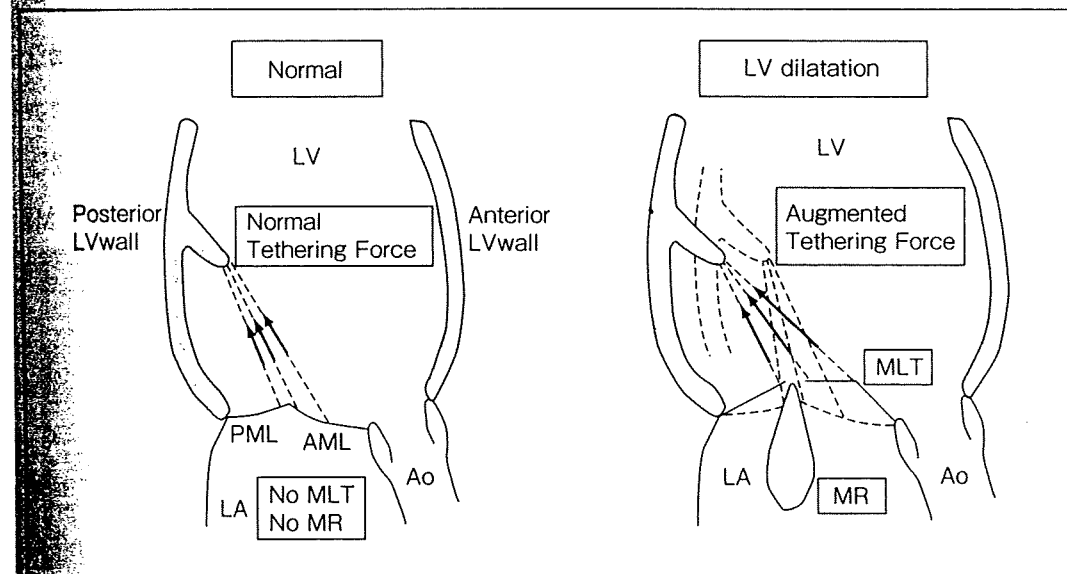
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冠動脈疾患

虚血性僧帽弁閉鎖不全症

1. 虚血性僧帽弁閉鎖不全の重要性と成因

虚血性僧帽弁閉鎖不全 (IMR) は、腱索延長や断裂により生じる器質的 MR と異なり、予後不良の慢性疾患である。IMR は、虚血性心筋症による心不全患者において半数以上に認められ、MR のない患者の予後に比べて2倍から10倍不良である。IMR は、虚血性心疾患の10~20%に認められ、その原因は、心筋梗塞や心室線維化による remodeling のためにおこる弁輪拡大に加えて、左室拡大により乳頭筋が偏位し、腱索が僧帽弁の腱索を左室内に引き込んで、いわゆる tethering を起こし弁尖の接合が不良となることで発生する¹⁾(図1)。いったん発生した IMR により、左室・僧帽弁輪はさらに拡大して、IMR を増



2. 虚血性僧帽弁閉鎖不全の発生機序

心筋梗塞や心室線維化による remodeling のために乳頭筋が偏位し、僧帽弁の腱索を左室内に引き込んで tethering を起こし、弁輪拡大が加わって、両弁尖の接合が不良となることで発生する。

左室, LA: 左房, Ao: 大動脈, AML: 前尖, PML: 後尖, MR: 僧帽弁閉鎖不全, MLT: 僧帽弁 tethering

(Kumanohoso T, et al. J Thorac Cardiovasc Surg 2003¹⁾ より)

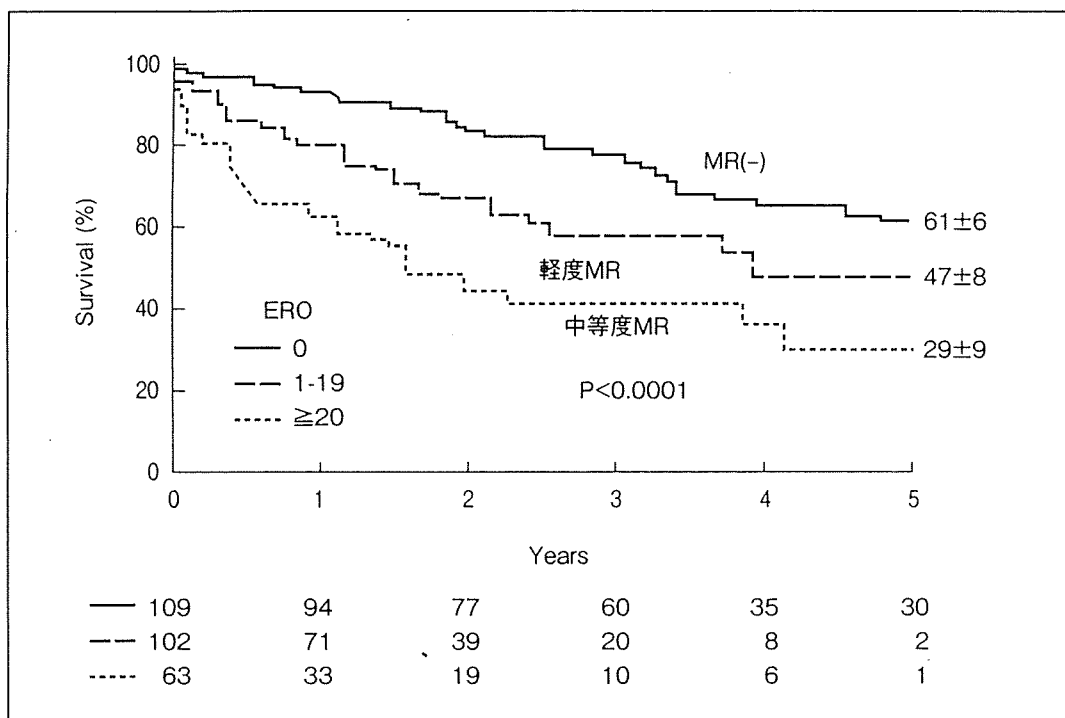


図2 梗塞後 MR の有無と重症度による生命予後

MRの有無とその程度により、生命予後に差がある。逆流孔面積（ERO）が 20mm^2 と器質的MRでは軽度とされる患者においても予後が悪い。

(Grigioni F, et al. Circulation 2001²⁾より)

大させる悪循環をきたす。乳頭筋の虚血による機能不全もIMRに関与するが、その程度は小さいと考えられる。

軽度のIMRは、一般的には、外科治療の対象にはならないと考えられるが、IMRを合併した患者の自然予後において、逆流孔面積が 20mm^2 と器質的MRでは軽度ないし中等度とされる患者においても、MRのない患者に比べて予後が悪いことが問題である²⁾ (図2)。

2. IMRの手術適応と単独CABGの効果

中等度のIMRを有する患者において、冠動脈バイパス術（CABG）と同時に僧帽弁手術（主として弁輪縫縮術）を行うべきか否かに関しては、CABGのみではMRは改善しないとの報告が多い。MRが中等度以下でも心機能不良例では、CABGに加えて積極的に弁輪縫縮術を行うべきであると考えられる³⁾。

3. IMRに対する手術術式

IMRに対する外科治療においても、弁置換術に比べて、弁形成術が優れて

いることが報告されているが⁴⁾、弁形成術ではMRが残存あるいは再発することがあり、すべての症例において弁形成術が可能となるわけではない。

弁形成術としては、一般的には縫合糸による縫縮よりも、小さなサイズの人工弁輪を使用した弁輪縫縮術が長期的に効果があるとされる。弁輪縫縮術は、僧帽弁の前後径を短縮させ、弁尖の接合性を改善させるが、術前に弁尖の tethering が強く、接合部が左室内に偏位しその程度が高度であれば、弁輪縫縮後もMRが残存する。僧帽弁輪から前後尖接合部までの距離を tethering height あるいは coaptation depth と呼び(図3)⁵⁾、正常では4mm以下で、10mm以上は高度 tethering と考えられ、弁輪縫縮術ではIMRが残存するため、前後尖の腱索を温存した弁置換術が望ましいとの考えもある⁶⁾。

僧帽弁尖形成術として、前後尖を縫合して僧帽弁を二つの弁口にする edge-to-edge repair や弁尖の弁腹をパッチで延長するなどにより前後尖の接合を深くする方法が行われている。最近、tetheringにより制限された弁尖の二次腱索を直接切断する方法が注目されているが、いまだ確立された方法ではない⁷⁾。

IMRは、左室自体の疾患であることから、左室あるいは乳頭筋に対して直接手を加える方法として、乳頭筋同士を縫合したり、乳頭筋間の左室や梗塞領域を縫合あるいは切除して乳頭筋を本来の位置に偏位させて tethering を軽減したりする手術が行われている。また、乳頭筋に人工腱索を付けて、僧帽弁輪へ縫合して短縮させ、乳頭筋と僧帽弁輪の距離を縮めて、tethering を軽減する方法も行われている。

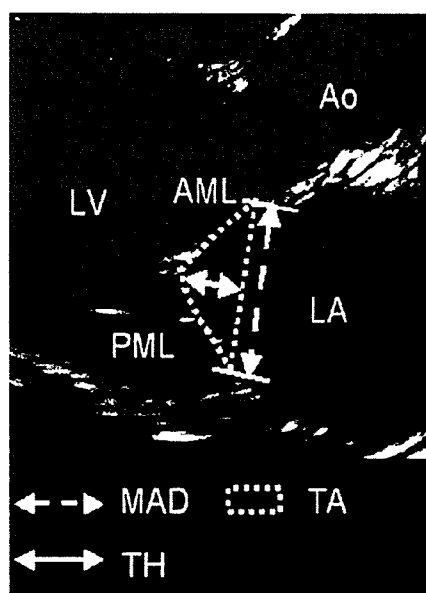


図3 僧帽弁 tethering の重症度評価

僧帽弁輪から、前後尖接合部までの距離を tethering height (TH) と呼び、正常では4mm以下で、10mm以上が高度と考えられる。

MAD: mitral annular diameter,

TA: tethering area (tenting area),

TH: tethering height (normal:<4mm) .

(Daimon M, et al. Circulation 2006⁵⁾ より)

4. IMR に対する手術成績および遠隔成績

日本胸部外科学会のデータベースによると 2002 年から 2006 年までの病院死亡率は, CABG 単独手術の 2~3 倍高い. Cleveland Clinic の遠隔成績でも, 1 年生存率 82%, 5 年生存率 58%と, 単独 CABG 後の成績に比べて不良である⁸⁾.

術後の MR 再発に関しては, 遠隔期の再発は少なからずあるとする報告が多く, 改善あるいは消失したと考えられた IMR が, 術後数か月の早期から 30%以上の症例で 2 度以上となっているとされている^{9,10)}. IMR の再発の危険因子として左室の球状化が指摘されており, IMR が左室の拡大・収縮性・形態といった病態と強く関係することを考慮して, 左室形成術を含めた外科治療戦略が必要となる.

(小林順二郎)

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Improved Long-Term Prognosis of Elderly Women in the Era of Sirolimus-Eluting Stents

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Background: The angiographic characteristics and prognosis in elderly women in relation to the therapeutic impact of sirolimus-eluting stents (SES) need to be clarified.

Methods and Results: Quantitative coronary angiography analysis was performed in 1,374 patients with coronary artery disease: 670 patients were treated with a bare metal stent (BMS) and the remaining 704 were treated with SES. Patients were divided into 4 groups according to gender and age (<75 years M/F, ≥75 years M/F), and major adverse cardiovascular events (MACE) were compared among them. Women ≥75 years old tended to have 3-vessel disease with small vessel size and the incidence of MACE in this group was high in the BMS era. However, in the SES era, this prognosis improved by reducing all-cause death and target vessel revascularization.

Conclusions: Using SES has a therapeutic advantage for the high-risk population of elderly women with angiographically unsuitable lesions for percutaneous coronary intervention. (Circ J 2009; 73: 1219–1227)

Key Words: Coronary artery disease; Elderly women; Sirolimus-eluting stent

Many pivotal trials have demonstrated that the sirolimus-eluting stent (SES) has significantly decreased the rate of restenosis and the need for recurrent intervention compared with bare metal stents (BMS).^{1,2} In the real world, the SES is used for more complex lesions and favorable results have been achieved for percutaneous coronary intervention (PCI), especially a reduction in the need for revascularization.^{3–7}

Coronary artery disease (CAD) is now the main cause of death in women.⁸ The Women's Ischemia Syndrome Evaluation (WISE) Study demonstrated that women, especially older women, are particularly at risk of increased morbidity and mortality.^{9–11} Other studies evaluating the outcome of PCI have also reported higher rates of mortality and major complications in women compared with men.^{12–16} Therefore, it is possible that the poor outcome of PCI in elderly women is related to the development of severe atherosclerotic changes, probably because of clustering of coronary risk factors. However, there is a lack of data regarding the characteristics and prognosis in elderly women with CAD, and it remains unknown whether SES reduces the major adverse cardiovascular events (MACE) and improves the prognosis in this particular population.

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Methods

Patients

From April 2000 through December 2005, 2,597 patients with CAD underwent PCI at the National Cardiovascular Center, Suita, Japan (Figure 1). In Japan, SES became commercially available in August 2004, so in the present study, the BMS era was defined as between April 2000 and July 2004, and the SES era was between August 2004 and December 2005.

Of the total, 1,232 patients were treated in the BMS era and 1,365 patients were treated in the SES era. Patients with a history of coronary artery bypass graft surgery and patients with chronic total occlusion were excluded from the study because of the difficulty of quantitative coronary angiography (QCA) analysis. In addition, patients treated with balloon angioplasty, rotational atherectomy or directional coronary atherectomy alone were also excluded. In the SES era, we excluded patients treated with BMS that had been indicated because of planned surgery, intolerance of ticlopidine or the presence of large vessels >4.0 mm diameter. In the Osaka area, the Committee of Reimbursement for Health Insurance recommends that SES should not be used for patients with acute coronary syndrome, so patients treated with a BMS for acute coronary syndrome in the SES era were also excluded. Thus, the number of patients treated with a BMS in the SES era was 216 and that with SES was 704, and the percentage use of SES in the SES era was 52%. Finally, 670 patients were included in the BMS era and 704 in the SES era. We then subdivided these populations into 4 groups according to gender and age: men <75 years old, men ≥75 years old, women <75 years old, women ≥75 years old.^{17,18} The Ethical Review Board gave approval and the study was conducted according to the ethical principles of the Declaration of Helsinki and Good Clinical Practice guidelines. All subjects gave signed informed consent.

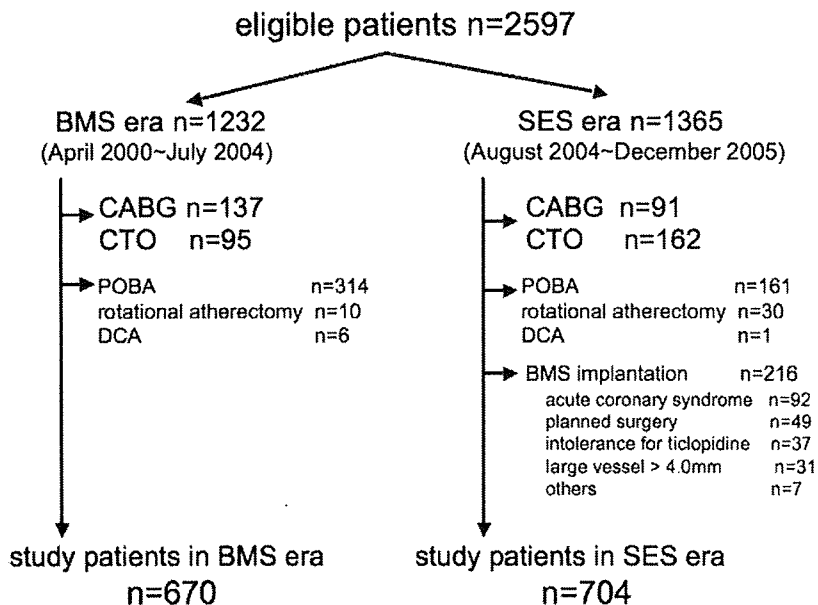


Figure 1. Flow chart of the present study. BMS, bare metal stent; SES, sirolimus-eluting stent; CABG, coronary artery bypass grafting; CTO, chronic total occlusion; POBA, plain old balloon angioplasty; DCA, directional coronary atherectomy.

Coronary Angiography and Quantitative Analysis

Selective coronary angiography was performed in multiple projections after administration of intracoronary nitroglycerin (0.125–0.25 mg). The angiographic characteristics of CAD were evaluated by computer-assisted quantitative analysis (CMS-QCA ver. 4.0, Medis, Leiden, The Netherlands), as reported previously.¹⁹ Briefly, we measured the diameter of the middle section in each major coronary segment (segments 1–3 of the right coronary artery, segments 6–8 of the left anterior descending artery, and segments 11 and 13 of the left circumflex artery) in order to calculate the average vessel diameter (AVD) for each patient. We defined segments with an irregular edge that narrowed to a diameter ≤ 1.5 mm as diseased lesions and calculated the average lesion length (ALL). In a previous study, lumen diameter < 1.5 mm was related with sufficient sensitivity and specificity to fractional flow reserve < 0.75 , a level highly inducive to causing myocardial ischemia.²⁰ The far distal portions of segments 8 and 13 that had a smooth and regular edge were not included in the ALL measurements. The QCA data were assessed by an experienced cardiologist (I.M.) who was unaware of the patients' status.

PCI Procedure

All procedural decisions, including device selection and adjunctive pharmacotherapy, were made at the discretion of the individual PCI operator. Intravenous heparin (5,000 IU) and intracoronary nitroglycerin (0.5 mg) were administered before PCI. After stent implantation, angiographic optimization was performed by high-pressure dilatation to achieve an acceptable angiographic result. Intravascular ultrasound was used according to the operator's decision. Procedural success was defined as residual stenosis $< 20\%$ without major complications. All patients received 324 mg/day of aspirin for at least 24 h before the procedure. Dual antiplatelet therapy (aspirin 300 mg and ticlopidine 200 mg) was given to all patients treated with BMS for 2 weeks and in those treated with SES for at 3–12 months. For the assessment of restenosis, exercise test or stress scintigraphy was routinely performed at 6–8 months after PCI. If myocardial ischemia was noted in this initial non-invasive testing, follow-up

coronary angiography was performed.

The following types of BMS were implanted: Multi-Link plus (Guidant, Santa Clara, CA, USA) 263 patients (39%); BX-Velocity (Cordis, Johnson & Johnson, Miami Lakes, FL, USA) 170 patients (25%); NIR (Medinol, Jerusalem, Israel; and Scimed, Boston Scientific, Maple Grove, MN, USA) 95 patients (14%); Multi-Link Penta (Guidant) 75 patients (10%); Duraflex (Avantec Vascular) 50 patients (7%); S670 (Medtronic, Shoreview, MN, USA) 17 patients (3%). In the SES era, Cypher (Cordis, Johnson & Johnson) was the only type of drug-eluting stent used.

Clinical Parameters and Follow-up

All the patients underwent assessment of coronary risk factors, angiography, and laboratory analyses including fasting glucose, hemoglobin A_{1c} (HbA_{1c}), total cholesterol (TC), triglycerides (TG), high-density lipoprotein-cholesterol (HDL-C), low-density lipoprotein-cholesterol (LDL-C) and creatinine levels. Body mass index (BMI) was calculated as weight (kg)/height (m)².

Follow-up information was obtained at the outpatient's clinic or by a review of the medical records. Follow-up was completed for all patients (100%). The primary endpoint was defined as all-cause mortality, and the secondary endpoint was the occurrence of the MACE, which included all-cause death, non-fatal myocardial infarction (MI), heart failure (HF) and target lesion revascularization (TLR) related to PCI procedure and occurring in the follow-up period.

HF was diagnosed if a patient showed signs of exertional dyspnea, orthopnea, rales in more than one-third of the lung fields, elevated jugular venous pressure or pulmonary congestion on chest X-ray related to cardiac dysfunction. MI was defined as 2 or more of the following: (1) typical chest pain > 20 min duration not relieved by nitroglycerin; (2) serial ECG recordings showing changes from baseline in ST-T and/or Q-waves in 2 or more contiguous leads; (3) elevation of serum creatine kinase > 2 -fold of normal. TLR was defined as repeat PCI or coronary bypass surgery, performed because of restenosis or a new stenotic lesion in the target vessel. Definite and possible stent thrombosis were defined on the basis of the Academic Research Consortium

Table 1. Patient Characteristics in the BMS Era

	Men		Women	
	<75 years (n=406)	≥75 years (n=132)	<75 years (n=65)	≥75 years (n=67)
Age (years)	64±8 [‡]	80±4	66±5	80±5 [‡]
BMI (kg/m ²)	23.4±2.7	23.2±2.8	23.7±3.7	23.7±3.7
UAP, n (%)	248 (61)	86 (65)	47 (72)	52 (77)
Coronary risk factors				
Hypertension, n (%)	288 (71) [‡]	110 (83)	50 (77)	58 (87)
Hypercholesterolemia, n (%)	292 (72)	82 (62)	50 (77)	62 (93) [#]
Diabetes mellitus, n (%)	205 (51)	56 (42)	32 (49)	42 (63) [#]
Smoking, n (%)	182 (45) ^{‡,¶}	41 (31)	17 (26)	4 (6) ^{#,‡}
Family history of CAD, n (%)	80 (20)	40 (31)	16 (24)	21 (31)
Serum creatinine ≥177 μmol/L, n (%)	26 (6)	29 (22)	9 (14)	8 (12) [#]
Peripheral vascular disease, n (%)	32 (8) [‡]	31 (24)	4 (6)	13 (19) [‡]
Stroke, n (%)	62 (15) [‡]	41 (31)	14 (22)	10 (15) [#]
Previous MI, n (%)	145 (36)	51 (39)	23 (35)	33 (49) ^{#,‡}
Previous HF, n (%)	53 (13)	20 (15)	8 (12)	11 (16)
No. of diseased vessels				
1	224 (55) [‡]	56 (42)	39 (60)	16 (24) ^{#,‡}
2	140 (35)	59 (45)	21 (32)	27 (40)
3	42 (10)	17 (13)	5 (8)	23 (36) ^{#,‡}
LVEF (%)	52±10	52±12	49±10	50±9
LVEF <40%, n (%)	81 (20)	21 (16)	12 (18)	11 (17)
Glycemic status				
Fasting glucose (mmol/L)	106±26	100±25	111±38	114±36 [#]
HbA _{1c} (%)	6.1±1.2	5.9±0.9	6.3±1.3	6.3±1.2 [#]
Lipid profile				
Total cholesterol (mmol/L)	189±35 [¶]	184±27	210±40	202±35 [#]
Triglycerides (mmol/L)	135±79 [‡]	109±57	123±67	107±40
HDL-cholesterol (mmol/L)	40±10 [¶]	42±13	49±12	46±13 [#]
LDL-cholesterol (mmol/L)	122±32	119±25	138±38	134±27 [#]
Hb (g/dl)	14.3±1.7 ^{¶,¶}	12.9±1.6	12.1±1.5	12.0±1.3 [#]
Medical treatment				
Aspirin, n (%)	367 (90)	110 (83)	64 (99)	56 (84) [‡]
β-blocker, n (%)	255 (63)	84 (64)	40 (62)	45 (67)
Calcium-channel blocker, n (%)	276 (68)	95 (72)	48 (74)	53 (79)
ACEI, n (%)	107 (26)	35 (27)	10 (15)	18 (26)
ARB, n (%)	52 (13)	25 (19)	14 (21)	14 (21)
Statin, n (%)	195 (48)	55 (42)	38 (59)	30 (45)
Average BMS diameter (mm)	3.2±0.3	3.1±0.3	3.0±0.3	2.9±0.3
Average BMS length (mm)	16.4±4.4	16.5±3.5	15.9±2.7	16.2±2.4
Complete revascularization in patients with multivessel disease, n (%)	264 (65)	84 (64)	33 (51)	35 (52) ^{#,‡}

*P<0.05 vs men ≥75 years, †P<0.05 vs women <75 years, ‡ vs men ≥75 years, ¶ vs men <75 years, † vs men <75 years.

BMS, bare metal stent; BMI, body mass index; UAP, unstable angina pectoris; CAD, coronary artery disease; MI, myocardial infarction; HF, heart failure; LVEF, left ventricular ejection fraction; Hb, hemoglobin; HDL, high-density lipoprotein; LDL, low-density lipoprotein; ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blocker.

stent thrombosis classification.²¹ Complete revascularization (CR) on QCA was defined as a residual stenosis <20% in the 3 major coronary arteries and their major branches (branch diameter >2 mm).

The clinical and angiographic characteristics and the incidence of MACE were compared among the 4 groups in the BMS and SES eras using the chi-square test (or Fisher's exact test) for categorical data, or analysis of variance (ANOVA) was performed for continuous data. For univariate analysis, the following clinical variables and risk factors were regarded as covariates: age, gender, glycemic status (fasting glucose and HbA_{1c} level), lipid profiles (TC, TG, HDL-C, LDL-C), creatinine level, BMI and the use of cardiovascular medications. On the basis of the results of univariate analysis, multivariate logistic regression analysis was performed to investigate the independent predictors of small AVD (<3.0 mm) and long ALL (>20 mm). Event-free survival was estimated using the Kaplan-Meier method, and differences were assessed using the log-rank test. A P value <0.05 was considered to be statistically significant. All

analyses were performed using Stat-View software, version 5.0 (SAS Institute Inc, Cary, NC, USA).

Results

Baseline Characteristics in the BMS Era

Table 1 shows the baseline characteristics of the 4 groups in the BMS era: 406 men <75 years old, 132 men ≥75 years old, 65 women <75 years old, and 67 women ≥75 years old. Compared with men ≥75 years old, women ≥75 years old had higher levels of fasting blood glucose, HbA_{1c}, TC and LDL-C, lower levels of hemoglobin, and higher prevalence of smoking. A higher prevalence of peripheral vascular disease was seen in women ≥75 years old compared with women <75 years old. Furthermore, among the 4 groups, the prevalence of previous MI and 3-vessel disease was the highest in women ≥75 years old. There were no significant differences in the medical treatment of groups except for aspirin use.

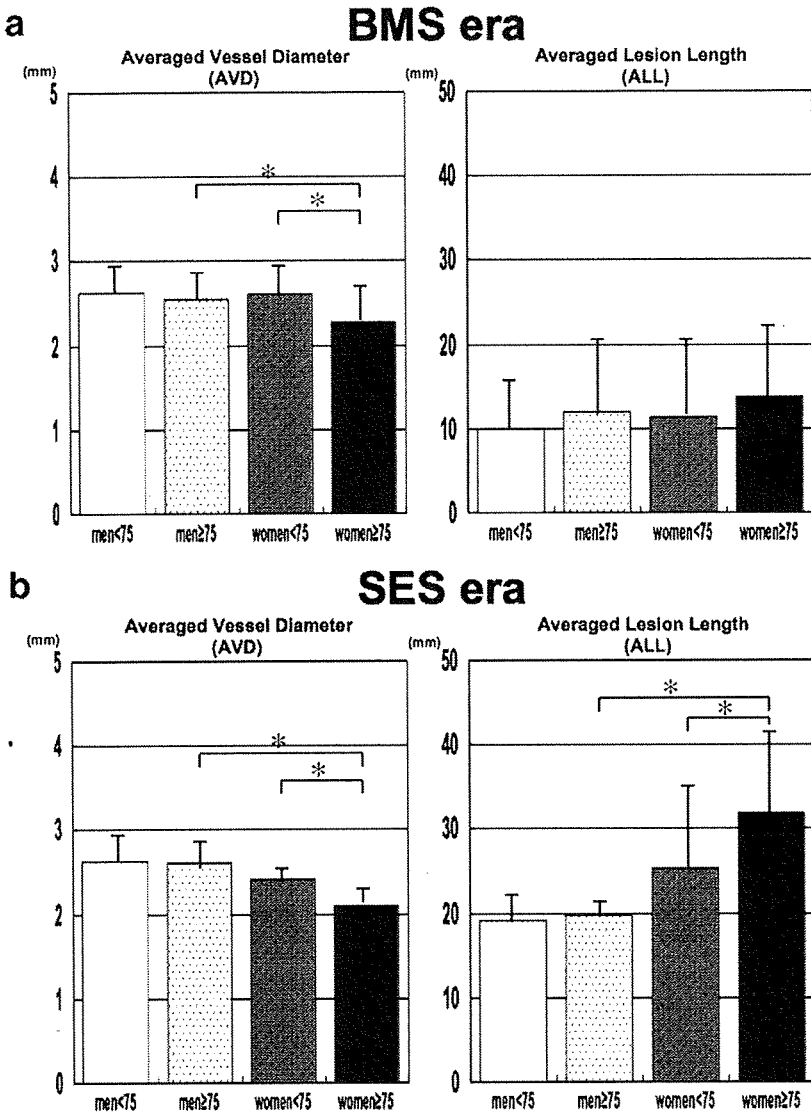


Figure 2. Comparison of quantitative coronary angiography results of AVD, ALL among the 4 groups in (a) bare metal stent (BMS) era and (b) sirolimus-eluting stent (SES) era. *P<0.05.

Table 2. Univariate and Multivariate Analyses of Data in the BMS Era

	Univariate analysis		Multivariate analysis	
	OR (95%CI)	P value	OR (95%CI)	P value
Predictors of small vessel diameter (AVD <3.0mm)				
Fasting glucose	0.996 (0.993–0.999)	0.0025	0.996 (0.994–0.999)	0.0155
Total cholesterol	1.002 (0.998–1.006)	0.4309		
Triglycerides	0.997 (0.996–0.999)	0.0002	0.998 (0.996–0.999)	0.0016
HDL-cholesterol	1.003 (0.992–1.015)	0.5773		
LDL-cholesterol	1.004 (1.000–1.009)	0.0755		
HbA _{1c}	1.002 (0.949–1.058)	0.9369		
Creatinine >177 μmol/L	0.937 (0.500–1.756)	0.8399		
Hypertension	0.819 (0.577–1.164)	0.2661		
Women ≥75 years old	28.566 (3.965–205.803)	0.0009	26.523 (3.676–191.357)	0.0011
Predictors of long lesion length (ALL >20mm)				
Fasting glucose	1.003 (1.001–1.006)	0.0124	1.003 (0.999–1.007)	0.0954
Total cholesterol	1.000 (0.997–1.004)	0.9786		
Triglycerides	1.001 (1.000–1.003)	0.0275	1.002 (1.000–1.004)	0.1088
HDL-cholesterol	0.987 (0.977–0.997)	0.0127	0.981 (0.966–0.996)	0.0135
LDL-cholesterol	0.999 (0.995–1.003)	0.5826		
HbA _{1c}	1.011 (0.970–1.054)	0.6035		
Creatinine >177 μmol/L	1.257 (0.743–2.125)	0.3938		
Hypertension	1.363 (1.013–1.834)	0.0409	1.080 (0.723–1.613)	0.7055
Women ≥75 years old	3.235 (2.144–4.881)	<0.0001	4.564 (2.533–8.223)	<0.0001

OR, odds ratio; CI, confidence interval; AVD, average vessel diameter; ALL, average lesion length. Other abbreviations see in Table 1.

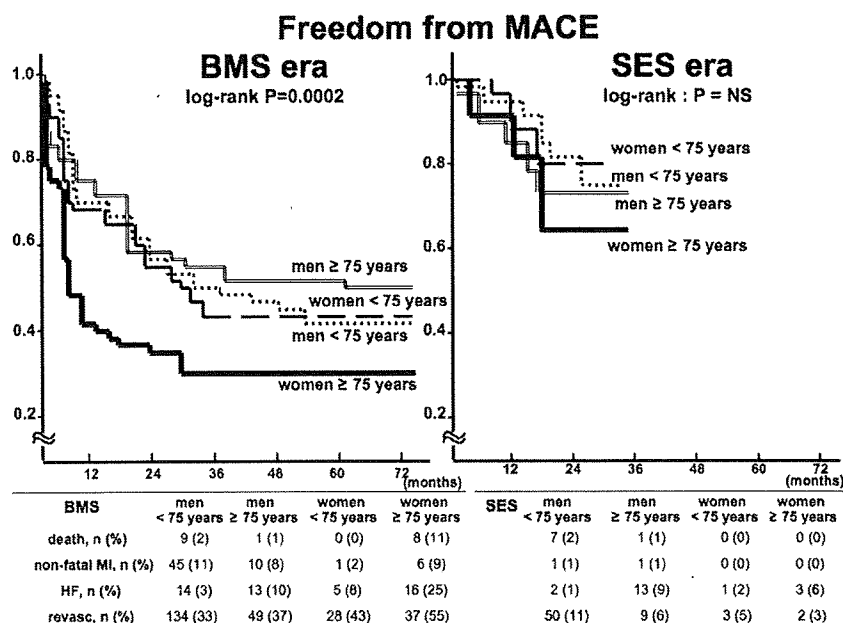


Figure 3. Kaplan-Meier curves of freedom from major adverse cardiovascular events (MACE) in bare metal stent (BMS, Left) and sirolimus-eluting stent (SES, Right) era. MACE includes death, non-fatal myocardial infarction (MI), heart failure (HF) and target lesion revascularization (revasc).

Table 3. Patient Characteristics in the SES Era

	Men		Women	
	<75 years old (n=450)	≥75 years old (n=145)	<75 years (n=57)	≥75 years (n=52)
Age (years)	63±8 [¶]	79±4	68±7	80±5 [†]
BMI (kg/m ²)	24.5±3.0	23.9±3.5	24.0±2.9	22.9±4.2
UAP, n (%)	54 (12) [¶]	35 (24)	16 (28)	20 (39) [#]
Coronary risk factors				
Hypertension, n (%)	352 (78)	113 (78)	49 (85)	45 (88)
Hypercholesterolemia, n (%)	278 (62) [¶]	77 (53)	46 (79)	43 (82) [#]
Diabetes mellitus, n (%)	249 (55)	88 (61)	28 (48)	28 (55)
Smoking, n (%)	180 (40) [¶]	51 (35)	17 (30)	7 (14) ^{#,†}
Family history of CAD, n (%)	154 (34) [‡]	27 (19)	24 (41)	7 (14) [†]
Serum creatinine ≥177 μmol/L, n (%)	21 (5)	5 (3)	2 (3)	5 (10) [#]
Peripheral vascular disease, n (%)	38 (8) [‡]	29 (20)	7 (12)	3 (6) [#]
Stroke, n (%)	40 (9) [‡]	25 (17)	10 (17)	6 (12)
Previous MI, n (%)	222 (49)	73 (50)	29 (49)	24 (48)
Previous HF, n (%)	72 (16)	25 (17)	9 (15)	9 (18)
No. of diseased vessels				
1	215 (48) [‡]	52 (36)	19 (33)	11 (22)
2	158 (35) [¶]	46 (32)	24 (42)	21 (40)
3	70 (17) [‡]	47 (32)	14 (25)	20 (38) [#]
LVEF (%)	48±9	46±11	48±10	50±10
LVEF <40%, n (%)	81 (18)	38 (26)	13 (22)	9 (18)
Glycemic status				
Fasting glucose (mmol/L)	128±47	126±45	118±41	123±53
HbA _{1c} (%)	6.6±4.4	6.1±1.0	6.1±1.0	6.3±1.2
Lipid profile				
Total cholesterol (mmol/L)	182±32 ^{‡,¶}	173±26	202±49	184±30 ^{#,†}
Triglycerides (mmol/L)	166±109	149±84	150±95	143±51
HDL-cholesterol (mmol/L)	41±10 [¶]	40±11	51±14	40±15 [†]
LDL-cholesterol (mmol/L)	110±28 ^{‡,¶}	104±23	122±46	117±27 [#]
Hb (g/dl)	13.8±1.8 ^{‡,¶}	13.1±1.3	12.4±1.5	11.3±1.5 ^{#,†}
Medical treatment				
Aspirin, n (%)	367 (90)	110 (83)	64 (99)	56 (84) [†]
β-blocker, n (%)	340 (76)	102 (70)	43 (74)	40 (78)
Calcium-channel blocker, n (%)	207 (46)	74 (51)	30 (52)	37 (73) ^{#,†}
ACEI, n (%)	121 (27)	38 (26)	9 (16)	11 (22)
ARB, n (%)	129 (29)	50 (35)	18 (31)	29 (55) ^{#,†}
Statin, n (%)	272 (60) ^{‡,¶}	72 (50)	46 (79)	26 (51)
Average SES diameter (mm)	2.9±0.3	2.9±0.3	2.9±0.3	2.8±0.3
Average SES length (mm)	21.6±4.3	21.0±3.9	25.9±3.2	30.8±3.6 [#]
Complete revascularization in patients with multivessel disease, n (%)	351 (77)	109 (75)	38 (71)	34 (72)

[#]P<0.05 vs men ≥75 years, [†]P<0.05 vs women <75 years, [‡] vs men ≥75 years, [¶] vs women <75 years. SES, sirolimus-eluting stent. Other abbreviations see in Table 1.

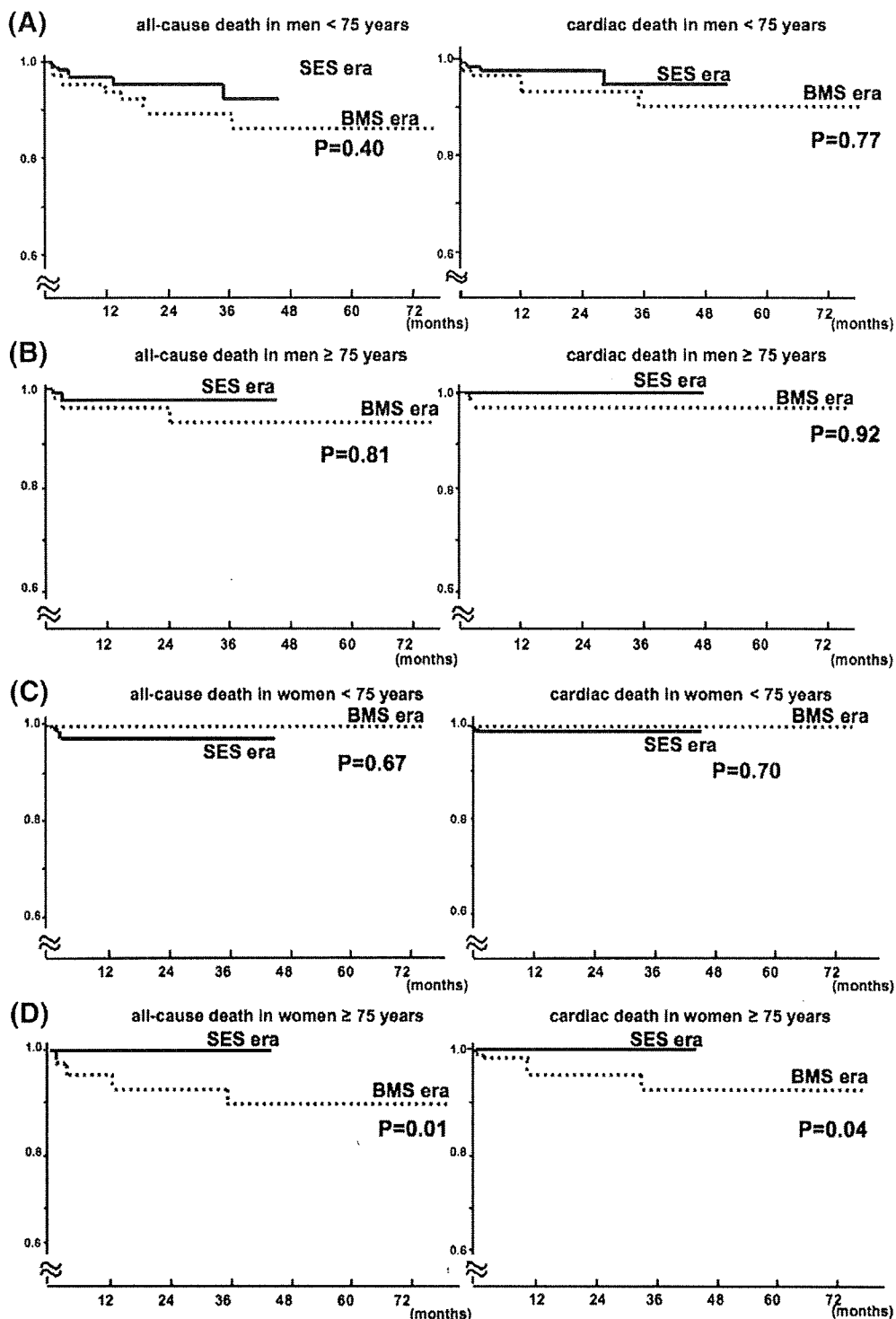


Figure 4. Kaplan-Meier curves of freedom from all-cause death and cardiac death in bare metal stent (BMS) era and sirolimus-eluting stent (SES) era. (A) men <75 years, (B) men ≥75 years, (C) women <75 years, (D) women ≥75 years.

QCA in the BMS Era

The results of QCA in the BMS era are summarized in **Figure 2a**. The AVD in women ≥75 years old was statistically significantly smaller than that in men ≥75 years old or <75 years old. ALL in women ≥75 years old was 13.8 ± 10.1 mm, which was not statistically significantly different from the other groups.

To investigate the independent predictors of small AVD (<3.0 mm) and long ALL (>20 mm), we performed univariate and multivariate logistic regression analysis (**Table 2**). Univariate analysis showed that hypercholesterolemia, TG, fasting blood glucose and women ≥75 years old were significant predictors for small AVD. By multivariate analysis, all of these variables were independent predictors of small

AVD. Regarding long ALL, TG, HDL-C, fasting blood glucose, hypertension and women ≥ 75 years old were significant predictors by univariate analysis. Multivariate analysis revealed that HDL-C and women ≥ 75 years old were strong independent predictors for long ALL.

MACE in the BMS Era

The event-free survival curve of the BMS era is shown in **Figure 3**. During the follow-up period of 75 months (median), women ≥ 75 years old had the highest incidence of cardiovascular events among the 4 groups. In particular, the incidence of TLR was high (55%), and the occurrence of death and HF was 11% and 25%, respectively, which were significantly higher in women ≥ 75 years old compared with other 3 groups. The prevalence of restenosis was 43% in elderly women with MACE.

Baseline Characteristics in the SES Era

Baseline characteristics of patients in the SES era are summarized in **Table 3**. The 4 groups consisted of 450 men < 75 years old, 145 men ≥ 75 years old, 57 women < 75 years old, and 52 women ≥ 75 years old. Overall, the patients' demographics were similar in the BMS era and the SES era, except for the prevalence of unstable angina pectoris and previous MI. When comparing elderly women in the BMS era and those in the SES era, their characteristics were similar except for the prevalence of unstable angina pectoris and peripheral vascular disease and the use of angiotensin-receptor blockers.

QCA in the SES Era

Figure 2b shows the results of QCA in the SES era. Although AVD was comparable between the 2 eras, ALL in the SES era (31.9 ± 10.2 mm) was approximately 3-fold longer than that in the BMS era. In the SES era, smaller AVD and longer ALL were observed in women ≥ 75 years old, compared with women < 75 years old and men ≥ 75 years old.

MACE in the SES Era

During the follow-up period of 34 months (median) in the SES era, there were no significant differences in MACE among the 4 groups (**Figure 3**). The incidence of TLR was low (3%) in women ≥ 75 years old.

As shown in **Figure 4**, the incidence of all-cause death and cardiac death in women ≥ 75 years old in the SES era was significantly lower than that of the BMS era. In detail, 9 patients died from: sepsis (n=1), cerebral bleeding (n=3), HF (n=3) and sudden death (n=2) in the BMS era, whereas no patients died in the SES era.

To clarify the role of CR, we compared the occurrence of MACE among the 4 groups, elderly women with and without CR in the BMS era (n=35 and 32, respectively) and those with and without CR in the SES era (n=34 and 18, respectively). As shown in **Figure 5**, there were no significant differences between patients with and without CR in the BMS era. In the SES era, patients with CR had a lower occurrence of MACE than patients without CR.

Discussion

In the present study, elderly women (women ≥ 75 years old) who underwent PCI had angiographically smaller and longer coronary atherosclerotic lesions than men and women aged < 75 years old. Although there was a high prevalence

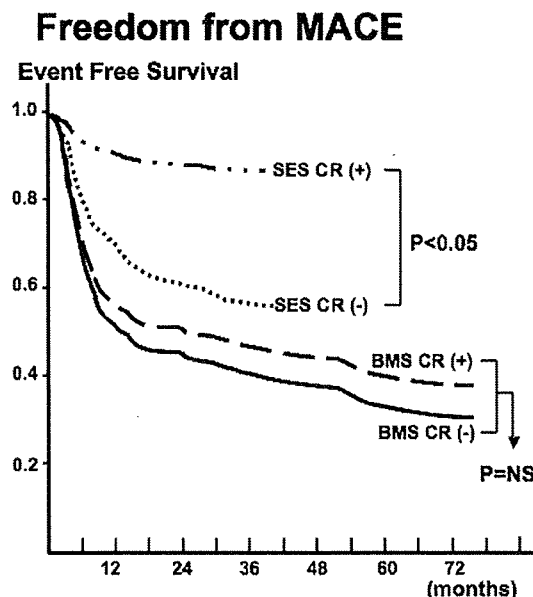


Figure 5. Kaplan-Meier curves of freedom from major adverse cardiovascular events (MACE) among women ≥ 75 years with and without complete revascularization (CR) in the bare metal stent (BMS) era (n=35 and 32, respectively) and those with and without CR in the sirolimus-eluting stent (SES) era (n=34 and 18, respectively).

of MACE in this particular population in the BMS era, the use of SES in the current era reduced the occurrence of MACE, primarily by reducing all-cause death and TLR.

Morphological Characteristics of CAD in Elderly Women

Sharaf et al using severity scores to describe the advanced and diffuse atherosclerotic changes in 323 women with CAD²² This score assesses the severity of a diseased lesion by its percentage diameter stenosis; however, that method can underestimate the severity of stenosis, particularly in patients with diffuse coronary narrowing, because it is difficult to identify a normal reference segment on angiography. Therefore, we used QCA to assess the whole coronary tree in a large population (n=1,374). As reported previously, QCA is more accurate, objective and reproducible than manual caliper measurements.^{19,23,24} The parameters we used (ie, AVD and ALL) enabled us to evaluate in detail the absolute values for the entire coronary tree, and our QCA analysis revealed that severe atherosclerotic changes had developed in women ≥ 75 years old (**Figures 2, 4**). In addition, the morphological characteristics of CAD were more severe in the SES era than in the BMS era, because the ALL was > 30 mm on average. We previously reported that morphological changes such as small vessels and diffuse narrowing developed in patients with diabetes mellitus or impaired glucose tolerance.¹⁹ As shown in **Table 1**, women ≥ 75 years old had higher fasting glucose and HbA_{1c} levels than similar aged men. Additionally, glucose metabolism, represented by the fasting glucose level, was a significant determinant for small vessels and diffuse coronary narrowing (**Table 2**). Therefore, elderly women (≥ 75 years old) may have a high prevalence of abnormal glucose tolerance than other patients and this metabolic abnormality seems to be an important factor in the development of severe coronary atherosclerotic changes (**Table 2**).

Improved Prognosis of Elderly Women With CAD in the SES Era

In the BMS population of the present study there was a high incidence of MACE in women ≥ 75 years old. Small vessel size and long lesion length were associated with development of restenosis in the BMS era^{25,26} and we found a strikingly high rate of TLR in women ≥ 75 years old in the present study. Because of the higher risk of developing restenosis, the benefit of CR on long-term prognosis might be traded off, as shown in **Figure 5**. The incidence of death and HF in women ≥ 75 years old were also higher than in other groups.

Many recent studies have demonstrated that SES strongly inhibit neointimal hyperplasia and reduce the need for TLR.^{1,2} SES can be used in complex lesions that seemed unsuitable for PCI in the BMS era.³⁻⁷ Considering the greater efficacy of SES and their increased use in lesions that were unsuitable for PCI in women ≥ 75 years old (eg, ALL > 30 mm on average), it can be proposed that the improved clinical outcomes, including all-cause and cardiac death, might be related to a reduction in ischemic events, which has resulted from the low restenosis rates associated with the use of SES. In addition, the reduction in ischemic events may prevent HF and arrhythmias.

Study Limitations

There are some biases and differences in patient selection for this retrospective study; for example, the difference between the BMS and SES eras for lesion length in elderly women may reflect a change in the indication for PCI. However, the general policy and procedure of PCI performed at our institution did not change from 1 era to the next. Moreover, the increased usage of angiotensin-converting enzyme inhibitors/angiotensin II receptor blockers and statins should be taken into consideration as modifiers of the results. Although the prevalence of unstable angina differed between the BMS and SES era, an unstable clinical presentation did not exert a significant impact on outcome as reported in previous studies.²⁷⁻²⁹

Conclusions

Elderly women with CAD have particular characteristics of coronary atherosclerosis, such as small vessels and diffuse coronary narrowing, which could be related to abnormal glucose tolerance and/or dyslipidemia. In the BMS era, this particular patient group had the worst long-term prognosis compared with men or women < 75 years old. However, in the SES era, this difference in prognosis has been alleviated, mainly because of a reduction in all-cause death and TLR.

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冠血行再建術

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心臓血管外科手術において、冠動脈バイパス術 (coronary artery bypass grafting : CABG) は症例数が最も多く、また虚血性心疾患に対する治療だけでなく、他の疾患に対する手術においても必要になる局面は多い。弁膜症、大血管疾患の患者で無症候性の冠動脈狭窄が見つかる場合もあり、また大動脈基部置換術などの冠動脈移植を伴う手技では、CABGが必要になることも想定に入れておかなければならない。したがってCABGの基本手技は、心臓血管外科医がまず最初に習熟するべきであり、また常に満足する結果を出さなければならない。

ここでは筆者が日常行っている標準術式としてのCABGをその手順通りに解説し、日常の臨床にすぐに役立てることができる参考書として利用できるようにすることを目的とする。

● グラフト採取

1 内胸動脈

胸骨正中切開の後、内胸動脈採取用のリトラクターを使用し、採取側の胸壁を挙上する。筆者は独自に開発した胸骨挙上器 (Mera社) を使用している (図1)。これを通常の開胸器と組み合わせて使用する。胸膜を内胸筋膜から、開胸にならないように注意深く剥離する。内胸筋膜を中枢側の筋膜が欠損している部分を突破口にして切開していくが、筆者はハーモニックスカルペルの腹側を使って、内胸静脈の直上を静脈を損傷しないように切開する。切開した筋膜の断端を上を持ち上げながら、内胸動脈にかぶさっている内胸静脈をハーモニックスカルペルで跳ね上げるようにして上方へ変移させると内胸動脈が露出する (図2a)。さらに内胸動脈上の脂肪組織を飛ばすと分枝が見えてくるのでそれをハーモニックスカルペルの蛋白凝固にて切離する (図2b)。

枝を処理し内胸動脈を展開するとその奥にもう1本の内胸静脈が現れるので、それを残し内胸動脈のみを剥離する。中枢側では胸壁、鎖骨下静脈、内胸静脈を三辺とする三角形の中に内胸動脈は位置し、特に右側は内胸静脈が胸壁から比較的遠位部から遊離しているため、この三角形の面積が大きく、右内胸動脈も胸壁から遊離してこの三角形の中の脂肪組織に埋もれている場合が多く、この部分の剥離の際には内胸動脈を損傷しないように注意を要する (図3)。中枢側は第1肋骨上縁まで遊離し、しばしば比較的大きな動脈 (外側肋骨動脈) が認められるので、切離またはクリップをかける。末梢側は内胸動脈の上腹壁動脈と筋横隔動脈への分岐を越えて剥離する。