

と静脈グラフトを使用した症例は、静脈グラフトのみの症例と比較して、早期死亡率を抑制するとされている<sup>18)</sup>。また、完全血行再建については、その有効性を認める報告と、有効でないとする報告があり、この点には議論の余地があり<sup>19, 20)</sup>、現時点では手術の安全を最大限考慮すべきものと考えられる。

Off-pump CABGの有効性についてのprospectiveな比較は報告されていないが、retrospectiveな比較においては、on-pump CABGと比較して手術死亡、術後脳梗塞、呼吸不全の発生頻度が低く、入院期間も短かったとされ<sup>21)</sup>、一般にoff-pump CABGの高齢者に対する有効性は認知されていると考えてよい。また、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懸念が大きい<sup>22)</sup>。加えて、当センターのCABG後のフォローでも、累積生存率は5年で50%以上で、長期生存例もまれではないことを考慮すると、上行大動脈吻合を要する静脈グラフトを安易に選択するべきではない。

これらのことから、高齢者は、off-pump CABGで、なおかつ大動脈に手術操作を行わないaorta no-touch術式の最も良い適応と考えられる。

## 女性

一般に女性は男性と比較して、CABGの手術リスクが高いとされている。女性がハイリスクである理由は、純粋に性別による影響なのか、もしくは女性がしばしば持ち合わせるCABGに不利な背景によるものなのかは、必ずしも明らかではない。具体的には、女性は体格的に男性より小さく、冠動脈も狭小であることから平均バイパス本数も少ないこと、内胸動脈もしくは両側内胸動脈グラフトの使用頻度が低いこと、糖尿病、高血圧、不安定狭心症の合併頻度が高いこと、さらには、手術時年齢などが関連して

いることが挙げられる。現在までのところ、グラフトや手術方法などのCABG治療方針について、性別をどのように反映させるべきかについては結論が出ていない。

## 糖尿病

糖尿病例においては、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とから、外科治療に困難を伴うこともしばしばである。しかしながら、これまでの大規模studyの結果によれば、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、糖尿病の合併は、好ましい治療法としてPCIより外科的な血行再建を選択する根拠となっている。

しかし一方で、外科的な血行再建には胸骨や創傷治癒遅延の問題があり、これはCABG術後の縦隔炎など深部感染症のリスクとなる。STSデータベースによれば、深部感染の頻度は1%未満であるが、発症後の死亡率は20%とも報告されている<sup>23)</sup>。縦隔炎と関連する術前因子としては、糖尿病とともに、肥満、再手術、慢性透析などが指摘されている<sup>24-26)</sup>。両側内胸動脈の使用についても、治癒遅延の原因になると広く考えられているが<sup>27, 28)</sup>、最近になり、内胸動脈の採取方法によっては治癒遅延に影響しないとする報告もされるようになってきている<sup>29)</sup>。縦隔炎に際しては、人工呼吸期間3日以上になると予後は不良で、縦隔炎例の長期生存率も不良である<sup>23)</sup>。

糖尿病には、しばしばびまん性に狭小化した冠動脈が見られる(図4)。当センターでは、off-pump CABGにおいて、狭小冠動脈に対しても積極的に吻合を行っており、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。術後早期のグラフト造影の結果によれば、off-pump CABGであっても、狭小冠動脈への動脈グラフトによるバイパスの

開存率および吻合部の形態は良好であった<sup>30)</sup>。一方で、静脈グラフトは有意に開存率が低かった。また、動脈グラフトの長期開存のために必須であるグラフト血流についての検討によれば、competitive flowの発生は、狭小冠動脈枝と内径1.5mm以上の冠動脈枝とでは、全く同等の頻度であった<sup>31, 32)</sup>。このことから、たとえ狭

小冠動脈であっても、狭窄が中等度の場合にはこの点を十分に留意し、グラフトのデザインや使用方法を決定すべきと考えられる。

### 再CABG

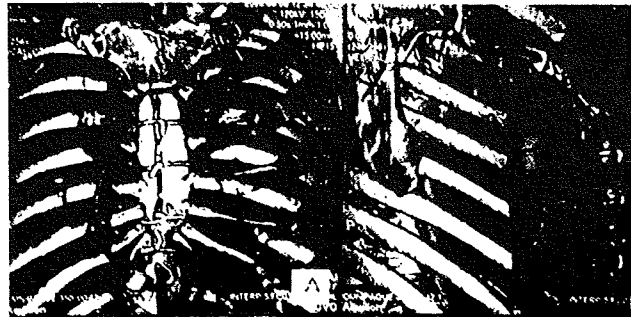
初回CABG手術と比較すると、再CABGでは、重症度や心拡大、癒着剥離のため人工心肺が必要となることが多く、手術リスクも高い。開存グラフトの存在が開胸、癒着剥離時に問題となることがしばしばで、最近の内胸動脈の多用がこの背景にある。このような症例に対しては、左冠動脈領域を標的とする場合には左開胸から、右冠動脈の末梢を標的とする際には胃大網動脈を用いての経腹腔的なアプローチも考慮すべきである。図5のように、胸骨後面に密着する開存内胸動脈グラフトがあり、左前下行枝へのバイパスを要する症例に対して、MIDCABによる内胸動脈-前下行枝バイパスは極めて有用である。

また、再手術の多くは静脈グラフトの狭窄や閉塞に伴うものであるが、現在は動脈グラフト、特にin-situ内胸動脈を使用することが多い。こういった場合の新たな問題としては、開存静脈グラフトの存在による、動脈グラフトでのcompetitive flowの発生が挙げられる。これは、通常上行大動脈に吻合された静脈グラフトは、鎖骨下動脈からの内胸動脈よりグラフトの内圧



■ 図4 糖尿病インスリン療法中の女性患者の術後グラフト造影

回旋枝、右冠動脈領域の狭小冠動脈枝4本に対して、撓骨動脈によるsequential吻合を行った。各枝1本1本への流量は少なく、静脈グラフトでは高い開存率は期待できない。動脈グラフトを第1選択として使用することで、外科治療のメリットをより生かすことができる。



■ 図5 再冠動脈バイパス手術例の術前造影CT  
胸骨後面のほぼ正中に、開存内胸動脈が癒着している。

が高いため, 特に静脈グラフトの狭窄が軽度の場合には新たに吻合された動脈グラフトの血流量が不十分となるものである。結果として期待される長期開存が得られず, 比較的早期の閉塞となってしまう懸念がある。

### グラフトの制限

近年, 動脈グラフトの長期開存のメリットが明らかとなり, 全動脈グラフトの完全血行再建が標準的となってきている。つまり, 動脈グラフトの使用を制限せざるを得ないことは, 新たなリスクとみなされ得る。腹部臓器疾患との合併例や, 橈骨動脈経路のカテーテルの増加により, グラフト使用が制限される機会は増えつつある。

高齢者やインスリン療法を要する糖尿病による両側内胸動脈使用の不可もしくは回避と, 腎機能障害やAllen testによる橈骨動脈の使用の不可もしくは回避が, 大伏在静脈グラフト使用の主な理由で, これ以外の症例では基本的に, 動脈グラフトのみでの十分な血行再建が可能であった。2000年以降の当センターでのデータでは, 全例off-pumpでのCABGの静脈グラフトの開存率は術後早期のカテーテル検査で94%と比較的良好であった。しかしながら5年後の生存率は約80%と予後が比較的不良で, その死亡原因としては, 約3/4近くは心臓以外の疾患(腎不全, 動脈瘤や肺炎など)によること, さらに完全血行再建例と不完全血行再建例の予後を比較すると完全血行再建のメリットは明らかでなかった。このことから, これらの患者群については, 必ずしも完全動脈グラフトに固執する必要はないと考えられる。

### 大動脈弁狭窄症

虚血性心疾患には, しばしば大動脈弁狭窄症の合併が見受けられる。2000年以降, 大動脈弁硬化の進行を伴う大動脈弁狭窄症に対する弁置

換術を同時に施行すべきかについては, 手術成績の向上, 弁狭窄の進行が速い症例があること, CABG後の再手術のリスクなどを考慮して, より中等度から軽度の大動脈弁狭窄に対してもCABGと同時に弁置換を行う傾向にある<sup>33-35)</sup>。

CABGと同時に弁置換を行う際のバイパスグラフト材料については, 通常は動脈グラフトを第1選択とするものの, 現時点では確立されたエビデンスがあるわけではない。逆に, 左室心筋の著明なhypertrophyに対して, 内胸動脈のflow capacityの不十分さの危惧もあり得る。この点について, 当センターにて大動脈弁置換とCABGを同時に施行した症例の遠隔期成績の検討によれば, 大動脈弁に機械弁を使用するか生体弁を使用するかでは予後に差を認めないのに対し, 動脈グラフト使用と不使用での比較では, 当然ながら両群の患者背景や手術時期に違いはあるものの, 使用群は不使用群より生命予後が有意に良好であった。大動脈弁置換と同時に行うCABGに際しても, やはり動脈グラフトの使用が推奨される結果となっている。

### 悪性腫瘍

悪性腫瘍の予後は一概に悪いとは限らないが, この存在は長期予後に少なからず影響を与える。これらの疾患の手術成績への影響については必ずしも明らかではない。当センターにおける悪性腫瘍合併例の成績によると, 術後1ヵ月生存率は98%以上であり, 悪性腫瘍の存在や既往は手術そのもののリスクとは考えられず, 悪性腫瘍の存在のみを理由として心臓手術適応から直ちに外れるものではない。しかしながら, これらの生存例の中には, リンパ腫治療後に呈した出血傾向, 放射線治療によると思われる癒着で内胸動脈剥離に長時間を要したものや, 反復する胸水貯留, 乳がん乳房切除後の内胸動脈の狭小化など(図6), 手術への影響については症例ごとに検討する必要がある。しかし当然



■ 図6 CTによる術前内胸動脈の評価  
左乳房切除後で、同側の内胸動脈が狭小化している。

ながら、人工心肺のリスクとなる下大静脈への進展や悪性度の高い腫瘍の合併例については、むしろ内科的な治療も十分に考慮するべきである。

#### まとめ

冠血行再建については、高齢化やカテーテル治療の変化と共に、ハイリスク例の割合が高まっている。今後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、整理して、各患者の特徴に合わせた治療方針を選択することが重要と考えられる。

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# Brain natriuretic peptide concentration in pericardial fluid is independently associated with atrial fibrillation after off-pump coronary artery bypass surgery

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**Objectives** Postoperative atrial fibrillation is associated with the increased incidence of morbidities and mortality. Predisposing determinants of atrial fibrillation development after off-pump coronary artery bypass grafting remain unclear. We hypothesized that pericardial fluid natriuretic peptide concentrations have a predictive value for developing postoperative atrial fibrillation in patients who have undergone off-pump coronary artery bypass grafting.

**Methods** We prospectively measured atrial natriuretic peptide and brain natriuretic peptide concentrations in plasma and pericardial fluid in 42 consecutive patients undergoing off-pump coronary artery bypass grafting, then continuously observed the occurrence of atrial fibrillation following off-pump coronary artery bypass grafting until the time of discharge.

**Results** Postoperative atrial fibrillation was documented in nine patients (21%, atrial fibrillation group), and not in 33 patients (no atrial fibrillation group). Between the groups, there was neither significant difference in plasma atrial natriuretic peptide concentrations nor in pericardial atrial natriuretic peptide concentrations. Plasma brain natriuretic peptide concentrations were comparable in both groups [56.2 (interquartile range 42.7–102.8) vs. 35.2 pg/ml (13.8–75.0),  $P=0.07$ ]. Pericardial fluid brain natriuretic

peptide concentrations were significantly higher in the atrial fibrillation group than in the no atrial fibrillation group [188.0 (124.8–411.0) vs. 39.3 pg/ml (10.0–88.4),  $P=0.0001$ ]. In a multivariable logistic regression model, pericardial brain natriuretic peptide concentration was significantly associated with a higher risk of postoperative atrial fibrillation (odds ratio=3.0 every 50 pg/ml increase; 95% confidence interval, 1.1–8.6;  $P=0.04$ ).

**Conclusion** Our results suggested that pericardial fluid brain natriuretic peptide concentration is independently associated with the development of atrial fibrillation after off-pump coronary artery bypass grafting. *Coron Artery Dis* 18:253–258 © 2007 Lippincott Williams & Wilkins.

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**Keywords:** arrhythmia, coronary disease, natriuretic peptides, pericardial effusion, postoperative complications

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## Introduction

Postoperative atrial fibrillation (AF) is a common complication of coronary artery bypass grafting (CABG), and has been associated with the increased incidence of morbidities, such as stroke, congestive heart failure, renal insufficiency, severe infection, and overall costs, principally owing to the prolongation of the duration of hospitalization [1–4]. A recent study [5] has suggested that postoperative AF was an independent predictor of in-hospital and long-term mortality following CABG. Off-pump CABG [off-pump coronary artery bypass grafting (OPCAB)], bypass surgery on the beating heart without the use of a cardiopulmonary bypass, has been expected to reduce postoperative complications, including postoperative AF [6–8]. Postoperative AF, however, appears at a rate of approximately 10–40% after OPCAB [9], and

predisposing determinants of AF development after OPCAB remain unclear. Numerous studies have attempted to identify predictors of postoperative AF; however, only older age has consistently predicted a higher incidence of AF after the cardiac surgery [3,10–16]. Recently, plasma natriuretic peptide concentrations for the diagnosis of cardiovascular disease have been established [17,18]. Several biomarkers, including natriuretic peptides, in pericardial fluid have been considered potentially valuable to add diagnostic information for the cardiac disease [19]. Some reports have suggested that natriuretic peptide concentrations in pericardial fluid were associated with left ventricular dysfunction [20], anterior myocardial infarction [21], and a pulmonary-to-system flow ratio greater than two in patients with congenital heart disease [22]. The aim of our study was to

evaluate the potential usefulness of pericardial fluid natriuretic peptide concentrations as a predictor of the development of AF after OPCAB.

## Methods

### Patients and study protocol

In consecutive 9 months, all the patients ( $n = 64$ ) who had undergone OPCAB through the Department of Cardiovascular surgery at Kyoto Prefectural University of Medicine were eligible for the inclusion. Patients with chronic AF ( $n = 5$ ), a documented past history of paroxysmal AF ( $n = 1$ ), the presence of a permanent pacemaker ( $n = 2$ ), prescribed antiarrhythmic agents (except  $\beta$ -blockers) ( $n = 2$ ), significant valvular disease ( $n = 2$ ), and renal insufficiency [serum creatinine concentration  $> 2.0$  mg/dL ( $177 \mu\text{mol/l}$ )] ( $n = 3$ ) were excluded from the study. Patients with decompensated congestive heart failure ( $n = 1$ ) and acute coronary syndrome within 6 months ( $n = 2$ ) before OPCAB and emergent surgery ( $n = 2$ ) were also excluded. Among the 44 patients, two patients missed collection of pericardial fluid. Finally, 42 patients were analyzed in this study. All were clinically evaluated before operation with echocardiography and cardiac catheterization according to standard techniques. Blood samples for routine chemistry, thyroid hormones, and natriuretic peptides were drawn after their referral to OPCAB. Pericardial fluid samples for natriuretic peptides were obtained during OPCAB. The occurrence of the first postoperative AF was the study end point. All study patients gave written informed consent. The study protocol was approved by ethics committees on human research of Kyoto Prefectural University of Medicine.

### Definition of postoperative atrial fibrillation

Patients were placed on continuous cardiac monitoring during their hospital stay, and 12-lead electrocardiogram was obtained when necessary to confirm rhythm abnormalities. In this study, we defined postoperative AF as atrial fibrillation that fulfilled the following two criteria: (i) it occurred within 7 days after OPCAB and was confirmed by a standard 12-lead electrocardiogram; (ii) it required intervention because of symptoms or hemodynamical instability. Self-limiting AF did not account for postoperative AF.

### Preoperative cardiac parameters

The left atrial diameter (LAD) was measured by echocardiography at the end-ventricular systole when the left atrial chamber is at its greatest dimension. LAD was measured by M-mode linear dimension which was measured from the trailing edge of the posterior aortic wall to the leading edge of the posterior LA wall obtained from the parasternal long-axis view. The left ventricular ejection fraction (LVEF) was evaluated from left ventricular cineangiography in the right anterior oblique projection. End-diastolic and end-systolic volumes were

calculated by an area-length method. Left ventricular end-diastolic pressure (LVEDP) was obtained from a water-filled catheter placed in the left ventricle during cardiac catheterization.

### Sampling of plasma and pericardial fluid

Venous blood samples were withdrawn on the morning before the cardiac surgery. After 30 min of rest, about 10 ml of venous blood was drawn from a venous cannula in the forearm. The pericardial fluid samples were obtained by suction with a sterile disposable syringe immediately after the incision of the pericardium before heparinization. At least each 0.5 ml of pericardial fluid samples was necessary to measure ANP or BNP. Thus 1.0 ml of pericardial fluid was required for the measurement of both natriuretic peptide concentrations. All the pericardial fluid samples obtained from the 42 patients were sufficient amounts for assay.

These samples were transferred to sterile disposable tubes containing ethylenediaminetetraacetic acid (1 mg/ml) and centrifuged at  $3000g$  for 15 min and stored in sample tubes at  $-30^\circ\text{C}$  until use. Measurements of plasma and pericardial fluid concentrations of ANP and BNP were performed using an immunoradioactive assay with commercially available kits (Shionogi Co. Ltd., Osaka, Japan). All assays were performed in duplicate.

### Statistical analysis

Numerical data, except ANP concentrations and BNP concentrations are expressed as the mean  $\pm$  SD. Plasma and pericardial fluid ANP and BNP concentrations were not distributed normally. Thus, the results of plasma and pericardial fluid ANP and BNP concentrations are expressed as the median value (25–75th percentile range), and nonparametric analysis was used. All statistical analyses were performed using commercially available statistical software (STATVIEW version 5.0, SAS Institute Inc., Cary, North Carolina, USA). Comparison of the continuous data between two groups was determined using Student's  $t$ -test. The frequency data were compared with the  $\chi^2$  test. Comparison of pericardial fluid and plasma natriuretic peptide concentrations in each patient was determined using the Wilcoxon signed-rank test. The correlation between plasma and pericardial fluid natriuretic concentrations was determined with Spearman's rank test. The correlation between the clinical variables and natriuretic peptide concentrations was also determined with Spearman's rank test. Comparisons of plasma and pericardial fluid natriuretic concentrations between two groups were determined with Mann-Whitney  $U$ -tests. We performed multivariate logistic regression analysis to adjust the risk factors of postoperative AF. A  $P$  value of less than 0.05 was considered statistically significant.

## Results

### Development of postoperative atrial fibrillation

Postoperative AF was documented in nine patients (21%), and developed at  $3.7 \pm 1.0$  day after operation. Among the nine patients who developed postoperative AF, seven patients were restored to a normal sinus rhythm by intravenous antiarrhythmic agents, and two patients required direct current cardioversion. Patients were divided into two groups on the basis of whether or not they developed postoperative AF (AF group and no AF group, respectively).

### Patient characteristics

The baseline characteristics are presented in Table 1. AF patients were significantly older and had higher free thyroxine concentrations. No statistically significant differences were seen between the groups in sex distribution, severity of angina, numbers of diseased coronary vessels, or major traditional coronary risk factors. LAD, LVEF, LVEDP, and the proportion of preoperative use of  $\beta$ -blocker were also similar in both groups.

### Pericardial fluid and plasma natriuretic peptide

Pericardial fluid ANP concentrations were significantly lower than plasma ANP concentrations [15.0 (interquartile range 10.0–24.0) vs. 18.4 pg/ml (8.2–33.0),  $P = 0.012$ ], whereas pericardial fluid BNP concentrations were significantly higher than plasma BNP concentrations [59.4 (14.6–121.0) vs. 36.9 pg/ml (16.8–76.0),  $P = 0.023$ ]. Figure 1 shows the correlation of natriuretic peptide concentrations in plasma and in pericardial fluid. Pericardial fluid BNP concentrations significantly and positively correlated with plasma BNP concentrations ( $R_s = 0.448$ ,  $P = 0.004$ ). No significant correlation was, however, seen between pericardial fluid ANP concentrations and plasma ANP concentrations ( $R_s = 0.297$ ,  $P = 0.059$ ).

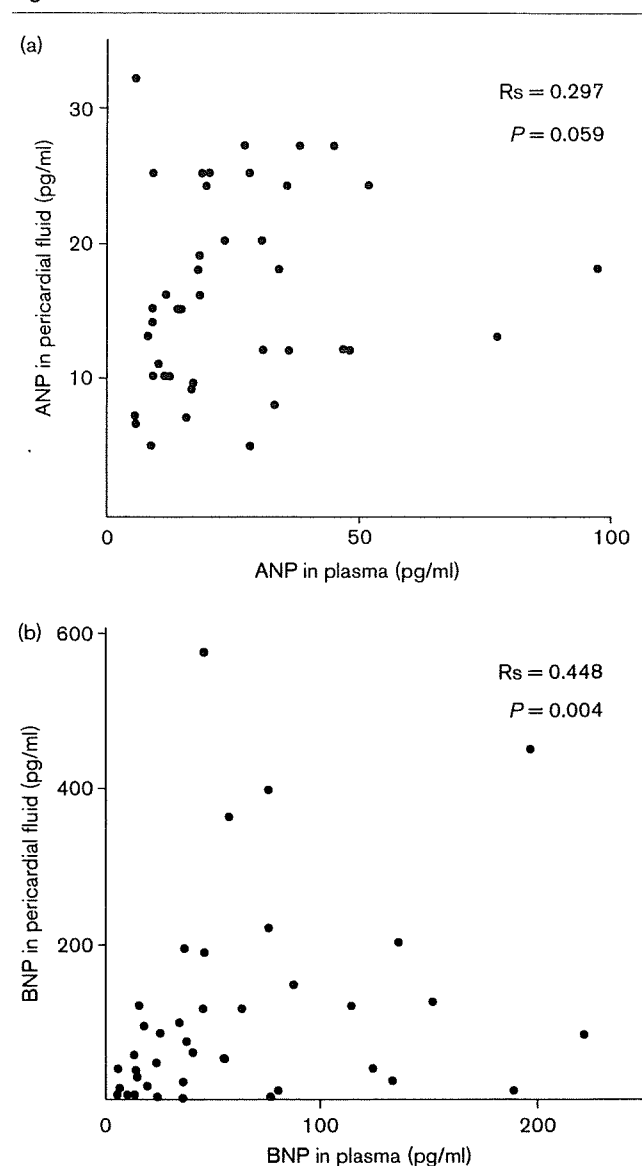
**Table 1** Patients' characteristics of both groups

	AF group (n=9)	No AF group (n=33)	P value
Age (years)	71 $\pm$ 6	63 $\pm$ 9	0.03
Men (%)	67	79	0.44
CCS class (I/II/III)	5/3/1	13/18/2	0.52
Diseased coronary arteries (1/2/3)	1/2/6	3/12/18	0.73
Hypertension (%)	33	64	0.10
Hyperlipidemia (%)	67	76	0.30
Diabetes mellitus (%)	56	39	0.39
TSH (mU/ml)	1.63 $\pm$ 1.11	2.22 $\pm$ 1.37	0.24
fT4 (ng/dl)	1.09 $\pm$ 0.21	0.95 $\pm$ 0.15	0.03
LAD (mm)	42.1 $\pm$ 4.7	39.8 $\pm$ 4.9	0.22
LVEF (%)	63.4 $\pm$ 13.6	66.0 $\pm$ 10.2	0.52
LVEDP (mmHg)	15.9 $\pm$ 4.0	13.5 $\pm$ 4.6	0.16
Beta-blocker use (%)	44	51	0.71

Data are presented as the mean value  $\pm$  SD or numbers or percentage of patients.

AF, atrial fibrillation; beta-blocker use, preoperative use of  $\beta$ -blocker; CCS class, Canadian Cardiovascular Society classification of angina pectoris; fT4, free thyroxine; LAD, left atrial diameter; LVEDP, left ventricular end diastolic pressure; LVEF, left ventricular ejection fraction; TSH, thyroid stimulating hormone.

**Fig. 1**



(a) Correlation of atrial natriuretic peptide concentrations in plasma and in pericardial fluid showing no significant correlation. (b) Correlation of brain natriuretic peptide concentrations in plasma and in pericardial fluid showing significant positive correlation.  $R_s$  indicates the Spearman's rank correlation coefficient. ANP, atrial natriuretic peptide; BNP, brain natriuretic peptide.

### Natriuretic concentrations and preoperative clinical parameters

Table 2 is a summary of the correlation between preoperative clinical variables and natriuretic peptide concentration in plasma or in pericardial fluid. A higher concentration of plasma and pericardial fluid BNP was significantly associated with older age. Plasma ANP concentrations, but not pericardial fluid ANP concentrations, showed a significant and weak-positive correlation with patient age and the LAD.

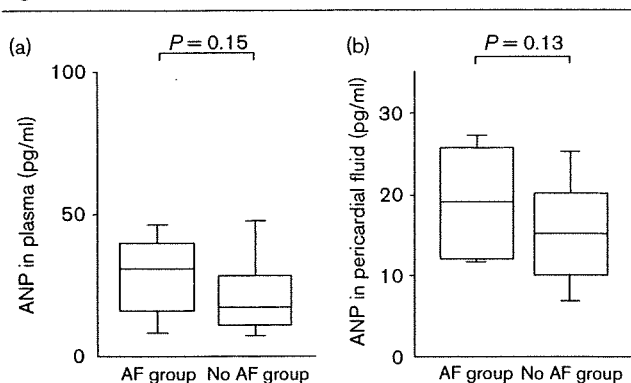


**Table 2 Correlation between clinical variables and plasma or pericardial fluid concentrations of atrial and brain natriuretic peptides**

	ANP in plasma		ANP in pericardial fluid		BNP in plasma		BNP in pericardial fluid	
	Coefficient	P value	Coefficient	P value	Coefficient	P value	Coefficient	P value
Age (years)	$R_s=0.364$	0.027	$R_s=0.264$	0.094	$R_s=0.480$	0.002	$R_s=0.486$	0.002
LAD (mm)	$R_s=0.362$	0.021	$-R_s=0.145$	0.344	$R_s=0.232$	0.138	$R_s=0.045$	0.778
LVEF (%)	$-R_s=0.150$	0.337	$-R_s=0.274$	0.076	$-R_s=0.225$	0.148	$-R_s=0.176$	0.259
LVEDP(mmHg)	$R_s=0.134$	0.402	$-R_s=0.021$	0.863	$R_s=0.249$	0.352	$R_s=0.247$	0.118

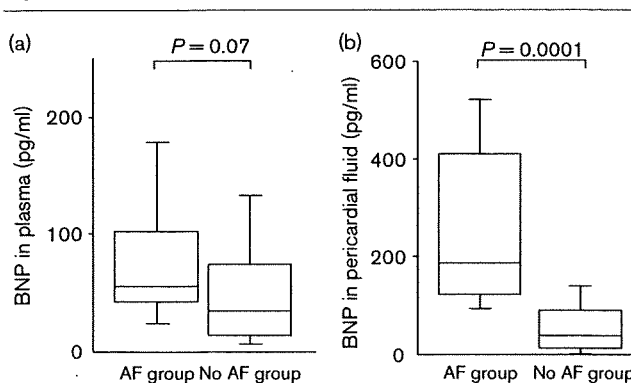
ANP, atrial natriuretic peptide; BNP, brain natriuretic peptide; LAD, left atrial diameter; LVEDP, left ventricular end diastolic pressure; LVEF, left ventricular ejection fraction;  $R_s$ , Spearman rank correlation coefficient.

**Fig. 2**



(a) Box plots of atrial natriuretic peptide (ANP) concentrations in plasma in the atrial fibrillation (AF) group and in the no AF group. (b) Box plots of ANP concentrations in plasma in the AF group and in the no AF group. The horizontal line in the box represents the median value; the boxed area is the interquartile range; and the whiskers are the 10–90% range.

**Fig. 3**



(a) Box plots of brain natriuretic peptide (BNP) concentrations in plasma in the atrial fibrillation (AF) group and in the no AF group. (b) Box plots of BNP concentrations in plasma in the AF group and in the no AF group. The horizontal line in the box represents the median value; the boxed area is the interquartile range; and the whiskers are the 10–90% range.

**Plasma and pericardial fluid natriuretic concentrations and postoperative atrial fibrillation**

Figure 2 shows plasma and pericardial fluid ANP concentrations in both groups. No significant difference was seen in plasma ANP concentrations between the AF

**Table 3 Multivariate predictors of postoperative atrial fibrillation**

Variables	OR	95% CI	P value
Age (1 year)	1.1	0.9–1.4	0.37
LAD (5 mm)	2.2	0.6–9.6	0.30
LVEF (5%)	0.7	0.3–1.6	0.40
LVEDP (1 mmHg)	1.0	0.7–1.4	0.94
ft4 (0.1 ng/dl)	1.3	0.5–3.0	0.40
Beta-blocker use (yes vs. no)	0.3	0.01–6.9	0.44
BNP in pericardial fluid (50 pg/ml)	3.0	1.1–8.6	0.04

Data are presented as odds ratio with 95% confidence intervals. OR, odds ratio of postoperative atrial fibrillation adjusted for age, LAD, LVEF, LVEDP, ft4,  $\beta$ -blocker use and BNP level in pericardial fluid. Beta-blocker use, preoperative use of  $\beta$  blocker; BNP, brain natriuretic peptide; CI, confidence interval; ft4, free thyroxine; LAD, left atrial diameter; LVEDP, left ventricular end diastolic pressure; LVEF, left ventricular ejection fraction; OR, odds ratio.

group and no AF group [30.6 (15.7–39.5) vs. 17.7 pg/ml (10.9–28.8),  $P=0.15$ ]. Pericardial fluid ANP concentrations between the AF group and no AF group [19.0 (12.0–25.5) vs. 15.0 pg/ml (9.9–20.0),  $P=0.13$ ] indicated no significant difference. Pericardial fluid and plasma BNP concentrations in both groups are presented in Fig. 3. Plasma BNP concentrations were comparable in both groups, with a higher trend in the AF group [56.2 (42.7–102.8) vs. 35.2 pg/ml (13.8–75.0),  $P=0.07$ ]. Pericardial fluid BNP concentrations were significantly higher in the AF group than in the no AF group [188.0 (124.8–411.0) vs. 39.3 pg/ml (10.0–88.4),  $P=0.0001$ ]. In a multivariable logistic regression model that was adjusted for age, LAD, LVEF, LVEDP, ft4, preoperative use of  $\beta$ -blocker and pericardial fluid BNP concentration, only the pericardial BNP concentration was associated with a higher risk of postoperative AF (odds ratio = 3.0 every 50 pg/ml increase; 95% CI, 1.1–8.6;  $P=0.04$ , Table 3).

**Discussion**

In this study, we found that pericardial fluid BNP concentration was an independent predictor for AF after OPCAB. To the best of our knowledge, no other study had shown that pericardial BNP concentration independently affected the risk of postoperative AF after OPCAB. Our result has shown that every 50 pg/ml increase of BNP concentration in pericardial fluid was associated with a three-fold increase in the odds of developing AF after OPCAB.

### Pericardial fluid and plasma natriuretic peptide

Pericardial fluid is mainly generated as an ultrafiltrate of plasma through the ventricular myocardium, including some overflow of the ventricular myocardial interstitial fluid and lymph. Therefore, pericardial fluid analysis is more sensitive in detecting increased substance synthesis and release into the myocardial interstitial fluid from ventricles than from atria [19]. The production of ANP takes place mainly in the atria, whereas BNP is produced both in the atria and in the ventricles [17,18]. Moreover, the higher concentrations of BNP and the lower concentrations of ANP in the pericardial fluid than in the plasma also suggest that BNP has a longer half-life in the pericardial fluid compared with in the plasma, and ANP has a shorter half-life in the pericardial fluid than in plasma [17,18]. A previous report [23] suggested that the affinity of the clearance receptor of ANP, which is expressed in a wide variety of tissues, was higher than that of BNP. These factors may partially be the reason why BNP concentrations were dominant in pericardial fluid, whereas ANP concentrations were dominant in plasma, and there was significant correlation between pericardial fluid concentrations and plasma concentrations of BNP, but not of ANP.

### Post operative atrial fibrillation and atrial natriuretic peptide in pericardial fluid and plasma

In this study, both pericardial fluid and plasma ANP concentrations were similar in the AF group and no AF group. The development of AF induced ANP production secondary to atrial stretch and atrial overload caused by AF [24]. Prolonged AF, by inflicting structural atrial damage, however, is associated with a reduced capacity to produce ANP [25]. In patients with mild congestive heart failure, Mabuchi and colleagues [26] revealed that high plasma BNP and relatively low plasma ANP compared with plasma BNP were independent risk factors of AF recurrence after direct current cardioversion. In another previous study [15] plasma ANP concentrations did not independently predict postoperative AF, with its markedly wide variation concentrations. Ellinor and colleagues [27] showed that plasma pro-ANP concentrations in the patients with paroxysmal AF without structural heart disease were similar to those in the control group. The primary pathophysiology of AF is confused by the secondary effect of the arrhythmia itself, and generally, the elevation of ANP concentrations has been considered to be the consequence of AF. The predictive value of plasma ANP concentrations for AF development is limited. Pericardial fluid ANP concentrations, which were significantly lower than plasma ANP concentrations, may have more limited additional information to predict postoperative AF.

### Postoperative atrial fibrillation and brain natriuretic peptide in pericardial fluid and plasma

Wazni and colleagues [14] have revealed plasma BNP concentrations to be a strong predictor for AF after cardiac

surgery. They suggested the common pathological and physiological changes associated with both the development of AF and increased BNP concentrations, such as age, atrial fibrosis, and increased left atrial pressure. In this study, pericardial fluid and plasma BNP concentrations were positively associated with patient age. Neither pericardial fluid BNP nor plasma BNP concentration, however, was associated with LVEDPs. In this study, LVEDPs were obtained by cardiac catheterization procedures that were performed several days or weeks before the surgery. Left atrial pressure is modified by intensive medical treatment before cardiac surgery, especially by depleting the cardiac preload. This may be the reason why the LVEDP data did not correlate with plasma and pericardial BNP concentrations that were obtained immediately before cardiac surgery. Higher pericardial fluid BNP concentrations may more accurately indicate higher left atrial pressure at the time of surgery than plasma BNP concentrations, and this may affect the development of postoperative AF. Other unknown common causes that synthesize BNP and result in AF after OPCAB were also suggested and pericardial fluid BNP concentrations possibly more accurately enhance this unknown common cause than plasma BNP concentrations.

### Clinical implication

Pericardial fluid can be collected easily, safely, and constantly in cases of open-heart surgery. Undergoing OPCAB, the measurement of pericardial fluid BNP concentrations may facilitate identifying patients at higher risk of developing postoperative AF. This may enable the treating physicians to initiate aggressive prophylactic therapy after OPCAB, such as administration of amiodarone. The prophylactic administration of amiodarone orally or intravenously has been shown to decrease the incidence of AF after CABG in higher risk patients [16,28,29]. Accurately identifying patients at higher risk of the development of postoperative AF will enable the decrease of the incidence of postoperative AF and to reduce the length of the stay, overall health care costs, and the morbidity associated with AF [16,28].

### Limitation

Firstly, the limitation of our study was the selection of patients. We selected patients who underwent OPCAB to limit the role of potential confounders, such as cardiopulmonary bypass and concomitant valvular surgery procedures. As we studied natriuretic peptide concentrations in participants with strictly defined criteria, limited numbers of the patients were included in our study. The larger study is warranted to duplicate our results and the further study is needed to amplify the results on various types of cardiac surgery. Second, in our study, self-limiting AF was not counted as postoperative AF. Therefore, the development of postoperative AF was probably underestimated. Self-limiting AF was sometimes missed,

however, even under continuous monitoring and in terms of the clinical implications of postoperative AF, self-limiting AF does not have clinical importance. We attempted to restore sinus rhythm when AF continued considerably to induced symptoms or hemodynamical instability. In this study, all the patients who were confirmed as AF by 12-leads electrocardiogram were required for intervention. The criteria for intervention for postoperative AF may differ at different institutions, and this may have affected the result. Third, our patient population had preserved cardiac function in terms of LVEF before surgery. This might affect the result that pericardial fluid BNP concentration was a stronger predictor than other preoperative parameters, especially plasma BNP, LVEF, and LVEDP. Fourth, unmeasured factors during operation or postoperative period, particularly hemodynamics, might affect development of AF after OPCAB. In this study, however, the issue was focused to identify predictors in preoperative parameters, which might be useful for risk stratification in preoperative period. Further study, including parameters during operation and postoperative period, is warranted.

### Conclusion

Our results suggested that the evaluation of pericardial fluid BNP concentration is independently associated with the development of AF after OPCAB.

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## Surgical ventricular restoration based on evaluation of myocardial viability with delayed-enhanced magnetic resonance imaging

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### Abstract

**Objective.** We examined whether the determination of myocardial viability by preoperative delayed-enhanced magnetic resonance imaging (DE-MRI) would be useful for planning surgical ventricular restoration (SVR).

**Methods.** Eight consecutive patients with poor cardiac function (ejection fraction <30%) due to ischemic cardiomyopathy underwent surgical treatment based on findings of preoperative cine-MRI and DE-MRI. Our surgical strategy consisted of (1) complete revascularization on viable segments; (2) SVR in a patient with extensive nonviable segments; and (3) mitral valve plasty in a patient with a more than moderate degree of mitral regurgitation. Based on the MRI assessments, four of the patients (group A) underwent isolated coronary bypass surgery, and the other four (group B) underwent SVR and mitral valve plasty concomitantly with coronary bypass surgery. Perioperative changes in ventricular function were quantitatively assessed in each group.

**Results.** The mean end-diastolic volume index was reduced from  $115 \pm 29 \text{ ml/m}^2$  to  $95 \pm 14 \text{ ml/m}^2$  in group A and from  $163 \pm 35 \text{ ml/m}^2$  to  $125 \pm 28 \text{ ml/m}^2$  in group B. The mean end-systolic volume index was reduced from  $91 \pm 25 \text{ ml/m}^2$  to  $68 \pm 16 \text{ ml/m}^2$  in group A and from  $135$

$\pm 36 \text{ ml/m}^2$  to  $98 \pm 28 \text{ ml/m}^2$  in group B. The mean ejection fraction increased from  $20\% \pm 6\%$  to  $28\% \pm 9\%$  in group A and from  $17\% \pm 6\%$  to  $22\% \pm 5\%$  in group B. The mean New York Heart Association (NYHA) functional class was reduced from  $3.0 \pm 0.8$  to  $1.8 \pm 0.6$  in group A and from  $3.5 \pm 0.5$  to  $2.2 \pm 0.2$  in group B.

**Conclusion.** DE-MRI was highly effective in helping to select which patients and which areas of the left ventricle are indicated for SVR, which contributed to excellent early clinical outcomes.

**Key words** Ischemic cardiomyopathy · Surgical ventricular restoration · Delayed-enhanced magnetic resonance imaging

### Introduction

Surgical ventricular restoration (SVR) is one of the important surgical treatments available as a nontransplantation therapy in patients with ischemic cardiomyopathy. Deciding whether to perform SVR and which area of the left ventricle (LV) should be excluded are critical issues to obtain good outcomes. For proper surgical planning, it is necessary to have accurate information on myocardial viability within dyssynergic ventricular walls.

Conventionally, dobutamine stress echocardiography or radionuclide studies have been used clinically to assess myocardial viability. However, radionuclide studies do not provide high spatial resolution, and dobutamine stress echocardiography cannot visualize all parts of the LV. Therefore, we eventually needed to decide whether to perform SVR and how much should be excluded by digital palpation of the LV walls or direct inspection of the areas during the operation.

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Delayed-enhanced magnetic resonance imaging (DE-MRI) is rapidly assuming a prominent role in the assessment of myocardial viability, as it is the only imaging modality that can reliably show the transmural extent of the infarcted myocardium. Kim et al. reported a strong relation between the transmural extent of the infarcted myocardium before revascularization and the likelihood of increased contractility after revascularization.<sup>1</sup>

Our hypotheses were as follows: (1) If patients have substantial myocardial viability even in the dilated LV, functional recovery could be obtained with revascularization alone. (2) By appropriate site selection based on accurate assessment of myocardial viability using DE-MRI, early and long-term outcomes could be improved after SVR. To this end, we assessed whether determining myocardial viability by preoperative DE-MRI would be useful when planning SVR.

## Methods

### Patient population

Eight consecutive patients (mean age  $60 \pm 7$  years) with poor cardiac function (ejection fraction  $<30\%$ ) due to ischemic cardiomyopathy underwent surgical treatment based on the results of assessments by preoperative cine-MRI and DE-MRI at our institution. The exclusion criteria were as follows: (1) contraindications for MRI assessment (i.e., pacemaker implantation in both preoperative and postoperative requirements, preoperative intraaortic balloon pumping, or percutaneous cardiopulmonary support use); and (2) emergency operation where MRI could not be performed preoperatively. The patients were divided into two groups according to the surgical procedure indicated based on the results of MRI assessments: isolated coronary artery bypass grafting (CABG)  $\pm$  mitral valve plasty (MVP) (group A) and SVR  $\pm$  MVP concomitant with CABG (group B). Perioperative changes in ventricular volume and function were studied quantitatively in the groups by MRI. Postoperative MRI was performed  $15 \pm 7$  days after the operation (range 9–29 days).

### MRI protocol

All cardiac MRI examinations were performed with a 1.5-T scanner (Giloscan; Philips Medical Systems, Eindhoven, the Netherlands). Images were obtained during breath-holding with electrocardiographic (ECG) gating. We used a segmented k-space steady-state free-precession sequence for cine imaging. With a previously described inversion recovery pulse sequence, delayed-enhanced

images at matching cine-image slice locations were obtained 10–15 min after intravenous administration of gadolinium (Gd)-DTPA at a dose of 0.2 ml/kg (Magnevist; Berlex Pharmaceuticals, Wayne, NJ, USA). We optimized the inversion time (250–350 ms) to null the normal myocardium and adjusted the views per segment and trigger delay according to the patient's heart rate to minimize any image blurring.

### MRI analysis

All images were reviewed and analyzed off-line with specialized postprocessing software (ViewForum; Phillips). Collection and interpretation of all imaging data were performed in a blind manner regarding the clinical data and outcome. We manually traced the LV endocardial border on all short-axis cine images at the end-diastolic and end-systolic frames to determine the end-diastolic and end-systolic volumes, respectively. LV mass was calculated by subtracting the endocardial volume from the epicardial volume at end-diastole and then multiplying by the tissue density (1.05 g/ml). The LV sphericity index (SI) was calculated as: end-diastolic volume/ $[(\text{long-axis diameter})^3 \times \pi/6]$ .<sup>2</sup> The higher the SI, the more spherical the LV. The endocardial and epicardial contours on delayed enhancement images were also outlined manually. Using a semiautomatic detection algorithm, we applied hyperenhancement (HE)—i.e., the infarcted region—with a signal intensity threshold of  $>3$  SDs and  $2\text{--}3$  SDs above remote normal myocardium; we then calculated the transmural extent, or “transmurality,” of hyperenhancement for all segments of the LV. The percentages of the hyperenhancement in the whole LV walls (%HE) were also calculated.

### Surgical strategies and procedures

Our surgical strategies for ischemic cardiomyopathy were as follows: (1) complete revascularization on viable segments (transmurality  $<75\%$ ); (2) SVR in a patient with extensive nonviable segments (transmurality  $\geq 75\%$ ); (3) SVR consisting of the Dor procedure, the SAVE (septal anterior ventricular exclusion) procedure, and linear infarction exclusion technique selected depending on the location of extensive nonviable segments; (4) mitral valve plasty in a patient with more than moderate mitral regurgitation; and (5) biventricular pacing if necessary.

In cases with isolated CABG, if the hemodynamic status was stable we performed CABG using an off-pump technique. Mitral annuloplasty was performed using a semirigid ring (Carpentier-Edwards Physio-Ring; Edwards Lifesciences, Irvine, CA, USA) in a patient

with ischemic mitral regurgitation. The Dor procedure<sup>3</sup> was performed without using patches (i.e., using purse-string stitches alone when nonviable areas were localized at the apex), and the SAVE procedure was performed when nonviable areas were extended from the apex to the anteroseptal segments. The SAVE procedure was performed as described.<sup>4</sup> The linear infarction exclusion technique was performed as the linear exclusion of the infarcted walls, not for resection as in Batista's operation<sup>5,6</sup> when extensive nonviable areas existed in the inferior or posterior segments.

Statistical analysis

Data are expressed as means ± standard deviation. Statistical analyses were performed with StatView 5.0 software (SAS Institute, Cary, NC, USA). Categorical data were analyzed with the chi-squared test or Fisher's exact test; and unpaired Student's *t*-tests were used to compare continuous variables with *P* < 0.05 considered to indicate statistical significance.

Results

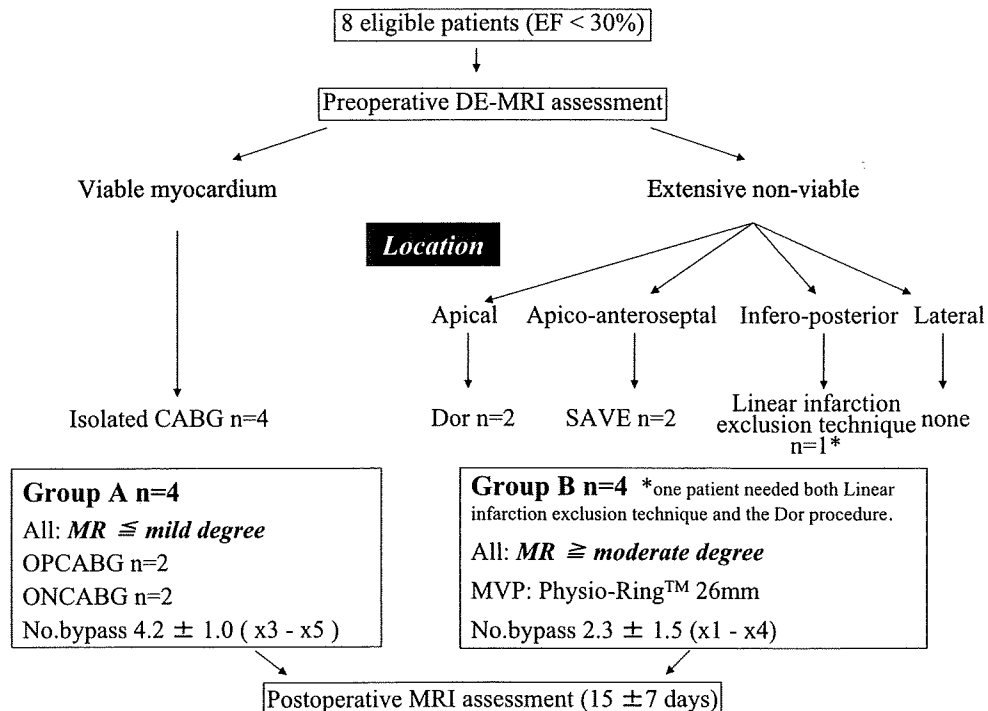
Surgical outlines based on the results of MRI assessments are shown in Fig. 1. Four of the patients (group A) underwent isolated CABG, and the other four patients (group B) underwent SVR and mitral valve plasty

concomitantly with CABG. Two patients in group A underwent CABG with an off-pump technique, and the other underwent beating bypass with cardiopulmonary bypass. The mean number of bypasses were 4.2 ± 1.0 (range 3–5) in group A and 2.3 ± 1.5 (range 1–4) in group B. Two patients in group B underwent the Dor procedure, and the other two patients underwent the SAVE procedure. One of the former patients underwent both the Dor procedure and the linear infarction exclusion technique. All of the patients in group B underwent mitral annuloplasty with a 26-mm Carpentier-Edwards Physio-Ring.

Characteristics of the patient population in each group are shown in Table 1. The mean ages of the patients in the two groups were similar (57 ± 2 years in group A, 63 ± 10 years in group B). All of the patients in this study were male. New York Heart Association (NYHA) functional classes were 3.0 ± 0.8 in group A and 3.5 ± 0.5 in group B.

Baseline data obtained by MRI are shown in Table 2. Baseline ejection fraction (EF) was 20% ± 6% (range 15%–27%) in group A and 17% ± 6% (range 11%–23%) in group B. The end-diastolic volume index (EDVI) and end-systolic volume index (ESVI) were significantly larger in group B than in group A. The %HE was significantly larger in group B than in group A. The proportion of hyperenhancement covering ≥75% of the regional wall thickness was also significantly larger in group B than in group A. Postoperative data are shown in Table 3. There

**Fig. 1** Patient and site selection in surgical ventricular restoration based on MRI assessment. *EF*, ejection fraction; *DE-MRI*, delayed-enhanced magnetic resonance imaging; *CABG*, coronary artery bypass grafting; *MR*, mitral regurgitation; *OPCABG*, off-pump coronary artery bypass grafting; *ONCABG*, on-pump coronary artery bypass grafting; *No.*, number; *SAVE*, septal anterior ventricular exclusion; *MVP*, mitral valve plasty



**Table 1** Patient population

Characteristic	Group A (isolated CABG, <i>n</i> = 4)	Group B (CABG + SVR + MAP, <i>n</i> = 4)
Age (years)	57 ± 2	63 ± 10
Male	4 (100%)	4 (100%)
Body surface area (m <sup>2</sup> )	1.6 ± 0.3	1.6 ± 0.1
Diabetes mellitus	4 (100%)	1 (25%)
Hypertension	2 (50%)	1 (25%)
Hyperlipidemia	2 (50%)	2 (50%)
Smoking history	3 (75%)	3 (75%)
NYHA functional class	3.0 ± 0.8	3.5 ± 0.5
Previous PTCA	0 (0%)	2 (50%)
History of CHF	3 (75%)	4 (100%)
Renal dysfunction	0 (0%)	1 (25%)
Peripheral vascular disease	0 (0%)	1 (25%)
Coronary anatomy		
One-vessel disease	0 (0%)	1 (25%)
Two-vessel disease	1 (25%)	0 (0%)
Three-vessel disease	3 (75%)	3 (75%)

CABG, coronary artery bypass grafting; SVR, surgical ventricular restoration; MAP, mitral annuloplasty; NYHA, New York Heart Association; PTCA, percutaneous transluminal coronary angioplasty; CHF, congestive heart failure

Data are expressed as means ± SD, or as numbers

There were no significant differences between groups A and B

**Table 2** MRI measurements: baseline data

Measurement	Group A (isolated CABG, <i>n</i> = 4)	Group B (CABG + SVR + MAP, <i>n</i> = 4)	<i>P</i>
End-diastolic volume index (ml/m <sup>2</sup> )	115 ± 29	163 ± 35	<0.05
End-systolic volume index (ml/m <sup>2</sup> )	91 ± 25	135 ± 36	<0.05
Ejection fraction (%)	20 ± 6	17 ± 6	NS
Cardiac index (l/min/m <sup>2</sup> )	1.4 ± 0.2	2.0 ± 0.3	NS
LV sphericity index	0.38 ± 0.01	0.40 ± 0.03	NS
LV mass (g)	131 ± 42	159 ± 49	NS
Hyperenhancement (%)	23 ± 4	48 ± 17	<0.05
Hyperenhancement ≥75% (%)	4.6 ± 2.9	25.5 ± 14.7	<0.05
Diastolic diameter <sup>a</sup> (mm)	60 ± 10	70 ± 9	NS

LV, left ventricular

Data are expressed as means ± SD

<sup>a</sup>Echocardiographic measurement

**Table 3** Postoperative data

Parameter	Group A (isolated CABG, <i>n</i> = 4)	Group B (CABG + SVR + MAP, <i>n</i> = 4)
Death	0	0
Inotropes >48 h	1 (25%)	1 (25%)
Ventilation >48 h	0 (0%)	0
Intubation time (h)	6.8 ± 7.1	8.8 ± 8.4
Renal failure	0	0
Atrial fibrillation	2 (50%)	3 (75%)
Mediastinitis	0	0
Reexploration	0	1 (25%)
PMI	0	0
ICU stay (day)	4.7 ± 5.5	3 ± 0
Hospital stay (day)	29 ± 23	30 ± 20

PMI, perioperative myocardial infarction; ICU, intensive care unit

Data are expressed as means ± SD, or as numbers (%)

There were no significant differences between groups A and B

**Table 4** MRI parameters at baseline and follow-up

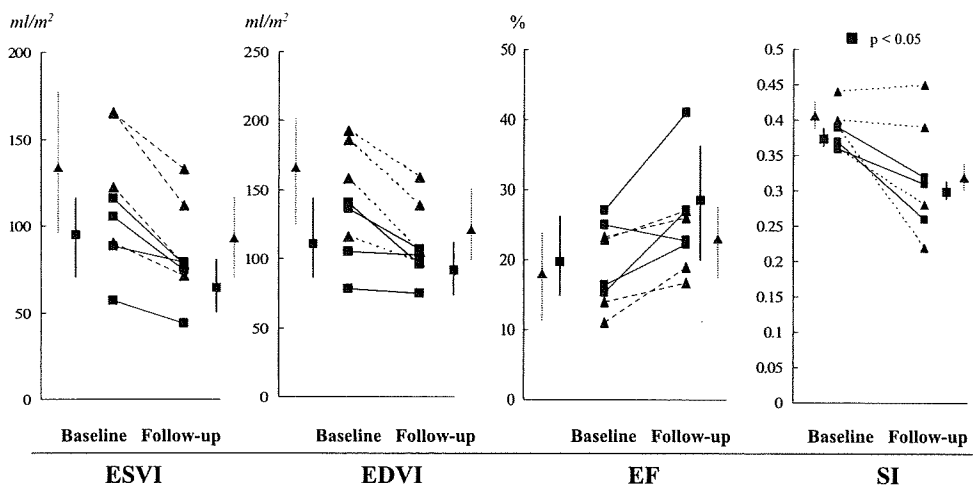
Parameter	Group A (n = 4)		Group B (n = 4)	
	Baseline	Follow-up	Baseline	Follow-up
End-diastolic volume index (ml/m <sup>2</sup> )	115 ± 29	95 ± 14	163 ± 35	125 ± 28
End-systolic volume index (ml/m <sup>2</sup> )	91 ± 25	68 ± 16	135 ± 36	98 ± 28
Ejection fraction (%)	20 ± 6	28 ± 9	17 ± 6	22 ± 5
Cardiac index (l/min/m <sup>2</sup> )	1.4 ± 0.2	1.9 ± 0.1*	2.0 ± 0.3	2.2 ± 0.4
LV sphericity index	0.38 ± 0.01	0.30 ± 0.02*	0.40 ± 0.03	0.33 ± 0.10
LV mass (g)	131 ± 42	137 ± 59	159 ± 49	142 ± 63
Diastolic diameter <sup>a</sup> (mm)	60 ± 10	56 ± 8	70 ± 9	59 ± 5

Data are expressed as means ± SD

<sup>a</sup>Echocardiographic measurement

\**P* < 0.05 vs. baseline

**Fig. 2** Individual changes in end-systolic volume index (ESVI), end-diastolic volume index (EDVI), ejection fraction (EF), and sphericity index (SI) from baseline to follow-up after the operation. Filled squares, group A; filled triangles, group B. Vertical bars, mean ± SD



were no cases of either hospital death or major complications in either group.

Perioperative changes in ventricular volume, ejection fraction, and LV sphericity index in each patient are shown in Fig. 2 and Table 4. EDVI was reduced from 115 ± 29 ml/m<sup>2</sup> to 95 ± 14 ml/m<sup>2</sup> in group A and from 163 ± 35 ml/m<sup>2</sup> to 125 ± 28 ml/m<sup>2</sup> in group B. EDVI was reduced in all four patients in both groups. ESVI was reduced from 91 ± 25 ml/m<sup>2</sup> to 68 ± 16 ml/m<sup>2</sup> in group A and from 135 ± 36 ml/m<sup>2</sup> to 98 ± 28 ml/m<sup>2</sup> in group B. ESVI was reduced in all four patients in both groups. EF increased from 20% ± 6% to 28% ± 9% in group A and from 17% ± 6% to 22% ± 5% in group B. EF was improved in three of the four patients in group A and in all four patients in group B. The LV sphericity index was significantly reduced from 0.38 ± 0.01 to 0.30 ± 0.02 in group A (*P* < 0.05) and slightly reduced from 0.40 ± 0.03 to 0.33 ± 0.10 in group B. NYHA functional class was reduced from 3.0 ± 0.8 to 1.8 ± 0.6 in group A and from 3.5 ± 0.5 to 2.2 ± 0.2 in group B.

## Discussion

Batista's operation,<sup>5,6</sup> first reported in 1996, has been unsuccessful. Based on an observational analysis of the literature, Ascione et al. reported that in-hospital mortality was 17% in 506 patients who underwent this operation for dilated cardiomyopathy, and the cause of death was low-output syndrome in 62% of cases.<sup>7</sup> In a follow-up series, they reported that late deaths occurred in 23% of 368 patients, and the cause of death was recurrence of congestive heart failure in 56% of cases. One of the main reasons for these unsuccessful results may be lack of consideration of myocardial viability in this procedure, and critical pump failure may occur after this operation because of resection of viable myocardium.

Although a recent study indicated poor late outcomes in patients with a severely dilated LV following CABG alone,<sup>8</sup> the unsuccessful results of Batista's operation indicated that volume reduction alone was insufficient and sometimes detrimental in patients with dilated car-



diomyopathy. It is important to select an appropriate area for resection based on accurate viability testing. The present study was performed to determine where and how much we should resect. Accordingly, we conducted a surgical strategy based on accurate assessments of myocardial viability using DE-MRI in this patient population and obtained good early outcomes. However, a longer follow-up is needed to determine whether these patients can achieve further functional recovery over time.

Cardiac MRI is a comprehensive imaging modality that can be used to measure accurately the LV volume, regional wall motion or thickening, coronary perfusion, and myocardial viability during a single imaging session. For determination of myocardial viability, several imaging methods, including stress echocardiography, single-photon emission tomography, positron emission tomography, and MRI, are now available. MRI offers certain inherent advantages over the other methods,<sup>9–13</sup> allowing the most comprehensive preoperative cardiac evaluation with less invasiveness and without radiation exposure. The greatest advantages of DE-MRI are that it can distinguish between reversible and irreversible myocardial ischemic injury and can reliably demonstrate, with higher spatial resolution, the transmural extent of the infarcted myocardium within akinetic or dyskinetic ventricular walls.<sup>14</sup> Therefore, it can also demonstrate subendocardial infarction that cannot be detected by other modalities.

The cellular-level mechanism for Gd-contrast hyperenhancement has not been fully clarified. However, it has been suggested that after infarction the myocyte membranes are ruptured, allowing passive diffusion of the Gd-contrast agent into the intracellular space, resulting in increased tissue-level contrast agent concentration and therefore hyperenhancement.<sup>15</sup>

As can be seen from the actual DE-MRI images shown in Fig. 3, it is easy to understand the condition of the regional walls (i.e., whether they are hyperenhanced). Kim et al. reported that the increased contractility after revascularization is related to the transmural extent before revascularization.<sup>1</sup> LV regions with delayed enhancement covering more than 75% of the regional wall thickness are not expected to recover function after revascularization, whereas if it is less than 75% there is a reasonable chance of recovering some degree of function after revascularization, even in regions with akinetic or dyskinetic ventricular walls.<sup>1</sup> The results of recent studies indicate that cardiac MRI can provide all the information needed for appropriate patient selection and surgical planning for SVR.

There is a lack of convincing evidence from randomized controlled trials for either of these treatment modalities—CABG alone or SVR concomitantly with

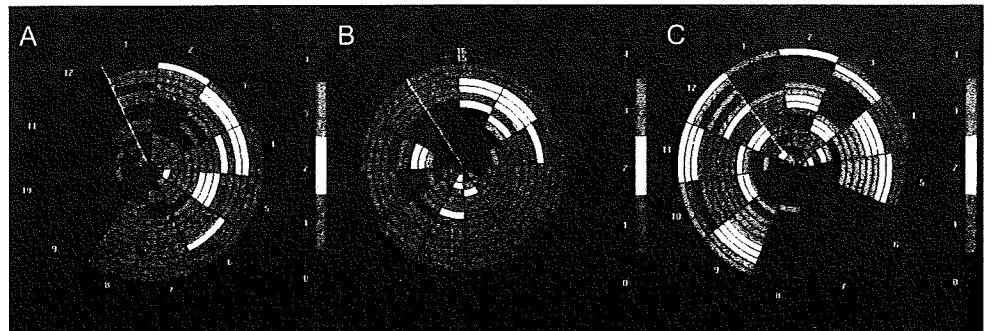
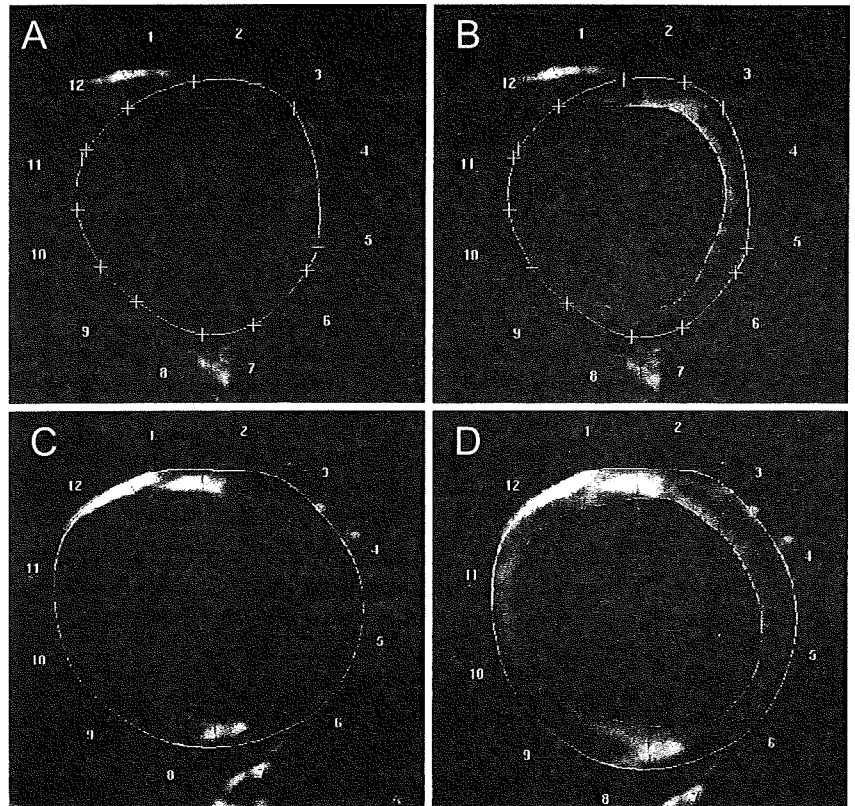
CABG—in this patient population. Using a retrospective database, Maxey et al. assessed morbidity and mortality in patients with ischemic cardiomyopathy who were referred for CABG. The outcome was significantly better in the groups who underwent CABG plus SVR than among patients who underwent CABG alone.<sup>16</sup> There was no viability testing in this study. One of the reasons for the inability to obtain strong evidence in this field is the difficulty of accurately assessing myocardial viability.

Several promising results of SVR have been reported. Isomura et al. reported an excellent 5-year survival rate for 83 patients who underwent elective SVR, with values of 80.3% after the SAVE procedure and 77.4% after the Dor procedure.<sup>17</sup> The patient population in this study had a large preoperative ESVI:  $135 \pm 38 \text{ ml/m}^2$  in the SAVE group and  $95 \pm 25 \text{ ml/m}^2$  in the Dor group. The RESTORE group reported that the ejection fraction improved on average by 10% ( $29.7\% \pm 11.3\%$  to  $40\% \pm 12.3\%$ ), and the 3-year survival was 89% in 662 patients with akinetic regions mainly in the anterior wall.<sup>18</sup> Although myocardial viability was not described in these reports, these midterm results were encouraging for cardiac surgeons and patients with severely dilated ischemic cardiomyopathy.

According to the excellent results of SVR, although we performed SVR in the LV regions with extensive delayed enhancements covering  $\geq 75\%$  in the present strategy, it may be better to perform aggressive SVR in those covering  $\geq 50\%$  to obtain more effective reverse-remodeling by reducing regional wall stress, especially in patients with severely dilated LV. Kim et al. reported that the likelihood of increased contractility after revascularization decreases rapidly in regions with  $\geq 50\%$  hyperenhancement, which can be considered nonviable.<sup>1</sup> In our experience, there may be a close correlation between DE-MRI findings and surgical findings. Scar formation can be seen directly in the LV regions with hyperenhancement of more than 75%, whereas the cardiac surface often seems normal in those with less than 50% hyperenhancement. Therefore, we could perform SVR in these regions if DE-MRI findings are reliable; that is, myocardial damage in these regions must be irreversible even when the surface is normal and the wall thickness is not very thin.

Site selection in SVR is also important for improving the clinical outcome. DE-MRI can demonstrate the accurate location of nonviable areas, and the procedures can then be selected depending on the location. Figure 4 shows bull's-eye expression of the transmural index of three patients. With DE-MRI, the hyperenhancement is distinguished by software in a semiautomated manner, and the transmural extent of the infarcted areas can be

**Fig. 3** Computer-assisted semiautomated technique for quantifying %HE on delayed-enhanced images of one patient in each group. **A, B** Patient with subendomyocardial infarction in group A. **C, D** Patient with extensive transmural infarction in the anteroseptal segments, partly including the inferior infarction in group B. A computer-assisted algorithm applied the signal-intensity thresholds of  $>3$  SDs and  $2-3$  SDs above the remote normal myocardial segment (blue) to delineate the infarct core (orange) HE, hyperenhancement



**Fig. 4** Preoperative bull's-eye expression of transmural extent of hyperenhancement, transmurality index, in three patients with ischemic cardiomyopathy. Transmurality index is indicated as: none (blue), 1%–24% (green), 25%–49% (yellow), 50%–74% (orange), 75%–100% (red). **A** Patient with a substantial amount of viable myocardium in group A (EF 15%, EDVI 136 ml/m<sup>2</sup>, ESVI 116 ml/m<sup>2</sup>). **B** Patient with nonviable myocardium in the apico-

anteroseptal segments in group B (EF 22%, EDVI 115 ml/m<sup>2</sup>, ESVI 90 ml/m<sup>2</sup>). This patient underwent surgical anterior ventricular exclusion (SAVE). **C** Patient with extensive nonviable myocardium in the inferoposterior segments in group B (EF 23%, EDVI 158 ml/m<sup>2</sup>, ESVI 122 ml/m<sup>2</sup>). This patient underwent linear infarction exclusion. EF, ejection fraction; EDVI, end-diastolic volume index; ESVI, end-systolic volume index

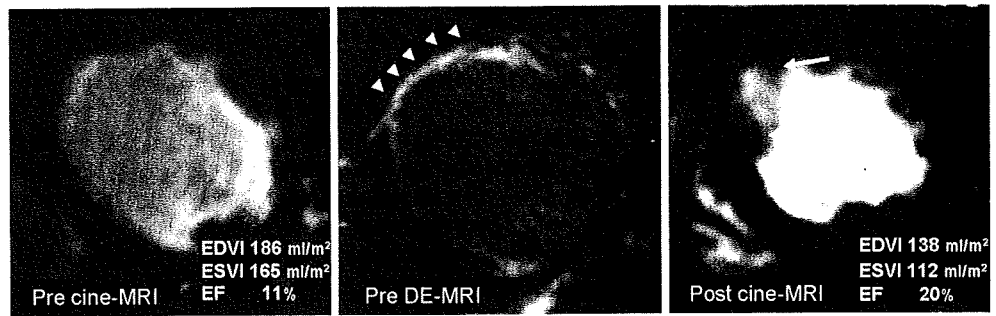
calculated for all segments of the LV walls. This information is highly effective for selecting which areas are indicated for SVR. If there are extensive nonviable areas in the inferior or posterior wall (Fig. 4C), we apply the linear infarction exclusion technique. We do not resect nonviable muscle but linearly exclude it to the borderline if possible.

Preoperative and postoperative MRI findings of a 54-year-old man who underwent the SAVE procedure

are shown in Fig. 5 to evaluate whether the ventricular exclusion could be performed effectively. Preoperative cine-MRI and DE-MRI demonstrated that the anteroseptal wall was particularly thin and had transmural hyperenhancement. Postoperative cine-MRI revealed that the regional area with the transmural infarction was excluded effectively by a patch.

Finally, it should be remembered that hibernating myocardium has sufficient potential for functional im-

**Fig. 5** Evaluation of the effectiveness of the ventricular exclusion (SAVE procedure). *Arrow heads*, area with transmural hyperenhancement; *arrows*, a patch. *Pre*, preoperative; *MRI*, magnetic resonance imaging; *DE-MRI*, delayed-enhanced magnetic resonance imaging; *Post*, postoperative



provement by revascularization alone.<sup>19–21</sup> We experienced a typical case that a 57-year-old man with dilated ischemic cardiomyopathy (ejection fraction 15%, EDVI 136 ml/m<sup>2</sup>, ESVI 116 ml/m<sup>2</sup>) could have improved cardiac function with CABG alone. Preoperative DE-MRI findings are shown in Fig. 3A,B and Fig. 4A. Although preoperative DE-MRI delineated extensive subendocardial infarction, the transmural extent of hyperenhancement was less than 30% in the whole ventricular wall, implying that there was substantial viable myocardium. Six months after the operation, catheterization demonstrated dramatic improvement in ventricular function, with the ejection fraction having increased to 35%. Carluccio et al. reported that patients with hibernating myocardium have altered LV volume and shape, which revert significantly after revascularization alone.<sup>21</sup> Myocardial viability was estimated by dobutamine stress echocardiography. Eight months after revascularization in 42 patients with a mean ejection fraction of 33%, ESVI was significantly improved from  $78 \pm 23$  ml/m<sup>2</sup> to  $56 \pm 23$  ml/m<sup>2</sup>. Although preoperative ESVI was relatively small in this study group, the study had sufficient power.

This report is based on our initial experience, and our study group was small. Therefore, longer follow-up and a larger study group are needed to elucidate the feasibility of the present strategy, which is based not on ventricular volume but on myocardial viability itself. This was not a comparative study, and it is therefore not possible to describe the superiority of MRI over other modalities.

## Conclusions

The surgical results of the two groups—CABG alone and SVR concomitantly with CABG—divided based on the assessment of myocardial viability by DE-MRI were satisfactory. DE-MRI was highly effective in helping to select which patients and which areas of the left ventricle are indicated for SVR, which helped obtain excellent clinical outcomes.

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## Invited commentary

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Ogawa et al. carefully documented the efficacy of delayed-enhanced magnetic resonance imaging (DE-MRI) for evaluating myocardial viability at the time of surgical ventricular restoration (SVR).<sup>1</sup> Kim and Manning reported a strong relation between the transmural extent of the infarct myocardium defined by DE-MRI before revascularization and the likelihood of increased contractility after revascularization.<sup>2</sup>

Examining the application of DE-MRI to surgical operations is important. Lloyd et al. also reported the effectiveness of DE-MRI for ventricular restoration.<sup>3</sup> It seems to be superior to other modalities in its ability to determine the location of scar tissue and viable tissue and to analyze the viability of the cardiac wall in the longitudinal direction.

Questions include the following: (1) The discussion is confusing about idiopathic DCM (although there is an article in which DE-MRI is effective for the diagnosis of DCM<sup>4</sup>); (2) Patients without LVR had a preoperative EDVI of  $115 \pm 29 \text{ ml/m}^2$  and an LVR of  $163 \pm 35 \text{ ml/m}^2$ , which means that even without DE-MRI almost all

cardiac surgeons are likely to select the same procedures. We want to know the significance of this strategy in small-heart and large-heart groups and individually whether SVR should be performed. (3) The differences in the MRI images before and after surgery could be useful for determining whether the exclusion was satisfactory.

As the authors pointed out, their study is limited. It was impossible to compare DE-MRI with other modalities because it was not a comparative study, the follow-up period was short, and the number of cases was small. However, this report is important regarding the establishment of preoperative evaluations for better surgical procedures including SVR.

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