# The Influence of Collateral Flow on the Antegrade and Retrograde Distribution of Cardioplegia in Patients with an Occluded Right Coronary Artery 

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Background: The predictive value of electrocardiography (ECG) and coronary angiography for cardioplegia distribution in patients with an occluded right coronary artery was evaluated.

Methods: Coronary angiograms and ECGs were evaluated in 15 patients with right coronary artery occlusion. Prediction of antegrade cardioplegia distribution was based on ECG evidence of infarction and coronary collateral flow determined from the angiogram. Antegrade and retrograde delivery of cardioplegia was directly assessed in all patients by myocardial contrast echocardiography. Intraoperative transesophageal echocardiographic images of the right ventricular free wall, the apex, and the intraventricular septum were recorded while $4 \mathbf{m l}$ of Albunex (Mallinckrodt Medical, St. Louis, MO) was injected into antegrade and retrograde cardioplegic catheters during cardioplegia delivery. The observed (myocardial contrast echocardiography) cardioplegia distribution was compared to the predicted cardioplegia distribution. Sensitivity, specificity, positive predictive values, and negative predictive values were calculated.

Results: Eighty seven of $90(97 \%)$ segments were analyzed. Angiography and ECG poorly predicted incomplete cardioplegia distribution. Electrocardiography was a better predictor of
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inadequate cardioplegia distribution to the right ventricle than was angiography. The negative predicted values of cardioplegia distribution ranged from 20 to $50 \%$ for the septum and right ventricle, respectively, with ECG criteria and from 0 to $33 \%$ for the septum and apex, respectively, with angiographic criteria. Antegrade cardioplegia delivery was distributed to the right ventricle in $31 \%$ of patients, despite $100 \%$ occlusion of the right coronary artery; whereas retrograde cardioplegia delivery to the right ventricle occurred $20 \%$ of the time.

Conclusions: In the presence of $100 \%$ right coronary artery occlusion, retrograde cardioplegia delivery is not often observed and antegrade delivery of cardioplegia to the right ventricle is not easily predicted. The preoperative angiography and ECG are not predictive of coronary collateral circulation and therefore not predictive of cardioplegia distribution to the right ventricle. (Key words: Angiography; cardioplegia distribution; contrast echocardiography; electrocardiography; right coronary artery.

IN the United States, more than $90 \%$ of coronary artery bypass graft (CABG) operations involve occlusion of the ascending aorta with cardioplegia administered to protect the heart during cardiopulmonary bypass. ${ }^{1-3}$ For cardioplegia to be effective, however, the solution should be distributed adequately to all regions of the heart. ${ }^{4}$ Underlying native coronary artery anatomy ${ }^{5,6}$ and collateral flow ${ }^{7}$ are critical factors for cardioplegia distribution and for preventing myocardial dysfunction.
It has been noted by some ${ }^{5,6,8}$ that in the presence of complete coronary artery obstruction, retrograde coronary sinus perfusion can be protective, whereas others ${ }^{9-11}$ have questioned the effectiveness of retrograde cardioplegia delivery for providing satisfactory protection. In particular, right ventricular dysfunction has been reported after CABG surgery, despite antegrade or retrograde cardioplegia administration. ${ }^{12-15}$ Total occlusion of the right coronary artery (RCA) can impede antegrade delivery of cardioplegia to the right ventricle, and retrograde cardioplegia delivery to the right ventricle has been shown to be unreliable. ${ }^{9,11,16-19}$ Protection of the right ventricle in particular therefore may be a clinical

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challenge in patients with an occluded RCA. Inadvertent maldistribution or nondistribution of cardioplegia to the right ventricle is not easily predicted clinically. We used intraoperative myocardial contrast echocardiography (MCE) in patients with total occlusion of the RCA to directly assess the distribution of cardioplegia delivery to the right ventricle, the left ventricle, the apex and the intraventricular septum during antegrade and retrograde delivery of cardioplegia and to determine collateral flow supplying the right ventricular free wall. We also evaluated the ability of preoperative ECG and coronary angiography for predicting cardioplegia distribution and compared predictions to cardioplegia distribution directly assessed with intraoperative MCE.

## Methods

After obtaining institutional approved and individual informed consent, 15 patients were observed during elective CABG surgery. All patients enrolled in the study had preoperative coronary angiographic evidence of RCA occlusion. Exclusion criteria included cerebral vascular insufficiency, aortic insufficiency, or a history of allergy to contrast dye. Routine anesthetic administration and monitoring were not modified at any point during the surgical procedure. All patients were evaluated and monitored with transesophageal echocardiography immediately after intubation until the end of surgery. Surgical techniques were modified to permit contrast injections. Cardiopulmonary bypass with moderate hypothermia was instituted via an ascending aortic and right atrial, two-stage, single-venous cannula. After cardiopulmonary bypass was instituted and the proximal aorta was occluded, all patients underwent initial cardioplegic induction with antegrade delivery of cold blood, crystalloid cardioplegic solution, or both for 3 $\min$ (average dose, 900 ml ). Antegrade cardioplegic induction was initiated at $150 \mathrm{ml} \cdot \mathrm{min}^{-1} \cdot \mathrm{~m}^{-2}$. Immediately after infusion of the antegrade-delivered cardioplegia solution, mild suction was placed on the aortic vent, and cardioplegic solution was administered retrogradely through a conventionally placed transatrial cannula with a self-inflating balloon-tip coronary sinus catheter (model 94315 T ; Medronic DLP, Grand Rapids, MI). Retrograde delivery of cardioplegic solution continued for 3 min . Retrograde cardioplegia delivery was administered to maintain a coronary sinus catheter pressure of $40-50$ mmHg . Catheter placement was confirmed by manual palpation, inspection of the coronary sinus pressure dur-


Fig. 1. Two-dimensional transesophageal echocardiogram of the right ventricular free wall, the apex, and the interventricular septum. The transducer was positioned to provide an echocardiographic window to view the right ventricular free wall, the interventricular septum, and the apex without shadowing or dropout of these regions. Note lateral wall dropout in this image.
ing retrograde flow, and imaging of the tip of the retrograde catheter in the coronary sinus with intraoperative transesophageal echocardiography. Albunex (Mallinckrodt Medical, St. Louis, MO) contrast medium ( 4 ml ) was injected into the antegrade (aortic root) cardioplegic catheter at 1 min after onset of antegrade cardioplegia delivery and into the coronary sinus catheter at 1 min after onset of retrograde cardioplegia delivery.
Transesophageal echocardiographic images of the right ventricular free wall, the apex, and the intraventricular septum were obtained in the long-axis imaging plane using a $5.0-\mathrm{mHz}$ transducer, (Sonos 2500 ; HewlettPackard, Andover, MA) (figs. 1 and 2). Images were recorded on $1 / 2$-inch videotape during each contrast injection. Optimal power- and time-gain settings were obtained for each patient before contrast injection and were kept constant throughout the rest of the study.
Distribution of antegrade- and retrograde-delivered cardioplegia solution was determined at the time of surgery by analysis of recorded images from the ultrasound video monitor (fig. 3). These images of contrast-enhanced perfusion patterns were again graded off-line by the original observer and an independent observer, (both blinded to the results of the on-line grade). Both observers assigned a score to each of the three regions of interest (septum, apex, and right ventricular free wall) using the following scale: $0=$ no enhancement; $1=$ partial enhancement; $2=$ complete enhancement; $3=$ unable to measure


Fig. 2. Schematic representation of the two-dimensional transesophageal echocardiogram obtained to evaluate cardioplegia distribution showing the long axis of the left ventricle. The right ventricular free wall, the apex, and the interventricular septum were scored region by region, as depicted in this cartoon representation of the echocardiogram.
because of inadequate image (i.e, lateral wall dropout). During the off-line analysis, if the two observers disagreed, then a third observer, blinded to the results of the initial observers, was asked to score the region in dispute. For the purpose of evaluation of the data, two separate analyses were performed. First a score of 2 was considered positive for cardioplegia distribution and a score of 0 or 1 was considered negative for cardioplegia distribution in a region. Second, an analysis was also reported with a score of 2 or 1 considered positive for distribution and a score of 0 considered negative for cardioplegia distribution. Inter- and intraobserver scoring variability was evaluated.

Two observers blinded to the intraoperative contrast enhanced cardioplegia distribution scores predicted antegrade cardioplegia distribution based on evaluation of the preoperative electrocardiogram and preoperative angiogram. The ECG criteria for predicting cardioplegia distribution were based on the presence or absence of a Q-wave myocardial infarction ${ }^{20}$ suggesting an occluded or severely stenotic vessel lumen. Inferior wall myocardial infarctions were considered when $Q$ waves were observed in leads II, III, and aVF. A septal wall myocardial infarction was considered when Q waves were observed in leads $V_{3}$ and $V_{4}$. An apical infarction was noted when $Q$ waves were observed in leads $V_{5}$ and $V_{6}$, and a posterior wall infarction was presumed when dominant R waves were seen in leads $\mathrm{V}_{1}$ and $\mathrm{V}_{2}$. By these ECG criteria, it was predicted that no cardioplegia was to be
delivered to the region with an infarction from the antegrade delivery route. The inferior and posterior regions were presumed to reflect right coronary flow.

## Statistical Methods

Ninety-five percent exact binomial confidence intervals for percent of patients with positive contrast scores, sensitivity, specificity, and predictive values were calculated using Stata (Stata Statistical Software, Release 5.0; Stata Corporation, College Station, TX). Sensitivity, specificity, positive predictive value, and negative predictive value were calculated when predictions were compared to regional cardioplegia distribution as determined by contrast echo evaluation. A true-positive was defined when ECG criteria predicted cardioplegia distribution to a region and MCE showed regional cardioplegia delivery to the same region. A false-positive was defined when ECG predicted cardioplegia distribution and MCE did not show cardioplegia delivery to that region. A false-negative was defined when ECG predicted no cardioplegia delivery and MCE showed cardioplegia delivery and, finally, a true-negative was defined when ECG predicted no regional cardioplegia delivery and MCE also did not show cardioplegia distribution to the region of interest.
Preoperative coronary angiograms were evaluated for native epicardial anatomy and for collateral coronary circulation supplying the right ventricle, the left ventricular apex, and the intraventricular septum. The classification of coronary collateral blood flow supplying a particular region was determined to be either good or poor. The degree of opacification of the epicardial segment of the recipient artery in the coronary angiogram and the faint visualization of collaterals and epicardial arteries distal to the occluded RCA was the basis for classification of poor coronary collateral circulation in the patients examined. All angiograms were interpreted by experienced observers. Sensitivity, specificity, positive predictive value, and negative predictive value were also calculated for predicting cardioplegia distribution based on the estimation of collateral circulation from angiography when compared to regional cardioplegia distribution determined by contrast enhanced echocardiography. Similar criteria were used to define truepositive (e.g., angiography predictive of cardioplegia delivery and MCE-confirmed delivery) true-negative, falsepositive, and false-negative as were used for ECG analysis.


Fig. 3. (A) Two-dimensional mid-atrial, four-chamber transesophageal echocardiogram of the myocardium, obtained immediately before antegrade contrast injection. (B) Same image obtained immediately after antegrade contrast injection. Note opacification within the myocardium is beginning to appear in the septum, the right ventricle, and the apex. ( $C$ ) The same image recorded a few frames later showing the appearance of contrast washout in the apical region of the myocardium and the right ventricular free wall. $(D)$ The same image a few more frames later (approximately 9 s after injection). The image now shows the contrast washout effect in the apical, septal, and right ventricular regions.

## Results

Thirty injections were evaluated in 15 patients. Ninety myocardial segments were evaluated at the time of cardiopulmonary bypass and (table 1) 87 of 90 possible regions $(96.7 \%$ ) were scored for the presence of cardioplegia delivery. Inadequate imaging of a region of interest (i.e., apex, septum, and right ventricular free wall) was the reason three segments were not analyzed.
In the presence of a $100 \%$ RCA-occlusive lesion, delivery of cardioplegia to the right ventricle was not reliable from either the antegrade or the retrograde delivery. However, antegrade delivery provided cardioplegia distribution to the right ventricle in approximately onethird of patients, despite the presence of $100 \%$ occlusion of the RCA (table 2). Retrograde delivery of cardioplegia
to the right ventricle only occurred in $20 \%$ of patients with $100 \%$ occlusion of the RCA. Preoperative ECG poorly predicted regions at risk for incomplete antegrade cardioplegia delivery (i.e., negative predictive value, $20 \%$ for the septum and $50 \%$ for the apex and right ventricle) (table 3). Preoperative angiography poorly predicted regions at risk for incomplete antegrade cardioplegia delivery as well (i.e., negative predictive value for the septum was $0 \%$, for the apex was $33 \%$, and for the right ventricle was $25 \%$ ) (table 4). Between ECG and angiography, preoperative electrocardiography was a better predictor of inadequate antegrade cardioplegia delivery to the right ventricle. Angiography did not predict inadequate retrograde cardioplegia distribution to the right ventricle.

INFLUENCE OF COLLATERAL FLOW

Table 1.

| Patient Number | Injury Type | Contrast Score |  |  | EKG Prediction |  |  | Angiogram Prediction |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | SEP | APX | RV | SEP | APX | RV | SEP | APX | RV |
| 1 | Antegrade | 1 | 0 | 0 | + | + | + | + | + | + |
|  | Retrograde | 1 | 1 | 0 |  |  |  |  |  |  |
| 2 | Antegrade | 2 | 2 | 1 | + | + | + | + | + | + |
|  | Retrograde | 2 | 2 | 0 |  |  |  |  |  |  |
| 3 | Antegrade | 2 | 2 | 2 | - | + | + | + | + | + |
|  | Retrograde | 2 | 3 | 0 |  |  |  |  |  |  |
| 4 | Antegrade | 1 | 0 | 0 | - | - | - | + | + | + |
|  | Retrograde | 1 | 1 | 0 |  |  |  |  |  |  |
| 5 | Antegrade | 2 | 2 | 0 | + | + | - | + | + | - |
|  | Retrograde | 2 | 2 | 2 |  |  |  |  |  |  |
| 6 | Antegrade | 2 | 2 | 1 | + | + | - | - | - | + |
|  | Retrograde | 2 | 2 | 0 |  |  |  |  |  |  |
| 7 | Antegrade | 0 | 0 | 0 | - | + | + | + | + | + |
|  | Retrograde | 2 | 2 | 1 |  |  |  |  |  |  |
| 8 | Antegrade | 2 | 1 | 3 | + | + | - | + | + | + |
|  | Retrograde | 1 | 1 | 0 |  |  |  |  |  |  |
| 9 | Antegrade | 2 | 2 | 2 | + | + | + | + | + | - |
|  | Retrograde | 2 | 2 | 0 |  |  |  |  |  |  |
| 10 | Antegrade | 1 | 1 | 3 | + | + | + | + | + | - |
|  | Retrograde | 2 | 2 | 0 |  |  |  |  |  |  |
| 11 | Antegrade | 2 | 0 | 0 | + | + | + | + | - | + |
|  | Retrograde | 2 | 2 | 1 |  |  |  |  |  |  |
| 12 | Antegrade | 1 | 1 | 1 | - | - | - | + | + | + |
|  | Retrograde | 1 | 1 | 0 |  |  |  |  |  |  |
| 13 | Antegrade | 2 | 2 | 2 | - | - | - | + | - | - |
|  | Retrograde | 2 | 2 | 2 |  |  |  |  |  |  |
| 14 | Antegrade | 2 | 2 | 2 | + | + | + | + | + | - |
|  | Retrograde | 2 | 2 | 1 |  |  |  |  |  |  |
| 15 | Antegrade | 2 | 0 | 0 | + | - | - | + | + | + |
|  | Retrograde | 2 | 2 | 2 |  |  |  |  |  |  |

$0=$ no opacification (enhancement); $1=$ partial opacification; $2=$ complete opacification; $3=$ unable to score; $+=$ cardioplegia should reach area;
cardioplegia should not reach area; RV = right ventricular free wall; SEP = septum; APX = apical regional.

There was complete concordance for intraobserver contrast scoring when on-line analysis of regional contrast enhancement at the time of surgery was compared by the same observer to off-line review of the videorecorded images. There was similarly no disagreement among observers who classified angiographic collateral flow to be either good or poor to the regions of interest that were evaluated.

When interobserver variability was evaluated, it was noted that 75 of 90 myocardial segments ( $84 \%$ ) were scored the same way by the two observers during independent review of the recorded video images. When interobserver scoring discordance necessitated a third observer to submit a score, ( 15 of 90 regions) the third score always agreed with one of the original two segmental contrast scores (table 5). Scoring discordance never differed by a score of more than 1 and was most commonly observed in the septal ( 6 of 15 ) and apical ( 6 of 15 ) regions.

The most common scoring discrepancy was between grades 2 and 1 (12 of 15) with scoring discrepancy between grades 0 and 1 being realized 3 of 15 times. Nine of 15 discordant scores were observed during retrograde injections, and 6 of 15 were observed during antegrade contrast injections.

## Discussion

Right ventricular dysfunction is common after CABG surgery. ${ }^{12-15}$ Right ventricular preservation is a clinical challenge, especially in a patient with occlusion of the RCA in whom antegrade cardioplegia is not expected to reach areas distal to the stenosis and in whom retrograde administration of cardioplegia is associated with inadequate right ventricular distribution and poor functional recovery. ${ }^{18,21-24}$ Although some ${ }^{4,5,7,25,26}$ reported the importance of identifying reversible predictors of func-

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Table 2. Number (\%) of Patients with a Contrast Score of 2 and a Score of 1 or 2 in the Intraventricular Septum, Apex, and Right Ventricular Free Wall (RV)

|  | Cardioplegia Distribution |  |  |
| :--- | :---: | :---: | :---: |
| Contrast Injection Site | Septum | Apex | RV |
| Contrast score of 2 |  |  |  |
| Antegrade | $10 / 15(67 \%)$ | $7 / 15(47 \%)$ | $4 / 13^{\star}(31 \%)$ |
| $95 \% \mathrm{Cl}$ | $38-88 \%$ | $21-73 \%$ | $9-61 \%$ |
| Retrograde | $11 / 15(73 \%)$ | $10 / 14^{\star}(71 \%)$ | $3 / 15(20 \%)$ |
| $95 \% \mathrm{Cl}$ | $45-92 \%$ | $42-92 \%$ | $4-48 \%$ |
| Contrast score of 1 |  |  |  |
| $\quad$ or 2 |  |  |  |
| Antegrade | $14 / 15(93 \%)$ | $10 / 15(67 \%)$ | $7 / 13^{\star}(54 \%)$ |
| $95 \% \mathrm{Cl}$ | $68-100 \%$ | $38-88 \%$ | $25-81 \%$ |
| Retrograde | $15 / 15(100 \%)$ | $14 / 14^{\star}(100 \%)$ | $6 / 15(40 \%)$ |
| $95 \% \mathrm{Cl}$ | $82-100 \%$ | $81-92 \%$ | $16-68 \%$ |

## $\mathrm{Cl}=$ confidence interval; $\mathrm{RV}=$ right ventricular free wall.

Numerator denotes the number of patients with a contrast score of either 1 or 2.

* Denominators $<15$ reflect inability to score due to inadequate image. (refer to Table 1 and text for definition).
tional outcome and maintaining an optimal global myocardial biochemical balance during the time of cardiopulmonary bypass to ensure myocardial protection, it remains that complete and homogeneous distribution of cardioplegia to all regions of the myocardium is an important predictor for preserving left ventricular function after cardiopulmonary bypass. The route of cardioplegic delivery, the presence of RCA stenosis, and the degree of coronary collateral blood flow are significant variables that influence myocardial protection, because agents designed to preserve myocardial function in jeopardized but viable tissue must be delivered to the target tissue to be effective. Retrograde administration of cardioplegia through the coronary sinus has been shown to provide only moderate cooling of the right ventricle after cold retrograde blood cardioplegia ${ }^{12,24,27}$ and inadequate delivery to the right ventricular free wall during contrast echocardiographic studies. ${ }^{9,16}$
Evidence confirmed significant anatomic variation of the coronary venous system. ${ }^{19}$ It was reported that the right ventricular free wall drains directly into the anterior cardiac vein (which empties into the small cardiac vein) or directly into the right atrium or thebesian veins. The small cardiac vein, if present, may empty into the coronary sinus, the middle cardiac vein, or the right atrium directly. The location of the self-inflated balloon of the coronary sinus catheter is unpredictable and may cause occlusion of the posterior interventricular vein (which drains blood from the right ventricle and the posterior two-thirds of the septum) as it empties into the
coronary sinus at the level of entry within the right atrium. ${ }^{9,16,28,29}$ Furthermore, back-leak of administered cardioplegia may contribute to poor distribution. ${ }^{30}$ All of these factors have contributed to right ventricular free wall maldistribution of cardioplegia from the retrograde coronary sinus route.
It appears that the development of collateral circulation and the influence of collateralization are other important factors that influence the distribution of cardioplegia. A well-developed myocardial collateral circulation can provide protection against myocardial ischemic injury, but, ironically, the presence of extensive coronary collateral circulation is a sign of advanced coronary occlusive disease. The importance of well-developed coronary collateral circulation for preserving myocardial performance has been documented by angiography, ${ }^{31}$ nuclear methods, ${ }^{32}$ and contrast ultrasonography. ${ }^{33}$ However, coronary angiography detects vessels of more than $100 \mu \mathrm{~m}$ in diameter and can underestimate collateral flow. ${ }^{33}$ Nuclear imaging technologies are impractical during surgery and may not predict cardioplegia flow delivery during cardiopulmonary bypass

Table 3. ECG Prediction of Antegrade Cardioplegia Distribution

|  | Septum | Apex | RV |
| :---: | :---: | :---: | :---: |
| Myocardial contrast echocardiography score 1 or $2=$ "+" cardioplegia distribution |  |  |  |
| Sensitivity | 10/14 (71\%) | 8/10 (80\%) | 4/7 (57\%) |
| 95\% CI | 42-92\% | 44-97\% | 18-90\% |
| Specificity | 1/1 (100\%) | $2 / 5$ (40\%) | 3/6 (50\%) |
| 95\% CI | 5-100\% | 5-85\% | 12-88\% |
| Positive predictive value | 10/10 (100\%) | 8/11 (73\%) | 4/7 (57\%) |
| $95 \% \mathrm{Cl}$ | $74-100 \%$ | 39-94\% | 18-90\% |
| Negative predictive value | 1/5 (20\%) | 2/4 (50\%) | 3/6 (50\%) |
| $95 \% \mathrm{Cl}$ | $0-72 \%$ | 7-93\% | 12-88\% |

Myocardial contrast echocardiography score 2 only = "+" cardioplegia distribution
$\left.\begin{array}{lccc}\text { Sensitivity } & 8 / 10(80 \%) & 6 / 7(86 \%) & 3 / 4(75 \%) \\ 95 \% \mathrm{Cl} & 44-97 \% & 42-100 \% & 19-99 \% \\ \text { Specificity } & 3 / 5(60 \%) & 3 / 8(38 \%) & 5 / 9(56 \%) \\ 95 \% \mathrm{Cl}\end{array} \mathrm{15-95} \mathrm{\%} \mathrm{9-76} \mathrm{\%}\right)$

[^0]Table 4. Angiogram Prediction of Antegrade Cardioplegia Distribution
$\left.\begin{array}{lccc}\hline & \text { Septum } & \text { Apex } & \text { RV } \\ \hline \begin{array}{l}\text { Myocardial contrast echocardiography } \\ \text { cardioplegia distribution }\end{array} & \text { MCE) score } 1 & \text { or } 2="+" \\ \begin{array}{lccc}\text { Sensitivity }\end{array} & 13 / 14(93 \%) & 8 / 10(80 \%) & 4 / 7(57 \%) \\ 95 \% \mathrm{Cl} & 66-100 \% & 44-97 \% & 18-90 \% \\ \text { Specificity } & 0 / 1(0 \%) & 1 / 5(20 \%) & 1 / 6(17 \%) \\ 95 \% \mathrm{Cl}\end{array} \quad 0-95 \%\right)$

MCE score 2 only = "+" cardioplegia distribution

| Sensitivity | $9 / 10(90 \%)$ | $5 / 7(71 \%)$ | $1 / 4(25 \%)$ |
| :--- | :---: | :---: | :---: |
| $95 \% \mathrm{Cl}$ | $55-100 \%$ | $29-96 \%$ | $1-81 \%$ |
| Specificity | $0 / 5(0 \%)$ | $1 / 8(13 \%)$ | $1 / 9(11 \%)$ |
| $95 \% \mathrm{Cl}$ |  |  |  |
| Positive | $0-45 \%$ | $0-53 \%$ | $0-48 \%$ |
| predictive value <br> $95 \% \mathrm{Cl}$ | $9 / 14(64 \%)$ | $5 / 12(42 \%)$ | $1 / 9(11 \%)$ |
| Negative <br> predictive value <br> $95 \% \mathrm{Cl}$ | $35-87 \%$ | $15-72 \%$ | $0-48 \%$ |
|  | $0 / 1(0 \%)$ | $1 / 3(33 \%)$ | $1 / 4(25 \%)$ |
|  | $0-95 \%$ | $1-91 \%$ | $1-81 \%$ |

$\mathrm{CI}=$ confidence interval; $\mathrm{RV}=$ right ventricular free wall.
because of changes induced in the microcirculation by cardioplegia administration. ${ }^{34}$ In the clinical setting, the role of collateral circulation is critical. In a study reported by Schirmer et al., ${ }^{23}$ the importance of correctly identifying the adequacy of collateral flow was shown by the finding of right ventricular dysfunction after CABG surgery in patients with moderate (nonsurgical) stenosis of the RCA that was not revascularized, whereas revascularization of more severely stenotic RCA lesions was associated with preservation of postoperative right ventricular function.
In our study, the presence of a Q-wave myocardial infarction implied that the vessel supplying the infarct zone was completely occluded at the time of the infarct. In addition, it was taken to mean that collateral blood supply was insufficient to provide adequate blood flow at the time of the infarct. Therefore, we presumed that in patients having coronary artery bypass surgery, the presence of a Q-wave infarction on the preoperative ECG suggested that antegrade delivery of cardioplegia would be compromised to the region of myocardium perfused by the infarcted vessel. However, we realize this may not always be the case because that the infarct-associated
vessel may recanalize (spontaneously or with thrombolytic agents) after the infarction. ${ }^{35}$
This study shows that in the presence of occlusive RCA disease, knowledge of regional distribution of cardioplegia is difficult to predict because of variability in the contribution of myocardial collateral flow and anatomic variation of the coronary venous system. These findings may help to explain the prevalence of right ventricular dysfunction, including atrial fibrillation, commonly reported, although these outcomes were not evaluated in this study. We provide evidence to motivate further investigation about the relation between cardioplegia distribution and functional recovery, without assuming that combination delivery techniques or isolated antegrade delivery may provide complete cardioplegia distribution to the entire myocardium. Direct knowledge of cardioplegia distribution may be used to modify myocardial protection strategies. For example, right ventricular protection after antegrade and retrograde delivery may still necessitate (1) initial saphenous vein grafting to bypass the myocardial region subtended by the RCA and (2) direct infusion of cardioplegic solution through the completed distal RCA graft to the myocardial target tissue. If adequate collaterals are shown by intraoperative MCE, then the need for any special modification (e.g., sequence of grafts or retrograde coronary sinus cannulation) in myocardial protective strategies would be obviated.

The limitations of this study include lack of demonstration of a functional outcome marker of cardioplegia distribution. Clearly, assessment of regional myocardial performance in regions that received cardioplegia and regions that did not receive cardioplegia would help to support the assumption that delivery of cardioplegia is essential for providing myocardial protection. This study did not assess the latter, because evidence of inadequate cardioplegia by intraoperative myocardial contrast echo prompted a change in cardioplegia delivery technique used by the surgeon to achieve complete myocardial delivery.

It could be argued that another limitation of this study is the lack of an established gold standard with which to compare the cardioplegic delivery measured with contrast echocardiography. Unfortunately no such clinical gold standard exists. However, the assumption that contrast echocardiography measures microcirculatory flow is not without supportive evidence ${ }^{9,11,36-41}$ and therefore is a reasonable standard on which to base other traditional monitoring techniques (e.g., electrocardiography, angiography).

Table 5. Interobserver Discordance

| Patient Number | Region | MCE Scores | Ante/Retro |  |
| :---: | :--- | :--- | :--- | :--- |
| 2 | Septum | 2 | 1 | Retro |
| 2 | Apex | 2 | 1 | Retro |
| 6 | Apex | 1 | 2 | Ante |
| 6 | Septum | 1 | 2 | Retro |
| 6 | Apex | 1 | 2 | Retro |
| 7 | Septum | 2 | 1 | Retro |
| 7 | RV | 1 | 0 | Retro |
| 8 | Apex | 0 | Ante | 2 |
| 10 | Apex | 1 | Ante | 2 |
| 10 | Septum | 1 | 2 | Ante |
| 10 | Septum | 2 | Retro | Retro |
| 10 | Septum | 2 | 2 | Ante |
| 12 | RV | 1 | 1 | Ante |
| 12 | RV | 1 | 2 | Retro |
| 13 |  | 2 | 0 | 1 |

Retro $=$ retrograde delivery of cardioplegia; Ante $=$ antegrade delivery of cardioplegia; RV $=$ right ventricular free wall; MCE $=$ myocardial contrast echocardiography.

Perioperative transesophageal echocardiography has been shown to significantly influence clinical decision making and to improve outcomes during mitral valvular surgery, ${ }^{42}$ congenital heart surgery, ${ }^{43}$ and postoperative management. ${ }^{44}$ Its benefit during routine use in patients undergoing elective coronary bypass surgery recently was shown. ${ }^{45}$ We report another application of intraoperative transesophageal echocardiography for patients scheduled for CABG surgery.

## References

1. Robinson LA, Schwarz GD, Goddard DB: Myocardial protection for acquired heart disease surgery: Results of a national survey. Ann Thorac Surg 1995; 59(2):361-72
2. Buckberg GD: Normothermic blood cardioplegia. Alternative or adjunct? J Thorac Cardiovasc Surg 1994; 107(3):860-7
3. Lichtenstein SV, Naylor CD, Feindel CM: Intermittent warm blood cardioplegia. Warm Heart Investigators. Circulation 1995; 92(suppl 9):II341-6
4. Zaroff J, Aronson S, Lee BK: The relationship between immediate outcome after cardiac surgery, homogenous cardioplegia delivery, and ejection fraction. Chest 1994; 106(1):38-45
5. Hilton CJ, Teubl W, Acker M: Inadequate cardioplegic protection with obstructed coronary arteries. Ann Thorac Surg 1979; 28(4):323-34
6. Grondin CM, Helias J, Vouhe PR: Influence of a critical coronary artery stenosis on myocardial protection through cold potassium cardioplegia. J Thorac Cardiovasc Surg 1981; 82(4):608-15
7. Caretta Q, Voci P, Acconcia MC: Collateral flow prevents unintentional myocardial ischemia during antegrade cardioplegia in patients undergoing coronary bypass grafting. J Thorac Cardiovasc Surg 1997; 113(3):585-93
8. Menasche P, Subayi JB, Veyssie L: Efficacy of coronary sinus cardioplegia in patients with complete coronary artery occlusions. Ann Thorac Surg 1991; 51(3):418-23
9. Aronson S, Lee BK, Liddicoat JR: Assessment of retrograde cardioplegia distribution using contrast echocardiography. Ann Thorac Surg 1991; 52(4):810-4
10. Villanueva FS, Spotnitz WD, Glasheen WP: New insights into the physiology of retrograde cardioplegia delivery. Am J Physiol 1995; 268:H1555-66
11. Allen BS, Winkelmann JW, Hanafy H: Retrograde cardioplegia does not adequately perfuse the right ventricle. J Thorac Cardiovasc Surg 1995; 109(6):1116-26
12. Mangano DT: Biventricular function after myocardial revascularization in humans: Deterioration and recovery patterns during the first 24 hours. ANESTHESIOLOGY 1985; 62(5):571-7
13. Wranne B, Pinto FJ, Hammarstrom E: Abnormal right heart filling after cardiac surgery: Time course and mechanisms. Br Heart J 1991; 66(6): 435-42
14. Christakis GT, Fremes SE, Weisel RD: Right ventricular dysfunc tion following cold potassium cardioplegia. J Thorac Cardiovasc Surg 1985; 90(2):243-50
15. Rabinovitch MA, Elstein J, Chiu RC: Selective right ventricular dysfunction after coronary artery bypass grafting. J Thorac Cardiovasc Surg 1983; 86(3):444-6
16. Winkelmann J, Aronson S, Young CJ: Retrograde-delivered cardioplegia is not distributed equally to the right ventricular free wall and septum. J Cardiothorac Vasc Anesth 1995; 9(2):135-9
17. Carrier M, Gregoire J, Khalil A: Myocardial distribution of retrograde cardioplegic solution assessed by myocardial thallium 201 uptake. J Thorac Cardiovasc Surg 1994; 108(6):1115-8
18. Noyez L, van Son JA, van der Werf T: Retrograde coronary sinus cardioplegia in myocardial revascularization: Hemodynamic evaluation of the influence on the right-ventricular function. Thorac Cardiovasc Surg 1992; 40(4):209-13
19. Partington MT, Acar C, Buckberg GD: Studies of retrograde cardioplegia. I. Capillary blood flow distribution to myocardium supplied by open and occluded arteries. J Thorac Cardiovasc Surg 1989; 97(4):605-12
20. Marriott HJL: Practical Electrocardiography. 8th edition. Baltimore, Williams \& Wilkins, 1988.
21. Boldt J, Kling D, Thiel A: Revascularization of the right coronary
artery: Influence on thermodilution right ventricular ejection fraction J Cardiothorac Anesth 1988; 2:140-6
22. Boldt J, Kling D, Dapper F: Myocardial temperature during cardiac operations: Influence on right ventricular function. J Thorac Cardiovasc Surg 1990; 100(4):562-8
23. Schirmer U, Calzia E, Lindner KH: Right ventricular function after coronary artery bypass grafting in patients with and without revascularization of the right coronary artery. J Cardiothorac Vasc Anesth 1995; 9(6):659-64
24. Gonzales AC, Brandon TA, Fortune RL: Acute right ventricular failure is caused by inadequate right ventricular hypothermia. J Thorac Cardiovasc Surg 1985; 89(3):386-99
25. Manciet LH, Fox KA, Copeland JG: Left ventricular function after extended hypothermic preservation of the heart is dependent on functional coronary capillarity. Circulation 1995; 92(suppl 9):II372-80
26. Quintilio Coci P, Bilotta F: Risk factors of incomplete distribution of cardioplegic solution during coronary artery grafting. J Thorac Cardiovasc Surg 1995; 109(103):439-47
27. Fisk RL, Ghaswalla D, Guilbeau EJ: Asymmetrical myocardial hypothermia during hypothermic cardioplegia. Ann Thorac Surg 1982; 34(3):318-23
28. Pan-Chih, Huang AH, Dorsey LM: Hemodynamic significance of the coronary vein valves. Ann Thorac Surg 1994; 57(2):424
29. Menasche P: Experimental comparison of manually inflatable versus autoinflatable retrograde cardioplegia catheters. Ann Thorac Surg 1994; 58(2):533-5
30. Voci P, Bilotta F, Caretta Q: Mechanisms of incomplete cardioplegia distribution during coronary artery surgery. An intraoperative transesophageal contrast echocardiography study. Anesthesiology 1993; 79(5):904-12
31. Helfant RH, Vokonas PS, Gorlin R: Functional importance of the human coronary collateral circulation. N Eng J Med 1971; 284(23): 1277-81
32. Berger BC, Watson DD, Taylor GJ: Effect of coronary collateral circulation on regional myocardial perfusion assessed with quantitative thallium-201 scintigraphy. Am J Cardiol 1980; 46(3):365-70
33. Sabia PJ, Powers ER, Ragosta M: An association between collateral blood flow and myocardial viability in patients with recent myocardial infarction. N Eng J Med 1992; 327(26):1825-31
34. McDonagh PF, Laks H: Use of cold cardioplegia to protect
against coronary microcirculatory injury due to ischemia and reperfusion. J Thorac Cardiovasc Surg 1982; 84(4):609-18
35. Topol EJ, Califf RM, Vandormael M: A randomized trial of late reperfusion therapy after acute myocardial infarction. Circulation 1992; 85:2090-9
36. Kaul S, Glasheen ME, Ruddy TD: The importance of defining LV area at risk in vivo during acute myocardial infarction: An experimental evaluation with myocardial contrast echo. Circulation 1987; 75:1249-60
37. Kaul S, Gilliam LD, Weymean AE: Contrast echocardiography in acute myocardial infarction II. Effect of site of injection of contrast agent on estimation of the area at risk for necrosis after coronary artery disease. J Am Coll Cardiol 1985; 6:825-30
38. Kaul S, Senior R, Daffroch H: Detection of coronary artery disease with myocardial contrast echocardiography: Comparison with 99mTc-sestamibi SPECT. Circulation 1997; 96(3):785-92
39. Feinstein SB, Shah PM, Bing RJ: Microbubble dynamics visualized in the intact capillary circulation. J Am Coll Cardiol 1984; 4:595600
40. Keller MW, Segal SS, Kaul S, Duling B: The behavior of sonicated albumin microbubbles with the microcirculation: a basis for their use during myocardial contrast echocardiography. Circ Res 1989; 65:458-67
41. Ragosta M, Camarano G, Kaul S: Microvascular integrity indicates myocellular viability in patients with recent myocardial infarction: New insights using myocardial contrast echocardiography. Circulation 1994; 89:256-69
42. Stewart WJ, Currie PJ, Salcedo EE: Intraoperative Doppler color flow mapping for decision-making in valve repair for mitral regurgitation. Technique and results in 100 patients. Circulation 1990; 81(2): 556-66
43. Muhiudeen IA, Roberson DA, Silverman NH: Intraoperative echocardiography for evaluation of congenital heart defects in infants and children. Anesthesiology 1992; 76(2):165-72
44. Chan KL: Transesophageal echocardiography for assessing cause of hypotension after cardiac surgery. Am J Cardiol 1988; 62(16): 1142-3
45. Savage RM, Lytle BW, Aronson S: Intraoperative echocardiography is indicated in high risk coronary artery bypass grafting. Ann Thorac Surg 1997; 64(2):367-74

[^0]:    $\mathrm{CI}=$ confidence interval; $\mathrm{RV}=$ right ventricular free wall.

