

『長期遠隔成績からみた糖尿病患者に対する至適冠血行再建法に関する研究』  
分担研究報告書要約

欧米では高齢者女性では心疾患の死亡率が高いことが報告されているが、本邦における高齢者冠動脈疾患の長期成績における性差は不明である。そこで本研究では 75 才を境界として高齢女性患者の冠動脈病変の特徴を明らかにするとともに、薬物溶出性ステント(SES)時代の心血管イベント(MACE: 死亡、非致死性心筋梗塞、心不全、再血行再建術の施行)に対する効果を従来型金属ステント(BMS)時代と比較検討した。その結果、本邦における高齢女性の冠動脈病変は血管径が小さく、病変長が長いことが特徴であった。また BMS 時代では、高齢女性は若年または男性に比して MACE が高率であったが、SES 時代では、高齢者または女性を問わず BMS 時代に比して MACE は減少していた。特に SES 時代の高齢女性においては、再血行再建術の施行頻度だけでなく死亡率(総死亡、心死亡)も有意に減少した。すなわち我が国における高齢女性の冠動脈疾患例は典型的な糖尿病による冠動脈狭窄例が集族している集団と思われる。そして、このような集団に対して従来の BMS を用いたカテーテル治療では長期予後改善効果は不十分であったが、SES を用いることにより再狭窄率が劇的に低下し 3 年程度の長期予後に関しては十分に良好な予後を得ることができるようになったと解釈される。このように小血管、びまん性病変を有する高齢女性は心血管イベントの高リスク群であるが、SES により予後改善効果が期待できると思われた。

所属施設・職名 近畿大学医学部循環器内科主任教授  
分担研究者名 宮崎俊一

厚生労働科学研究費補助金(循環器疾患等総合研究事業) 分担研究報告書  
長期遠隔成績からみた糖尿病患者に対する至適冠血行再建法に関する研究

分担研究者 宮崎俊一 近畿大学医学部循環器内科

研究要旨 BARI 研究により治療中の糖尿病例に対しては冠動脈バイパス術(CABG)施行例の方が経皮的冠動脈形成術(PCI)施行例よりも長期予後が良好であると報告されている。この原因として糖尿病症例における冠動脈病変は瀰漫性でかつ絶対径が小さい小血管病変を示すことが多く、このため PCI では十分な開大に至らないことが考えられる。このことは高齢女性における心血管事故の要因とも重複する可能性がある。本研究では PCI 施行例の長期予後を調査し、冠動脈狭窄形態と臨床指標との因果関係を統計解析することで、なぜ糖尿病例では CABG の方が PCI 施行例よりも長期予後が良いのかを明らかにする。

#### A. 研究目的

糖尿病症例における冠動脈病変形態の特徴として瀰漫性かつ小血管であることが知られている。このことがPCI治療に置いて再狭窄の発生頻度を増加させ、従ってCABG施行例の方が長期予後が良くなる可能性がある。一方、高齢女性の心死亡は男性よりも多いという報告がある。そこで本研究ではPCI施行例の冠動脈狭窄形態と長期予後の関連を調査し、糖尿病と高齢女性の要因に着目して要因解析することを目的とした。

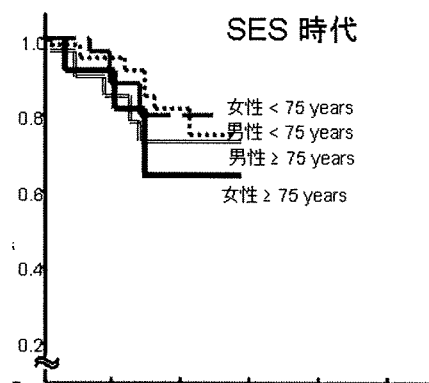
#### B. 研究方法

2000年4月から2005年12月までの間に国立循環器病センターへ入院したPCI施行例を対象としてコンピュータを用いた定量的冠動脈造影解析(QCA)をおこなった。これらのデータを年齢(75才以上かどうか)と性別によって4群に分けて背景因子及び長期予後調査を行うこととした。

#### C. 研究結果

2000年4月から2005年12月までの間に入院となったPCI施行例は2597例であった。これらの症例のうち、初回PCI施行例でQCA可能例は2000年4月から2004年7月の間(通常型金属ステント時代;BMS era)に670例、以後の薬剤

溶出性ステント時代(SES era)に704例であった。本年はDES適用後の予後調査を行ったところ下図のように4群間で有意差は出なかった。



#### D. 考察

BMS時代では、高齢女性は他の群に比して主要心血管イベント発生が高率であったが、SES時代では主要心血管イベントは減少し、4群間の差は認められなかった(図)。特にSES時代高齢女性においては、MACEが有意に減少した。

#### E. 結論

BMS時代には75才以上の高齢女性において心事故の発生が多い。

#### F. 健康危険情報 なし

#### G. 研究発表 なし

#### H. 知的財産の出願、登録状況 なし

共同研究者 片岡有

## Reference List

1. Kosuge M, Kimura K, Kojima S et al. Impact of body mass index on in-hospital outcomes after percutaneous coronary intervention for ST segment elevation acute myocardial infarction. *Circ J*. 2008;72:521-525.
2. Niizuma S, Iwanaga Y, Yahata T et al. Plasma B-type natriuretic peptide levels reflect the presence and severity of stable coronary artery disease in chronic haemodialysis patients. *Nephrol Dial Transplant*. 2008.
3. Otsuka Y, Kawamura A, Miyazaki S. Isolated right ventricular dysfunction without myocardial infarction. *Int J Cardiol*. 2008;124:e1-e3.
4. Takeno M, Yasuda S, Otsuka Y et al. Impact of metabolic syndrome on the long-term survival of patients with acute myocardial infarction: potential association with C-reactive protein. *Circ J*. 2008;72:415-419.
5. Arakawa K, Yasuda S, Hao H et al. Significant association between neutrophil aggregation in aspirated thrombus and myocardial damage in patients with ST-segment elevation acute myocardial infarction. *Circ J*. 2009;73:139-144.
6. Kataoka Y, Yasuda S, Morii I et al. Improved long-term prognosis of elderly women in the era of sirolimus-eluting stents. *Circ J*. 2009;73:1219-1227.
7. Kimura T, Morimoto T, Nakagawa Y et al. Antiplatelet therapy and stent thrombosis after sirolimus-eluting stent implantation. *Circulation*. 2009;119:987-995.
8. Kosuge M, Kimura K, Morita S et al. Combined prognostic utility of white blood cell count, plasma glucose, and glomerular filtration rate in patients undergoing primary stent placement for acute myocardial infarction. *Am J Cardiol*. 2009;103:322-327.
9. Mori S, Yasuda S, Kataoka Y et al. Significant association of coronary artery calcification in stent delivery route with restenosis after sirolimus-eluting stent implantation. *Circ J*. 2009;73:1856-1863.
10. Niizuma S, Iwanaga Y, Yahata T et al. Plasma B-type natriuretic peptide levels reflect the presence and severity of stable coronary artery disease in chronic haemodialysis patients. *Nephrol Dial Transplant*. 2009;24:597-603.

長期遠隔成績からみた糖尿病患者に対する至適血行再建法に関する研究  
～当院における経皮的カテーテル治療患者の解析～

分担研究者 住吉徹哉 財団法人日本血圧研究振興会附属榊原記念病院 循環器内科  
高見澤格 同

### 研究要旨

人口の高齢化や食生活の変化により、糖尿病の罹患者数は1997年には1370万人であったのに対し2006年には1870万人にまで増加している。糖尿病の大血管障害である虚血性心疾患も増加しており、今後冠動脈バイパス術(CABG)と経皮的冠動脈カテーテル治療(PCI)は増加することが予想される。糖尿病患者では多枝病変やびまん性狭窄病変が多く、腎機能低下や心機能低下例が多いため、以前からCABGとPCIのどちらを選択すべきかという議論がなされてきた。しかし、近年の体外循環を使用しない off-pump 技術や動脈グラフトを用いたCABGとステント治療が主流となったPCIを比較した研究は少なく、本邦独自のデータを集積・解析しそれぞれの長期予後を評価する必要性は高い。本研究により本邦独自の糖尿病患者における虚血性心疾患治療法の選択基準の確立が期待できる。

#### A. 研究目的

当院においてPCI治療を受けた患者のうち、糖尿病合併例の長期予後を調査する。

#### B. 研究方法

2001年から2004年に当院でPCIを施行された虚血性心疾患1390例のうち、糖尿病を合併した症例を後ろ向きに解析し長期遠隔成績を調査した。主要心血管イベント(MACE)は心血管死亡、心不全、心筋梗塞、狭心症、再血行再建(TLR)とした。急性心筋梗塞症例およびPCIまたはCABGの既往例は除外した。

#### C. 研究結果

該当症例は119例(平均年齢66±9歳)であった。119例の平均HbA1cは7.2±1.5%であった。平均追跡期間は50±29か月で、1年以上のフォローアップができた症例は104例(87%)であった。このうち死亡は3例(2.8%)で1例が術後19か月後の突然死であった。PCI手技に関連する合併症は7例にみられたが、術中の心室細動が1例、CABGが2例、手技

関連の心筋梗塞が2例、コレステロール塞栓が1例、造影剤アレルギーが1例であった。MACEは35例(34%)にみられ、冠血行再建としてPCIを施行したのが26例で、そのうちTLRが24例であった。CABGは8例施行され全例TLRの症例であった。

#### D. 考察

PCIを施行した糖尿病合併患者におけるMACEの発生は34%と高かったがTLRがそのうちの69%を占めており、糖尿病での再狭窄率の高さが再確認された。非糖尿病患者との比較が今後必要である。循環器関連の死亡は1例のみで心筋梗塞は認めず、比較的PCIの予後は良好であったため、CABGとの比較検討が必要である。

#### E. 結論

PCIを施行した糖尿病合併の狭心症例でのMACEは34%と高いためCABGとのより大規模かつ詳細な比較検討が必要である。また、血糖コントロールによる層別化を行うことで成績が異なるか検討することも必要である。

別紙 4 研究成果

学会発表

発表者名	学会・研究会名	日時	場所	演題名
高見澤 格	第 71 回日本循環器学会総会	2007 年 3 月 17 日	神戸	Relationship between adiponectin level and restenosis in patients with myocardial infarction
高見澤 格	第 21 回日本冠疾患学会学術集会	2007 年 12 月 14 日	京都	心筋梗塞患者におけるレプチンの動態に関する検討
高見澤 格	第 8 回日本心血管カテーテル治療学会	2008 年 11 月 25 日	京都	Histopathological and immuno-histochemical analysis of materials captured by a distal protection device
高見澤 格	第 18 回日本心血管インターベンション治療学会	2009 年 6 月 25 日	札幌	Histopathological and immuno-histochemical analysis of materials captured by a distal protection device
高見澤 格	第 57 回日本心臓病学会	2009 年 9 月 18 日	札幌	心筋梗塞患者における Bare Metal Stent の再狭窄に関わるアディポサイトカインの検討

刊行物

書籍

著者	著書	項目	頁	発行年	会社
高見澤 格	EBM 循環器疾患の治療	無症候性心筋虚血に対する冠血行再建	P130-134	2009 年 9 月	中外医
住吉徹哉	2010-2011	(PCI、CABG)の適応は？			学社

長期遠隔成績からみた糖尿病患者に対する至適血行再建法に関する研究  
～当院における経皮的カテーテル治療患者に関する研究～

分担研究者 財団法人日本 hypertension 研究振興会 附属 榊原記念病院 心臓外科

高梨秀一郎 主任外科部長

福井寿啓 医長

当院において CABG を受けた患者のうち、糖尿病合併の割合と長期予後を調査した。ただし、急性心筋梗塞症例および以前 PCI と CABG を施行された症例は除外した。2003 - 2004 年度に当院において CABG を施行された症例のうち、糖尿病合併症例は 59 例であった。平均 HbA1c は  $7.1 \pm 1.1\%$  であった。手術死亡は 2 例、遠隔死亡は 1 例であった。CABG が必要である虚血性心疾患症例の 40.1% に糖尿病を合併していて、手術死亡率は 3.4%、遠隔死亡率は 1.7% に認めた。

長期遠隔成績からみた糖尿病患者に対する至適血行再建法に関する研究  
～当院における経皮的カテーテル治療患者に関する研究～

分担研究者 財団法人日本血圧研究振興会附属榊原記念病院心臓外科  
高梨秀一郎 主任外科部長  
福井寿啓 医長

研究要旨

本邦では、冠動脈バイパス術(CABG)に対する経皮的冠動脈カテーテル治療(PCI)の比率が高いこと、CABG においては動脈グラフトの使用頻度が高いこと、体外循環を使用しない off-pump CABG の割合が高いこと、など、欧米諸国との大きな隔たりがあり本邦独自のデータの集積・解析の必要性が高い。本邦では患者の追跡率が高いため、糖尿病の重症度と冠動脈の特徴を含め詳細に検討を行うことができ、本邦独自の糖尿病患者における虚血性心疾患治療法の選択基準の確立が期待できる。

A. 研究目的

2003 - 2004 年度 2 年間に当院において CABG を受けた患者のうち、糖尿病合併の割合と長期予後を調査する。

B. 研究方法

2003 - 2004 年度に、当院で CABG を施行された患者をレトロスペクティブに解析をし、糖尿病を合併していた割合と長期遠隔成績を調べた。ただし、急性心筋梗塞症例および以前 PCI と CABG を施行された症例は除外した。

C. 研究結果

2003 - 2004 年度に当院において CABG を施行された症例のうち、糖尿病合併症例は 59 例であった。平均 HbA1c は  $7.1 \pm 1.1\%$  であった。手術死亡は 2 例、遠隔死亡は 1 例であった。

D. 考察

糖尿病患者では非糖尿病患者に比較して虚血性心疾患の頻度が 2~4 倍に増加することが明らかにされており、海外の大規模臨床研究においても、虚血性心疾患での糖尿病合併は 20~40% と報告されている。当院での成績も同様であった。年齢に関しては、平均  $66.3 \pm 8.3$  歳と比較的若く、糖尿病を合併している症例では、早期より虚血性心疾患を合併する可能性があることが示唆された。今後症例を積み重ねることで、HbA1c を指標として糖尿病のコントロール状態を把握し、予後に対する寄与度を評価することや、内服薬の予後への影響を考察することが可能であると考えられる。

E. 結論

CABG が必要である虚血性心疾患症例の 40.1% に糖尿病を合併していた。手術死亡率は 3.4%、遠隔死亡率は 1.7% であった。

薬剤溶出性ステント留置後の再狭窄 - 糖尿病の関与についての検討

分担研究者 伊藤 彰 大阪市立総合医療センター循環器内科

研究要旨 薬剤溶出性ステント(DES: drug eluting stent)は金属ステントと比較して PCI 後の再狭窄率を低減したが、実臨床においては DES を使用してもなお 10-15%の再狭窄がみられており、さらなる対策が必要である。今回、DES(Cypher stent)を留置した連続例を検討し、再狭窄と関連する因子について検討した。その結果、慢性腎不全による透析、糖尿病、病変長が DES 留置後の再狭窄と関連する因子であった。

A. 研究目的

DES 留置後の再狭窄に影響する因子について検討する。

B. 研究方法

狭心症または無症候性心筋虚血の治療のため DES(Cypher stent)を留置した連続 225 例(男性 126、女性 99、平均年齢 66 歳)を対象とした。ステント留置 12 ヶ月目までに冠動脈造影を施行し再狭窄の有無を確認できたのは 176 例(222 病変)であった。ステント内部またはステント端から 5mm 以内に 50%以上の狭窄がみられた場合に再狭窄と定義した。

C. 研究結果

全対象患者の臨床像を表 1 に示す。冠危険因子では 66%が高血圧、46%が糖尿病、64%が高脂血症を有していた。30%に心筋梗塞の既往があり、9%が慢性腎不全で透析療法を受けていた。222 病変のうち再狭窄は 29 病変(再狭窄率 13.1%)にみられた。再狭窄例は非再狭窄例と比較して糖尿病を高頻度に合併しており、透析例が多く、病変長が長かった(表 2)。

D. 考察

DES 留置後の再狭窄は金属ステントと比較して低率ではあるが今回の検討では 13.1%にみられた。糖尿病、腎不全に伴う透析、長い病変長が再狭窄と関係しており、これらを合併する患者にお

いては注意深い術後の経過観察が必要であると同時に、多枝病変の場合には冠動脈バイパス術の適応をより積極的に検討する必要があると考えられた。

E. 結論

今回の検討から糖尿病、血液透析、病変長が薬剤溶出性ステント(Cypher stent)留置後の再狭窄と関係する因子であった。

F. 健康危険情報

なし

G. 知的財産権の出願・登録状況

なし

表 1

Age (yrs)	66 ± 9
Male (%)	126 (72)
Stable angina pectoris (%)	79 (45)
Silent myocardial ischemia (%)	49 (28)
Unstable angina pectoris (%)	29 (16)
Previous myocardial infarction (%)	53 (30)
Previous PCI (%)	60 (34)
Previous CABG (%)	10 (6)
Hypertension (%)	116 (66)
Hyperlipidemia (%)	113 (64)
Diabetes mellitus (%)	81 (46)
Smoker (Current or Ex-) (%)	114 (65)
Familial history (%)	45 (26)
Obesity (%)	49 (28)
Hemodialysis (%)	16 (9)



表2

	No- restenosis (n=193)	Restenosis (n=29)	P
Age (yrs)	66.7 ± 9.3	64.0 ± 9.9	NS
Male (%)	77.1	75	NS
Hypertension (%)	64.2	75.9	NS
Hyperlipidemia (%)	64.2	58.6	NS
Diabetes mellitus (%)	43	65.5	< 0.05
Smoking (%)	65.8	65.5	NS
Hemodialysis (%)	7.3	27.6	< 0.01
Lesion type B1 (%)	7.8	0	
B2 (%)	47.2	34.5	
C (%)	43.5	62.1	< 0.05
Reference vessel diameter (mm)	2.80 ± 0.48	2.92 ± 0.48	NS
Post-intervention MLD (mm)	2.62 ± 0.42	2.67 ± 0.41	NS
Lesion length (mm)	20.1 ± 11.2	27.6 ± 18.5	< 0.01

## 研究成果の刊行に関する一覧表

## 書籍

著者氏名	論文タイトル名	書籍全体の編集者名	書籍名	出版社名	出版地	出版年	ページ
伊藤彰	薬物療法、PCI、CABGの対比	小川久雄	最新狭心症治療の実際	永井書店	東京	2009	274-280

## 雑誌

発表者氏名	論文タイトル名	発表誌名	巻号	ページ	出版年
Takagi T, Okura, H*, Kobayashi, Y, Kataoka, T, Taguchi, H, Toda, I, Tamita, K, Yamamuro A, Sakanoue Y, Ito A, Yanagi S, Shimeno K, Waseda K, Yamasaki Y, Fitzgerald PJ, Ikeno F, Honda Y, Yoshiyama M, Yoshikawa J, for the POPPS Investigators.	A Prospective, Multicenter, Randomized Trial to Assess Efficacy of Pioglitazone on In-Stent Neointimal Suppression in Type 2 Diabetes POPPS (Prevention of In-Stent Neointimal Proliferation by Pioglitazone Study).	J Am Coll Cardiol Intv	2	524-531	2009
Yunoki K, Naruko T, Komatsu R, Ehara S, Shirai N, Sugioka K, Nakagawa M, Kitabayashi C, Ikura Y, Itoh A, Kusano K, Ohe T, Haze K, Becker AE, Ueda M.	Enhanced expression of haemoglobin scavenger receptor in accumulated macrophages of culprit lesions in acute coronary syndromes.	Eur. Heart J.	30	1844 - 1852	2009

<p>Abe Y, Yagishita D, Tagawa Y, Furukawa A, Nakagawa E, Yunoki K, Shirai N, Komatsu R, Naruko T, Yoshiyama M, Yoshikawa J, Haze K, Itoh A.</p>	<p>A novel echocardiographic index of inefficient left ventricular contraction resulting from mechanical dyssynchrony.</p>	<p>J Cardiol.</p>	<p>55</p>	<p>248-255</p>	<p>2009</p>
<p>Yunoki K, Naruko T, Komatsu R, Shirai N, Nakagawa M, Sugioka K, Ikura Y, Kusano KF, Itoh A, Haze K, Yoshiyama M, Becker AE, Ueda M.</p>	<p>Relation of elevated levels of plasma myeloperoxidase to impaired myocardial microcirculation after reperfusion in patients with acute myocardial infarction.</p>	<p>Am J Cardiol.</p>	<p>105</p>	<p>922-929</p>	<p>2010</p>

## 研究成果の刊行物・印刷

# Radial Artery as a Graft for Coronary Artery Bypass Grafting

Junjiro Kobayashi, MD

The radial artery (RA) graft was revived in late 1980s when it was found that the graft was patent 13–18 years after coronary artery bypass grafting (CABG) after improvement of the technique in harvesting and the use of calcium-channel blockers. Recently, the RA became a reasonable alternative to the saphenous vein (SV) graft with the trend toward complete arterial revascularization and more frequent off-pump CABG to avoid aortic manipulation. To improve the quality of the RA conduit, harvesting technique and topical and systemic antispasmodic medication are important. The RA should be grafted to severe proximal stenosis (>90%) in the native coronary arteries to avoid flow competition, especially in the right coronary territory. The RA graft could be used as an aortocoronary or composite configuration with similar graft patency. Early graft patency of the RA conduit was as good as other arterial grafts, and better than SV graft in the circumflex and right coronary territories, in many studies, especially in diabetic patients. Long-term results of graft patency and cardiac-event-free survival compared with SV graft are still controversial in randomized controlled trials, probably because the incidence of flow competition and the definition of graft patency varied. (*Circ J* 2009; 73: 1178–1183)

**Key Words:** Coronary artery bypass; Left internal thoracic artery; Radial artery; Saphenous vein

**T**he superiority of the left internal thoracic artery (LITA) over the saphenous vein (SV) in coronary artery bypass grafting (CABG) was widely accepted in angiographic studies in the 1980s.<sup>1,2</sup> The clinical importance of the LITA to the left anterior descending artery (LAD) graft was emphasized in a long-term follow-up study comparing it with the SV over 20 years.<sup>3</sup> The graft patency rate of the LITA to the LAD graft was approximately 90%, and that of SV grafts was 50–60% at 10 years after CABG.<sup>4,5</sup> Because the SV developed intimal hyperplasia and graft atherosclerosis, which caused late graft occlusion, various arterial grafts have been adopted over the past 30 years. The right internal thoracic artery (RITA),<sup>6,7</sup> the right gastroepiploic artery (GEA),<sup>8,9</sup> the radial artery (RA),<sup>10,11</sup> and the inferior epigastric artery (IEA)<sup>12,13</sup> have been used in addition to the LITA. According to the database of Japanese Association for Coronary Artery Surgery in 2004, the LITA comprised 37.5% of the total grafts. Other arterial grafts were 14.5% (RITA), 14.7% (RA), and 9.1% (GEA). Arterial grafts accounted for 76% of total grafts in Japan, which is significantly higher than in Western countries. Here I review the current status of the RA graft as the second choice of arterial graft after the LITA.

## Historical Perspective

The RA was first used in CABG by Carpentier et al in 1971.<sup>14</sup> However, 2 years later, they recommended not using the RA because of the 35% incidence of narrowing or occlusion of this conduit, which was much higher than in

the SV graft by control angiography.<sup>15</sup> Graft failure was caused by spasm and intimal hyperplasia after endothelial denudation from mechanical dilatation and the trauma of skeletonized harvesting. RA grafts were revived in late 1980s when, after initially believing that they were occluded, they were found to be patent 13–18 years after CABG.<sup>10</sup> The technique of harvesting and the use of calcium-channel blockers has improved the early and late graft patency, and revived the use of the RA. The 5-year graft patency rate of the RA was 84% compared with 90% for the LITA. The study showed that the RA is a reasonable alternative to other graft materials that complement the LITA. Recently, the SV graft is being widely replaced by the RA. With the trend toward complete arterial revascularization and more frequent off-pump CABG (OPCAB) to avoid aortic manipulation, the use of the RA as a composite graft with the internal thoracic artery (ITA) has become more common.<sup>16,17</sup>

## Harvesting Technique

The RA is easily harvested and has excellent handling characteristics. However, preoperative evaluation and proper harvesting technique is mandatory for good short- and long-term patency rates and the possibility of improved survival. The most widely used clinical test for assessment of adequate ulnar collateral circulation to the hand is the Allen test. Other assessment techniques, such as pulse oximetry, digital plethysmography, and Duplex scanning, have been reported.<sup>18</sup> Contraindications in addition to forearm ischemia are severe atherosclerosis with calcification, and dissection from prior cannulation. Thrombotic occlusion immediately before CABG because of preoperative cardiac catheterization is not a contraindication to use the RA after thrombectomy in the operating room. The most common complications after RA harvest are sensory abnormality and numbness, which occurs in 3–15% of patients.<sup>19,20</sup>

The options for RA harvest are pedicled or skeletonized with or without using the ultrasonic scalpel, and open vs endoscopic harvesting. Significantly greater blood flow is

(Received May 8, 2009; revised manuscript received May 11, 2009; accepted May 12, 2009; released online June 9, 2009)

Department of Cardiovascular Surgery, National Cardiovascular Center, Suita, Japan

Mailing address: Junjiro Kobayashi, MD, Department of Cardiovascular Surgery, National Cardiovascular Center, 5-7-1 Fujishiro-dai, Suita 565-8565, Japan. E-mail: jkobayas@hsp.ncvc.go.jp

All rights are reserved to the Japanese Circulation Society. For permissions, please e-mail: cj@j-circ.or.jp

**Table 1. Advantages and Disadvantages of the SV, RA, RITA, and GEA for CABG as a Second Graft to the LITA**

	Advantage	Disadvantage
SV	Good handling Enough length for many anastomosis as for individual graft Decreased transfusion than with bilateral ITA use Decreased harvesting time than with bilateral ITA use	Poor short- and long-term patency Not available in varix patients Postoperative leg edema Poorer wound healing than the RA
RA	Length >20cm Luminal diameter slightly larger than that of coronary arteries Good handling Decreased transfusion than with bilateral ITA use Decreased harvesting time than with bilateral ITA use	Very spasmodic Not always available (Allen test positive, unsuitable quality, CRF) Numbness and risk of motor dysfunction Arm wound
RITA	Excellent long-term patency Less spastic than RA Almost always usable Graftable to any territory as a composite free graft	Longer harvesting time Not graftable to PL or PDA as in-situ More bleeding and sternal infection than with RA harvest Difficult handling as a composite graft Thin arterial wall not suitable for aortic anastomosis
GEA	Graftable to any territory as in-situ graft Substitute for RA composite graft Available in redo CABG Suitable for MICS RCA anastomosis	Laparotomy (delayed oral intake) More spasmodic than the ITA Not better than SV patency Size variety not appropriate in some patients

SV, saphenous vein; RA, radial artery; RITA, right internal thoracic artery; GEA, gastroepiploic artery; CABG, coronary artery bypass grafting; LITA, left internal thoracic artery; ITA, internal thoracic artery; CRF, chronic renal failure; PL, posterolateral branch; PDA, posterior descending artery; MICS, minimally invasive cardiac surgery; RCA, right coronary artery.

reported in RA grafts harvested by ultrasonic scalpel than in traditionally harvested RA grafts<sup>21</sup> probably because of the larger RA caliber with the skeletonizing technique and better pharmacological preparation. In addition to systemic administration of nitroglycerin and diltiazem, antispasmodic agents are used topically. Papaverine, which is a short-acting phosphodiesterase inhibitor, is a widely used vasodilator for ITA and RA harvesting. As it is very acidic, a mixture of blood as a buffer is mandatory when it is infused into the lumen of the RA. Milrinone, which is a long-acting phosphodiesterase inhibitor, systemically used for heart failure as a dilator, has been administered intraluminally to prevent RA spasm, with good clinical results<sup>22</sup> Verapamil and nitroglycerin (VG solution) can effectively prevent spasm against a wide range of vasoconstrictors, with better preservation of endothelial function than papaverine<sup>23</sup> The alpha-adrenoreceptor antagonist, phenoxybenzamine, and verapamil in heparinized blood are also used intraluminally and topically<sup>24</sup>

### Advantage of RA Use

In Western countries, conventional CABG consists of LITA to the LAD and SV grafts to other coronary branches under cardiac arrest with cardiopulmonary bypass. Despite the easy access and adequate length for aortocoronary bypass, SV grafts have poor long-term patency<sup>3-5</sup> In any patient category, bilateral ITA use has been reported as better than only LITA use in late clinical results<sup>25-27</sup> However, bilateral ITA harvesting has shown a higher incidence of sternal wound infection in patients taking insulin or steroids, who are obesity or have chronic obstructive lung disease<sup>28,29</sup> In addition, the RITA to LAD graft crossing the midline of the chest may obstruct future reoperations for aortic valve surgery, but to avoid this situation the RITA is unable to reach the posterolateral coronary artery even if it passes through the transverse sinus.

The RA is more than 20 cm in length on average and able to reach any coronary territory when it is used as a composite graft. The RA has an inner diameter of 2-3 mm without size mismatch to the coronary arteries. Harvesting

of the RA is concurrently possible with LITA and SV harvesting. There are several observational studies that showed better early and late mortality and morbidity compared with SV grafts<sup>30,31</sup> Unlike the SV grafts, the RA grafts adapted to arterial pressure and flow, and changed diameter for optimal flow velocity. As the second arterial graft in addition to LITA to LAD anastomosis, cohort studies comparing the RITA and the RA showed the same clinical and angiographic results<sup>32,33</sup> In addition, perioperative bleeding and sternal wound infection are favorable with the RA compared with the RITA<sup>33</sup>

Other arterial grafts have their own disadvantages. The GEA, which is able to reach any coronary territory as an in-situ graft, has been widely used in Japan compared with Western countries. Use of in-situ GEA for CABG was first reported in 1987, and early graft patency ranged from 90% to 100%<sup>8,9</sup> Long-term graft patency at 10 years was not better than with SV grafts<sup>34</sup> probably because of the size variation. GEA harvesting requires a longer skin incision and laparotomy, which delays oral intake. The GEA is also prone to flow competition compared with the LITA because the GEA is the third branch of the abdominal aorta and has 10-15 mmHg lower pressure at its end compared with the end of the LITA<sup>35-37</sup> Although skeletonized and composite use of the GEA for larger internal diameter and flow has been reported<sup>38</sup> avoiding flow competition has not been proved<sup>39-41</sup>

The IEA was first reported as an alternative arterial graft to the SV in 1990<sup>12</sup> It is relatively short and only suitable for grafting to diagonal or intermediate branches. The major complication of IEA harvesting is abdominal wall hematoma or infection. As the graft patency of the IEA is not better than SV grafts, it is no longer used widely.

### Disadvantages of RA Use

One of disadvantages of the RA is the intense spasm. Basic study has delineated that the mechanism of severe spasm in the RA is more difficult to reverse compared with the LITA<sup>42</sup> The functioning of the RA in releasing endothelium-derived relaxing factors such as nitric oxide is the same

Table 2. Patency Rate of RA and Other Grafts

Reference	Year	Interval	RA	% of AC	LITA	RITA	GEA	IEA	SV
Acar <sup>10</sup>	1992	<3 weeks	56/56 (100%)	100%	48/48 (100%)	11/11 (100%)			8/9 (88.9%)
		9.2 months	29/31 (93.5%)		28/28 (100%)	9/9 (100%)			
Calafiore <sup>55</sup>	1995	3.6 months	75/76 (98.7%)	0%				67/70 (95.7%)	
		21.2 months	33/35 (94.3%)					25/25 (100%)	
da Costa <sup>56</sup>	1996	8.7 months	59/61 (96.7%)	100%	21/32 (96.8%)	12/13 (92.3%)	1/1 (100%)		13/14 (92.8%)
Brodman <sup>57</sup>	1996	11.9 weeks	86/90 (95.5%)	100%					
Chen <sup>58</sup>	1996	11.6 weeks	90/94 (95.7%)	100%	62/62 (100%)				22/24 (93.3%)
Possati <sup>59</sup>	1998	59 months	57/62 (91.9%)	100%	57/58 (98.2%)	3/4 (75%)	9/10 (90%)		43/58 (74.1%)
Tatoulis <sup>60</sup>	1998	4.2 months	21/22 (95.7%)	90%	16/16 (100%)				
Acar <sup>61</sup>	1998	5.6 years	54/64 (84.4%)	100%	44/47 (93.6%)				
Bhan <sup>62</sup>	1999	16.2 months	60/62 (96.8%)	100%	56/57 (98.2%)				
Amano <sup>63</sup>	2001	<3 months	137/139 (98.6%)	69%	99/100 (99.0%)	27/27 (100%)	48/50 (96.0%)		34/38 (89.5%)
		1.5 years	213/229 (93.0%)	65%	168/171 (98.2%)	27/27 (100%)	75/82 (91.4%)		71/79 (89.8%)
Iacò <sup>64</sup>	2001	18 days	88/89 (98.9%)	11%	82/82 (100%)		13/13 (100%)	12/12 (100%)	4/4 (100%)
		48 months	87/91 (95.6%)	22%	63/93 (100%)		11/12 (91.7%)	10/11 (90.9%)	8/9 (88.8%)
Possati <sup>65</sup>	2003	105 months	77/84 (91.6%)	100%	80/82 (97.5%)	6/7 (85.7%)	14/15 (93.3%)		39/73 (53.4%)
Cameron <sup>66</sup>	2004	5.2 years	55/62 (88.7%)	96%	51/51 (100%)	17/18 (94.4%)			33/36 (91.6%)
Zacharias <sup>67</sup>	2004	1.8 years	111/157 (70.7%)	NA	370/394 (93.9%)				95/161 (59.0%)
Khot <sup>68</sup>	2004	565 days	204/398 (51.3%)	NA	243/269 (90.3%)	61/77 (79.2%)			174/272 (64.0%)

IEA, inferior epigastric artery; AC, aortocoronary bypass; NA, not available. Other abbreviations see in Table 1.

as for other arterial grafts, as is its constriction function to vasoconstrictive factors. However, the RA has multiple tight muscle layers in the media, which has a higher density of muscle cells than other arterial grafts. Because of this, the RA wall has a higher maximum contractile force in response to vasoconstrictive agents, such as norepinephrine, serotonin, endothelin I, and angiotensin II. These chemical mediators are released after endothelial damage caused by surgical trauma and platelet aggregation.

RA grafts frequently show the flow competition phenomenon with mildly stenotic native coronary arteries.<sup>43-51</sup> The use of the RA in composite grafts with the LITA as Y or T grafts showed similar graft patency as RA grafts used as an aortocoronary bypass.<sup>45-47</sup> However, Gaudino et al found flow competition more frequently in the composite RA conduits than in the aortocoronary RA conduit.<sup>48</sup> Long-term patency of these competitive RA grafts was poor by angiographic analysis, though it was better than the SV when good forward flow was present.<sup>44,49,50</sup> Other potential disadvantages of composite grafts compared with aortocoronary grafts are the relative technical difficulty and the reliance of a single inflow to supply all or many coronary territories.<sup>51</sup> The SV graft still has a role as a graft to the moderately stenotic right coronary territory because of the high incidence of flow competition of composite RA grafts to the right coronary branches,<sup>1,43,44,47,51,52</sup> and the poor early graft patency of the RITA to the right coronary artery.<sup>53,54</sup> The advantage and disadvantage of the grafts are listed in Table 1.

### Patency of RA Grafts

The long-term outcome after CABG depends on graft patency. Previous angiographic observational studies have shown that the RA achieved excellent short- (96-100%), mid- (94-97%), and long-term graft patency (84-96%) when used as either an aortocoronary bypass or a composite graft (Table 2).<sup>10,55-67</sup> Patency rates of the RA have exceeded those of SV grafts at all time points and are comparable to other arterial grafts. Many reports have shown better outcomes of the RA compared with the SV,<sup>10,56,58,59,63-65,67</sup> though some reported similar long-term graft patency.<sup>33,45,48,66</sup>

Only the Cleveland Clinic reported worse graft patency of the RA than the SV.<sup>68</sup>

Possati et al reported the long-term (105±9 months) graft patency of RA grafts in a series of 90 consecutive CABG patients.<sup>65</sup> The RA graft patency was 88%, which was less than that of the LITA (96%), but better than that of the SV (53%). Although these results are encouraging the use of the RA as a complementary arterial conduit with the LITA, there are only a few long-term studies assessing RA graft patency in the setting of a randomized controlled trial.

### Randomized Controlled Trials

The Radial Artery Patency Study (RAPS) Investigators enrolled 561 patients in 13 centers.<sup>69</sup> In this trial, the RA graft was randomly assigned to bypass the major artery in either the right coronary territory or the circumflex coronary territory, with the SV graft used for the opposing territory, which had proximal lesions at least 70% diameter narrowing. Angiography for 440 RA grafts and 440 SV grafts was performed in 440 patients in 1 year. Desai et al reported that 8.2% of RA grafts and 13.6% of SV grafts were completely occluded (P=0.009).<sup>69</sup> Diffuse narrowing of the graft (string sign) was present in 7.0% of the RA grafts and only 0.9% of SV grafts (P=0.001). The absence of severe native vessel stenosis was a risk of graft occlusion and diffuse narrowing of the RA conduit (70-89% proximal stenosis: 81.7%; >90% proximal stenosis: 91.5%). Patency of the RA grafts was similar in the right coronary and circumflex arteries. These results are compatible with previous reports suggesting that the RA should be limited to grafting to native coronary vessels with a high degree of stenosis (>70%) because of graft sensitivity to competitive flow and diffuse narrowing.<sup>43-51</sup> Diffuse narrowing of the RA graft is thought to be of little or no clinical consequence because the narrowed graft may improve or work well late in the follow-up. However, cardiologists consider the string sign of the RA graft as a failure. As the string sign at 1 year is unfavorable toward a functioning RA or SV graft, 15.2% of RA grafts and 14.5% of SV grafts are occluded or functioning poorly. In an early postoperative study, composite RA grafts with competitive flow without diffuse narrowing were present in 7.3% of

total conduits.<sup>70</sup> The actuarial patency rate of these grafts on late angiography was only 33.9% at 3 years after OPCAB. RA grafting should not be considered in the setting of <75% proximal coronary obstruction, especially in the right coronary branches.

The RAPS Investigators also reported that diabetes (RR: 1.45,  $P=0.03$ ), female gender (RR: 1.78,  $P=0.02$ ), and small target vessel diameter (RR: 2.28,  $P<0.01$ ) are multivariate predictors of graft failure.<sup>71,72</sup> Graft occlusion was more common among diabetic patients (14% vs 10%) because of more frequent SV occlusion (19%) than RA occlusion (10%). The RA is protective in the small-sized coronary arteries with diffuse diabetic disease. With regard to gender, RA graft occlusion rate at 1 year was similar in men (8.6%) and women (5.3%) ( $P=0.6$ ), whereas SV graft occlusion rates were lower in men (12.0%) than in women (23.3%). A history of peripheral vascular disease was associated with an elevated risk of RA occlusion, but not with SV occlusion. On the contrary, angiographic studies of patients at the Cleveland Clinic found poor graft patency in the RA (51%) compared with the SV (64%). With regard to sex, women had significantly worse RA graft patency (39%) than men (56%).<sup>67</sup>

The Radial Artery Patency and Clinical Outcome (RAPCO) study was undertaken to compare angiographic patency and cardiac-event-free survival of the RA graft with that of the free RITA and SV during a 10-year period after CABG.<sup>73</sup> The RA was compared with the free RITA in patients <70 years of age and with the SV in patients aged >75 years. The 5-year interim results of this single center trial conducted by Buxton et al in Australia reported that there were no differences in angiographic graft failure and cardiac events of the patients with the RA compared with the RITA or SV. The 5-year patency rates between the RA and RITA were 95% vs 100%, respectively, and those between the RA and SV were 87% vs 94%. However, these results were based on a small number of angiographic studies, and SV graft patency was very much better than in previous reports. The final results up to 10 years should clarify the long-term RA graft patency.

The Radial Artery Versus Saphenous Vein Graft Patency (RSVP) trial was a single-center, prospective, randomized clinical trial designed to compare 5-year patency rates of RA and SV aortocoronary grafts to the circumflex coronary artery.<sup>74</sup> At 5 years, 103 patients among 142 enrolled patients underwent angiography. The graft patency of the RA (98.3%) was significantly ( $P=0.04$ ) better than that of the SV (86.4%). Graft narrowing occurred in 10% of patent RA grafts and 23% of SV grafts ( $P=0.01$ ).

Total arterial myocardial revascularization with a composite RITA or RA was compared with conventional CABG in a prospective randomized fashion by Muneretto et al.<sup>75</sup> At a mean follow-up of 12 months, the total arterial CABG group had a better outcome in terms of angina recurrence, need for percutaneous cardiac intervention, and actuarial freedom from cardiac events. The 1-year results for total arterial revascularization, in which the RA was used as a composite or aortocoronary conduit in addition to in-situ bilateral ITA grafting, vs conventional coronary CABG (CARRPO trial) showed similar graft patency, and cardiac-event-free rates at 1 year after CABG.<sup>76</sup>

### Summary and Recommendation

To improve the quality of the RA conduit, harvesting

technique and topical and systemic antispasmodic medication are important. The RA should be grafted to severe proximal stenosis (>90%) in the native coronary arteries to avoid flow competition. The RA graft can be used as an aortocoronary or composite configuration with the same graft patency. Early graft patency of the RA conduit is as good as other arterial grafts and better than the SV graft in the circumflex and right coronary territories in many studies, especially in diabetic patients. Long-term results of graft patency and cardiac-event-free survival compared with SV graft are still controversial in randomized controlled trials, probably because both the incidence of flow competition and the definition of graft patency varied.

### References

1. Loop FD, Lytle BW, Cosgrove DM, Stewart RW, Goormastic M, William GW, et al. Influence of the internal mammary artery graft on 10-year survival and other cardiac events. *N Engl J Med* 1986; **314**: 1–6.
2. Lytle BW, Loop FD, Cosgrove DM, Ratliff NB, Easley K, Taylor PC. Long-term (5 to 12 years) serial studies of internal mammary artery and saphenous vein coronary artery bypass grafts. *J Thorac Cardiovasc Surg* 1985; **89**: 248–258.
3. Boylan MJ, Lytle BW, Loop FD, Taylor PC, Borsh JA, Goormastic M, et al. Surgical treatment of isolated left anterior descending coronary stenosis: Comparison of the left internal mammary artery and venous autograft at 18 to 20 years of follow up. *J Thorac Cardiovasc Surg* 1994; **107**: 657–662.
4. Bourassa MG, Fischer LD, Campeau L, Gillespie MJ, McConney M, Lespérance J. Long-term fate of bypass graft: The Coronary Artery Surgery Study (CASS) and Montreal Heart Institute experience. *Circulation* 1985; **6**(Suppl V): V-71–V-78.
5. Ura M, Sakata R, Nakayama Y, Arai Y, Saito T. Long-term results of bilateral internal thoracic artery grafting. *Ann Thorac Surg* 2000; **70**: 1991–1996.
6. Ioannidis JP, Galanos O, Katritsis D, Connery CP, Drossos GE, Swistel DG, et al. Early mortality and morbidity of bilateral versus single internal thoracic artery revascularization: Propensity and risk modeling. *J Am Coll Cardiol* 2001; **37**: 521–528.
7. Tector AJ, Mc Donald ML, Kress DC, Downey FX, Schmahl TM. Purely internal thoracic artery grafts: Outcomes. *Ann Thorac Surg* 2001; **72**: 450–455.
8. Suma H, Fukumoto H, Takeuchi A. Coronary artery bypass grafting by utilizing in situ right gastroepiploic artery: Basic study and clinical application. *Ann Thorac Surg* 1987; **44**: 394–397.
9. Mills NL, Everson CT. Right gastroepiploic artery: A third arterial conduit for coronary bypass. *Ann Thorac Surg* 1989; **47**: 706–711.
10. Acar C, Jebara VA, Portoghese M, Beyssen B, Pagny JY, Grare P, et al. Revival of the radial artery for coronary artery bypass grafting. *Ann Thorac Surg* 1992; **54**: 652–660.
11. Tatoulis J, Royse AG, Buxton BF, Fuller JA, Skillington PD, Goldblatt JC, et al. The radial artery in coronary surgery: A 5-year experience-clinical and angiographic results. *Ann Thorac Surg* 2002; **73**: 143–148.
12. Vincent JG, van Son JAM, Skotnicki SH. Inferior epigastric artery as a conduit in myocardial revascularization: The alternative free arterial graft. *Ann Thorac Surg* 1990; **49**: 323–325.
13. Perrault LP, Carrier M, Hebert Y, Cartier R, Leclerc Y, Pelletier LC. Early experience with the inferior epigastric artery in coronary artery bypass grafting: A word of caution. *J Thorac Cardiovasc Surg* 1993; **106**: 928–930.
14. Carpentier A, Guermontprez JL, Deloche A, Frechette C, DuBost C. The aorta-to-coronary radial artery bypass graft: A technique avoiding pathological changes in grafts. *Ann Thorac Surg* 1973; **16**: 111–121.
15. Curtis JJ, Stoney WS, Alford WC Jr, Burrus GR, Thomas CS Jr. Intimal hyperplasia: A cause of radial artery aortocoronary bypass graft failure. *Ann Thorac Surg* 1975; **20**: 628–635.
16. Kobayashi J, Tagusari O, Bando K, Niwaya K, Nakajima H, Ishida M, et al. Total arterial off-pump coronary revascularization with only ITA and composite radial artery grafts. *Heart Surg Forum* 2002; **6**: 30–37.
17. Tagusari O, Kobayashi J, Bando K, Niwaya K, Nakajima H, Ishida M, et al. Total arterial off-pump coronary artery bypass grafting for revascularization of the total coronary system: The clinical outcome and angiographic evaluation. *Ann Thorac Surg* 2004; **78**: 1304–1311.



18. Abu-Omar Y, Mussa S, Anastasiadis K, Steel S, Hands L, Taggart DP. Duplex ultrasonography predicts safety of radial artery harvest in the presence of an abnormal Allen test. *Ann Thorac Surg* 2004; **77**: 116–119.
19. Greene MA, Malias MA, Fuller JA. Arm complications after radial artery procurement for coronary bypass operation. *Ann Thorac Surg* 2001; **72**: 126–128.
20. Budillon AM, Nicolini F, Agostinelli A, Beghi C, Pavesi G, Fragnito C, et al. Complications after radial artery harvesting for coronary artery bypass grafting: Our experience. *Surgery* 2003; **133**: 283–287.
21. Ronan JW, Perry LA, Barner HB, Sundt TM III. Radial artery harvest: Comparison of ultrasonic dissection with standard technique. *Ann Thorac Surg* 2000; **69**: 113–114.
22. He GW, Yang CQ. Vasorelaxant effect of phosphodiesterase-inhibitor milrinone in the human radial artery used as coronary bypass graft. *J Thorac Cardiovasc Surg* 2000; **119**: 1039–1045.
23. He GW, Yang CQ. Use of verapamil and nitroglycerin solution in preparation of radial artery coronary bypass grafting. *J Thorac Cardiovasc Surg* 1996; **61**: 610–614.
24. Mussa S, Guzik TJ, Black E, Dipp MA, Channon KM, Taggart DP. Comparative efficacies and durations of action of phenoxybenzamine, verapamil/nitroglycerin solution, and papaverine as topical antispasmodics for radial artery coronary bypass grafting. *J Thorac Cardiovasc Surg* 2003; **126**: 1789–1805.
25. Endo M, Nishida H, Tomizawa Y, Kasanuki H. Benefit of bilateral over single internal mammary artery grafts for multiple coronary artery bypass grafting. *Circulation* 2001; **104**: 2164–2170.
26. Berreklouw E, Rademakers PP, Koster JM, van Leur L, van der Wielen BJ, Westers P. Better ischemic event-free survival after two internal thoracic artery grafts: 13 years of follow-up. *Ann Thorac Surg* 2001; **72**: 1535–1541.
27. Stevens LM, Carrier M, Perrault LP, Hébert Y, Cartier R, Bouchard D, et al. Single versus bilateral internal thoracic artery grafts with concomitant saphenous vein grafts for multivessel coronary artery bypass grafting: Effects on mortality and event-free survival. *J Thorac Cardiovasc Surg* 2004; **127**: 1408–1415.
28. Grossi EA, Esposito R, Harris LJ, Croke GA, Galloway AC, Colvin SB, et al. Sternal wound infections and use of internal mammary artery grafts. *J Thorac Cardiovasc Surg* 1991; **102**: 342–347.
29. Matsa M, Paz Y, Gurevich J, Shapira I, Kramer A, Pevny D, et al. Bilateral skeletonized internal thoracic artery grafts in patients with diabetes mellitus. *J Thorac Cardiovasc Surg* 2001; **121**: 668–674.
30. Cohen G, Tamariz MG, Sever JY, Liaghati N, Guru V, Christakis GT, et al. The radial artery versus the saphenous vein graft in contemporary CABG: A case match study. *Ann Thorac Surg* 2001; **71**: 180–186.
31. Zacharias A, Habib RH, Schwann TA, Riordan CJ, Durham SJ, Shah A. Improved survival with radial artery versus vein conduits in coronary bypass surgery with left internal thoracic artery to left anterior descending artery grafting. *Circulation* 2004; **109**: 1489–1496.
32. Calafiore AM, Di Mauro M, D'Alessandro S, Teodori G, Vitolla G, Contini M, et al. Revascularization of the lateral wall: Long-term angiographic and clinical results of radial artery versus right internal thoracic artery grafting. *J Thorac Cardiovasc Surg* 2002; **123**: 225–231.
33. Lemma M, Gelpi G, Mangini A, Vanelli P, Carro C, Condemi A, et al. Myocardial revascularization with multiple arterial grafts: Comparison between the radial artery and the right internal thoracic artery. *Ann Thorac Surg* 2001; **71**: 1969–1973.
34. Suma H, Tanabe H, Takahashi A, Horii T, Isomura T, Hirose H, et al. Twenty year experience with the gastroepiploic artery graft for CABG. *Circulation* 2007; **116**(Suppl I): I-188–I-191.
35. Hashimoto H, Isshiki T, Ikari Y, Hara K, Sacki F, Tamura T, et al. Effect of competitive blood flow on arterial graft patency and diameter: Medium-term postoperative follow-up. *J Thorac Cardiovasc Surg* 1996; **111**: 399–407.
36. Shimizu T, Suesada H, Cho M, Ito S, Ikeda K, Ishimaru S. Flow capacity of gastroepiploic artery versus vein grafts for intermediate coronary artery stenosis. *Ann Thorac Surg* 2005; **80**: 124–130.
37. Ochi M, Hatori N, Fujii M, Saji Y, Tanaka S, Honma H. Limited flow capacity of the right gastroepiploic artery graft: Postoperative echocardiographic and angiographic evaluation. *Ann Thorac Surg* 2001; **71**: 1210–1214.
38. Suma H, Tanabe H, Yamada J, Mikuriya A, Horii T, Isomura T. Midterm results for use of the skeletonized gastroepiploic artery graft in coronary artery bypass. *Circ J* 2007; **71**: 1503–1505.
39. Asai T, Tabata S. Skeletonization of the right gastroepiploic artery using an ultrasonic scalpel. *Ann Thorac Surg* 2002; **74**: 1715–1717.
40. Gagliardotto P, Coste P, Lazreg M, Dor V. Skeletonized right gastroepiploic artery used for coronary artery bypass grafting. *Ann Thorac Surg* 1998; **66**: 240–242.
41. Amano A, Li R, Hirose H. Off-pump coronary artery bypass using skeletonized gastroepiploic artery, a pilot study. *Heart Surg Forum* 2004; **7**: 101–104.
42. Verma S, Szmilko PE, Weisel RD, Bonneau D, Latter D, Errett L, et al. Should radial arteries be used routinely for coronary artery bypass grafting? *Circulation* 2004; **110**: e40–e46.
43. Royse AG, Royse CF, Ttoulis J, Grigg LE, Shah P, Hunt D, et al. Postoperative radial artery angiography for coronary artery bypass surgery. *Eur J Cardiothorac Surg* 2000; **17**: 294–304.
44. Nakajima H, Kobayashi J, Tagusari O, Bando K, Niwaya K, Kitamura S. Competitive flow in arterial composite grafts and effect of graft arrangement in off-pump coronary revascularization. *Ann Thorac Surg* 2004; **78**: 481–486.
45. Lemma M, Mangini A, Gelpi G, Innorta A, Spina A, Antona C. Is it better to use radial artery as a composite graft? Clinical and angiographic results of aorta-coronary versus Y-graft. *Eur J Cardiothorac Surg* 2004; **26**: 110–117.
46. Yie K, Na C, Oh SS, Kim J, Shinn S, Seo H. Angiographic results of the radial artery graft patency according to the degree of native coronary stenosis. *Eur J Cardiothorac Surg* 2008; **33**: 341–348.
47. Maniar HS, Barner HB, Bailey MS, Prasad SM, Moon MR, Pasque MK, et al. Radial artery patency: Are aortocoronary conduits superior to composite grafting? *Ann Thorac Surg* 2003; **76**: 1498–1504.
48. Gaudino M, Alessandrini F, Pragliola C, Cellini C, Glieca F, Luciani N, et al. Effect of target artery location and severity of stenosis on midterm patency of aorta-anastomosed vs internal artery-anastomosed radial artery grafts. *Eur J Cardiothorac Surg* 2004; **25**: 424–428.
49. Nakajima H, Kobayashi J, Tagusari O, Niwaya K, Funatsu T, Kawamura A, et al. Angiographic flow grading and graft arrangement of arterial conduits. *J Thorac Cardiovasc Surg* 2006; **132**: 1023–1029.
50. Nakajima H, Kobayashi J, Tagusari O, Bando K, Niwaya K, Kitamura S. Functional angiographic evaluation of individual, sequential, and composite arterial grafts. *Ann Thorac Surg* 2006; **81**: 807–814.
51. Maniar HS, Sundt TM, Barner HB, Prasad SM, Peterson L, Absi T, et al. Effect of target stenosis and location on radial artery graft patency. *J Thorac Cardiovasc Surg* 2002; **123**: 45–52.
52. Légaré JF, Buth KJ, Sullivan JA, Hirsch GM. Composite arterial grafts versus conventional grafting for coronary artery bypass grafting. *J Thorac Cardiovasc Surg* 2004; **127**: 160–166.
53. Shah PJ, Durairaj M, Gordon I, Fuller J, Rosalion A, Seevanayagam S, et al. Factors affecting patency of internal thoracic artery graft: Clinical and angiographic study in 1434 symptomatic patients operated between 1982 and 2002. *Eur J Cardiothorac Surg* 2004; **26**: 118–124.
54. Shah PJ, Bui K, Blackmore S, Gordon I, Hare DL, Fuller J, et al. Has the in situ right internal thoracic artery been overlooked? An angiographic study of the radial artery, internal thoracic arteries and saphenous vein graft patencies in symptomatic patients. *Eur J Cardiothorac Surg* 2005; **27**: 870–875.
55. Calafiore AM, Di Giammarco G, Teodori G, D'Annunzio E, Vitolla G, Fino C, et al. Radial artery and inferior epigastric artery in composite grafts: Improved midterm angiographic results. *Ann Thorac Surg* 1995; **60**: 517–523.
56. da Costa FD, da Costa IA, Poffo R, Abuchaim D, Gaspar R, Garcia L, et al. Myocardial revascularization with the radial artery: A clinical and angiographic study. *Ann Thorac Surg* 1996; **62**: 475–480.
57. Brodman RF, Frame R, Camacho M, Hu E, Chen A, Hollinger I, et al. Routine use of unilateral and bilateral radial arteries for coronary artery bypass graft surgery. *J Am Coll Cardiol* 1996; **28**: 959–963.
58. Chen AH, Nakao T, Brodman RF, Greenberg M, Charney R, Menegus M, et al. Early postoperative angiographic assessment of radial artery grafts used for coronary artery bypass grafting. *J Thorac Cardiovasc Surg* 1996; **111**: 1208–1212.
59. Possati G, Gaudino M, Alessandrini F, Luciani N, Glieca F, Trani C, et al. Midterm clinical and angiographic results of radial artery grafts used for myocardial revascularization. *J Thorac Cardiovasc Surg* 1998; **116**: 1015–1021.
60. Tattoulis J, Buxton BF, Fuller JA. Bilateral radial artery grafts in coronary reconstruction: Technique and early results in 261 patients. *Ann Thorac Surg* 1998; **66**: 714–720.
61. Acar C, Ramsheyyi A, Pagny J, Jebara V, Barrier P, Fabiani J, et al. The radial artery for coronary artery bypass grafting: Clinical and angiographic results at five years. *J Thorac Cardiovasc Surg* 1998; **116**: 981–989.
62. Bhan A, Gupta V, Choudhary SK, Sharma R, Singh B, Aggarwal R, et al. Radial artery in CABG: Could the early results be compatible to internal mammary artery graft? *Ann Thorac Surg* 1999; **67**: 1631–1636.

63. Amano A, Hirose H, Takahashi A, Nagano N. Coronary artery bypass grafting using the radial artery: Midterm results in Japanese institute. *Ann Thorac Surg* 2001; **72**: 120–125.
64. Iacò AL, Teodori G, Di Giammarco G, Di Mauro M, Storto L, Mazzei V, et al. Radial artery for myocardial revascularization: Long-term clinical and angiographic results. *Ann Thorac Surg* 2001; **72**: 464–469.
65. Possati G, Gaudino M, Prati F, Alessandrini F, Trani C, Glieca F, et al. Long-term results of the radial artery used for myocardial revascularization. *Circulation* 2003; **108**: 1350–1354.
66. Cameron J, Trivedi S, Stafførd G, Bett JH. Five-year angiographic patency of radial artery bypass grafts. *Circulation* 2004; **110**(Suppl II): II-23–II-26.
67. Zacharias A, Habib RH, Schwann TA, Riordan CJ, Durham SJ, Shah A. Improved survival with radial artery versus vein conduit in coronary bypass surgery with left internal thoracic artery to left anterior descending artery graft. *Circulation* 2004; **109**: 1489–1496.
68. Khot UN, Friedman DT, Pettersson G, Smedira NG, Li J, Ellis SG. Radial artery bypass grafts have an increased occurrence of angiographically severe stenosis and occlusion compared with left internal mammary arteries and saphenous vein grafts. *Circulation* 2004; **109**: 2086–2091.
69. Desai ND, Cohen EA, Naylor CD, Fremes SE; Radial Artery Patency Study Investigators. A randomized comparison of radial-artery and saphenous vein coronary bypass grafts. *N Engl J Med* 2004; **351**: 2302–2309.
70. Nakajima H, Kobayashi J, Funatsu T, Shimahara Y, Kawamura M, Kawamura A, et al. Predictive factors for the intermediate-term patency of arterial grafts in aorta no-touch off-pump coronary revascularization. *Eur J Cardiothorac Surg* 2007; **32**: 711–717.
71. Desai ND, Naylor CD, Kiss A, Cohen EA, Feder-Elituv R, Miwa S, et al. Impact of patient and target-vessel characteristics on arterial and venous bypass graft patency: Insight from a randomized trial. *Circulation* 2007; **115**: 684–691.
72. Singh SK, Desai ND, Petroff SD, Deb S, Cohen EA, Radhakrishnan S, et al. The impact of diabetic status on coronary artery graft patency: Insights from the radial artery patency study. *Circulation* 2008; **118**(Suppl 1): S222–S225.
73. Buxton BF, Raman JS, Ruengsakulrach P, Gordon I, Rosalion A, Bellomo R, et al. Radial artery patency and clinical outcomes: Five-year interim results of a randomized trial. *J Thorac Cardiovasc Surg* 2003; **125**: 1363–1371.
74. Collins P, Webb CM, Chong CF, Moat NE; Radial Artery Versus Saphenous Vein Patency (RSVP) Trial Investigators. Radial artery versus saphenous vein patency randomized trial: Five-year angiographic follow-up. *Circulation* 2008; **117**: 2859–2864.
75. Muneretto C, Negri A, Manfredi J, Terrini A, Rodella G, ELQarra S, et al. Safety and usefulness of composite grafts for total arterial myocardial revascularization: A prospective randomized evaluation. *J Thorac Cardiovasc Surg* 2003; **125**: 826–835.
76. Damgaard S, Wetterslev J, Lund JT, Lilleør NB, Perko MJ, Kelbæk H, et al. One-year results of total arterial revascularization vs conventional coronary surgery: CARRPO trial. *Eur Heart J* 2009; **30**: 1005–1011.

## 虚血性僧帽弁閉鎖不全症

小林順二郎

### はじめに

日本胸部外科学会の統計によると、冠動脈バイパス (CABG) 単独手術は薬物溶出ステントの導入により、経皮的冠動脈インターベンション (PCI) が激増して、2003年の約22,000例をピークに2006年までに約18,000例と20%減少した(表1)。一方、虚血性僧帽弁閉鎖不全 (IMR) に対する手術症例数は、2003年の220例から、2006年の332例へと1.5倍増加している。手術死亡率も、単独CABGの1.5%に比べて6~8%と高く、心臓外科医に残された数少ないチャレンジングな領域となっている。

本稿では、このIMRの重要性と治療法について述べる。

### I. 虚血性僧帽弁閉鎖不全の原因および重要性

IMRの原因は、側壁あるいは後下壁の心筋梗塞や心室線維化によるremodelingのため

#### Key word

ischemic heart disease  
mitral regurgitation  
cardiac surgery  
congestive heart failure  
left ventricular remodeling

#### Ischemic Mitral Regurgitation

Junjiro Kobayashi :  
Department of Cardiovascular Surgery,  
National Cardiovascular Center  
国立循環器病センター 心臓血管外科

に起こる左室拡大と、僧帽弁輪拡大に加えて乳頭筋が偏位し、これ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(図1)<sup>1)</sup>。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を増大させる悪循環を来す。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。

IMRは機能的MRとも呼ばれ、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、虚血性心疾患の10~20%、虚血性心筋症による心不全患者の半数以上に認められ、MRの無い患者の予後に比して2~10倍不良である<sup>2,3)</sup>。

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<sup>2</sup>と器質的MRでは軽度とされる患者においても、MRの無い患者に比べて予後が悪いことが問題である(図2)<sup>4)</sup>。IMRはその頻度と予後から考えて、非常に重要な疾患であるが、循環器内科医の認識は低く、心臓外科への紹介も少ないため、多数の経験を有する施設は少ない。

### II. 虚血性僧帽弁閉鎖不全の手術適応と単独CABGの効果

中等度のIMRを有する患者において、CABGと同時に僧帽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

表1. 本邦における冠動脈バイパス手術と虚血性僧帽弁閉鎖不全に対する外科治療成績

年度	2002年	2003年	2004年	2005年	2006年
単独冠動脈バイパス術総数	21,626	21,046	19,930	18,054	17,941
病院死亡率	2.7%	2.9%	2.8%	3.1%	2.7%
虚血性MRに対する手術					
弁形成術総数	N/A	188	238	261	270
弁置換術総数	N/A	26	41	55	36
全症例数	193	220	287	323	332
病院死亡率	7.3%	5.5%	8.0%	7.2%	7.4%

単独冠動脈バイパス術は減少しているが、虚血性MRに対する症例数は増加傾向にある。病院死亡率は、両者とも大きな変化は無い。

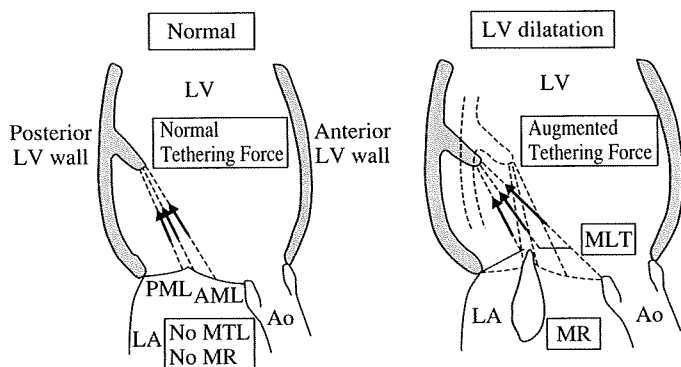


図1. 虚血性僧帽弁閉鎖不全の発生機序  
心筋梗塞や心室線維化による remodeling のために乳頭筋が偏位し、僧帽弁の腱索を左室内に引き込んで tethering を起こし、弁輪拡大が加わって、両弁尖の接合が不良となることで発生する。

LV：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  
(文献1より改変)

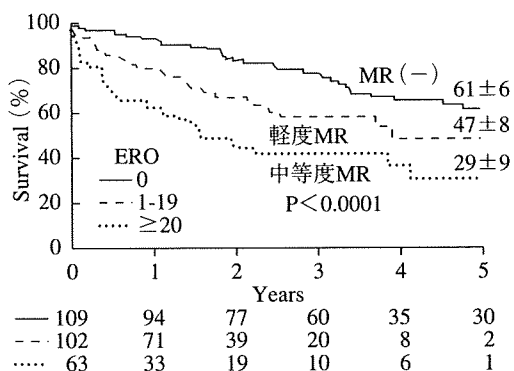


図2. 梗塞後MRの有無と重症度による生命予後  
MRの有無とその程度により、生命予後に差がある。逆流孔面積(ERO)が20mm<sup>2</sup>と器質的MRでは軽度とされる患者においても予後が悪い。

(文献3より改変)

しないとの報告が多い。Aklogら<sup>4)</sup>は、中等度のIMRに対して、CABGのみを行った場合に、51%では軽度になるが<sup>5)</sup>、40%の症例で不変か悪化し、術中の経食道エコーでの評価は過小評価で、信頼性に欠けると報告している。我々も、中等度のIMRに対してCABGのみを行った場合に、46%の症例で不変か悪化し、10年の生存率55%、心事故回避率49%にとどまることを報告している<sup>6)</sup>。心事故発生の危険因子としては、左室駆出率30%未満、術後早期からの2/4度以上のMR、下壁梗塞の無いこと、左内胸動脈の非使用であった。同様に、Schroderら<sup>6)</sup>は、術中食道エコーで軽度以上のIMRがあればMRが無いが、わずかの症例に比べて1.34倍