Intraoperative Flow Measurement in Coronary Artery Surgery

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Intraoperative Flow Measurement in Coronary Artery Surgery:
Present Applications and Future Perspectives

Meten van bloedstroom tijdens coronaire bypass chirurgie:
Huidige toepassingen en toekomstige ontwikkelingen

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General Introduction

"Wir müssen wissen, wir werden wissen."
("We must know, we shall know.")

David Hilbert (German mathematician, 1862–1943)

INTRODUCTION

Although most cardiac surgeons perform coronary surgery on microscopic structures, not often any sort of direct quality control method to test patency of the constructed anastomoses is applied.

In most cases, simple evaluation of the immediate perioperative hemodynamic performance is considered as an acceptable marker of operative success.

In this regard, it is very provocative that in surgical myocardial revascularization, electrocardiographic and hemodynamic parameters may remain postoperatively unchanged, even with a malfunctioning coronary graft.

In the light of the new transitions in cardiac surgery, we must concentrate on optimizing the quality of care we are giving to our patients.

Every medical procedure requires a quality control method, and this is particularly true for complex procedures such as heart operations. This may be difficult to accept as it requires maturity and self-judgment.

The present thesis summarizes clinical experience with intraoperative graft patency verification in cardiac surgery.

Intraoperative graft patency verification after coronary surgery has been proposed since the early 60's, when coronary surgery was at its infancy. The first flow measurement devices were based on electromagnetic technology and were soon abandoned for their many limitations.

As experience with coronary surgery grew, surgeons felt less and less obliged to document the quality of their coronary anastomoses and, until recently, coronary graft testing was seldom adopted.

Thanks to the technological improvements, ultrasound based flow meters (mainly Doppler) were available on the market in the early 80's.

Although these devices offered many advantages when compared to the electromagnetic technology, they still had many limitations.

In the late 90's, the introduction and popularization of beating heart "off-pump" coronary surgery stimulated interest upon intraoperatively documenting patency of coronary grafts.

At the same time, a further technological achievement was available with the introduction of transit time flow meters (TTFM) that offered a reproducible and simple method for testing coronary graft flow.

Construction of the anastomoses on the beating heart was supposedly technically more challenging than on the arrested bloodless heart and, for this reason, surgeons, at least some of them, felt the urgency to guarantee and proof the

technical feasibility of this innovative procedure and its good outcome in terms of quality of coronary grafting.

The present research focused on understanding and documenting the clinical applicability of this technology and its possible benefits. All the initial impetus was mainly focused at justifying the applicability of beating heart coronary surgery by proofing that patent anastomoses could be constructed even on the beating heart.

As experience with TTFM grew, a number of pitfalls in coronary grafting became clear and a number of technical mistakes that would have remained otherwise missed were detected.

After over 2 years of clinical experience, it was very evident that coronary bypass flow was a complex and multifactorial entity that was dependent on many other variables.

When looking at TTFM of coronary grafts, certain parameters can be defined, such as flow curve shape, percentage of diastolic flow, pulsatility index, and absolute flow value that, when simultaneously all accounted for, could help in better defining the quality of the anastomoses.

Interestingly, the absolute flow value was not, "per se", a good indicator of graft quality.

Although the correct interpretation of TTFM finding is complex, it is easy to discern completely occluded grafts from fully patent ones but there will be no detectable modifications in the flow parameters until the stenosis of the anastomosis has reached a hemodynamically significant critical level of 75%.

Although at this stage TTF has resulted a sensitive tool for intraoperative quality assessment of newly constructed grafts, its application can not be extended to the evaluation of coronary targets.

Transit time probes are formed by two piezoelectric crystals and one metal reflector placed on the opposite side of the probe itself. The vessel under evaluation is placed within the probe and interposed between the crystals and the reflector. For this reason, accurate dissection of the vessel is required before applying the TTFM probe.

Differently from TTFM probes, Doppler epi-coronary probes are formed by a single crystal and do not require dissecting and encircling the target artery under study and, therefore, are more easily applicable to test the status of the native coronaries and their blood flow before and after the revascularization has been performed.

Furthermore, TTF allows for a purely functional analysis of the graft-anastomosis unit and does not add any anatomical information about the degree of patency of the anastomosis.

As we understand more about coronary grafts flow patterns, we feel the necessity to better investigate intraoperatively the rheology of the coronary arteries via newly designed epicardial Doppler micro-probes.

Intraoperative epicardial coronary ultrasound has been proposed since the 1980's as a possible tool to guide cardiac surgeons on selection of appropriate coronary targets and to assess coronary anastomosis quality.

In spite of initial enthusiasm, this technology was soon abandoned due to its limitations in terms of technological designing and interpretation of findings.

Very recently, Doppler technology has resurged as a valuable intraoperative armamentarium to help cardiac surgeons selecting adequate coronary targets for revascularization and depicting both anatomical and functional features of newly constructed anastomosis.

Moreover, micro-probe Doppler has allowed for safe graft vessel harvesting (left internal mammary artery) and for selection of optimal anastomotic target site.

A newly designed Doppler micro-probe allows for recording of purely functional values (flow velocity) at the level of the anastomosis and directly on the coronary vessel.

PROSPECTS

As technology evolves, and research continues, we hope that multiple features will be included in the same vascular flow meter device to allow for simultaneous coronary graft flow measurement, epicardial coronary blood flow velocity and flow direction detection, and ultrasound imaging reconstruction of coronary targets and coronary anastomosis.

At that stage, cardiac surgeons will be able to demonstrate consistently and intraoperatively the quality of their surgical efforts.

Chapter 1

Graft Patency Verification in Coronary Artery Bypass Grafting: Principles and Clinical Applications of Transit Time Flow Measurement

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ABSTRACT

The increasing popularity of beating-heart coronary surgery has raised concerns and doubts about the quality of the coronary anastomoses performed. Intraoperative graft patency verification methods are not commonly used after coronary surgery and, most of the cardiac surgeons rely on the simple clinical signs (electrocardiogram tracings and hemodynamic stability) to make a diagnosis of coronary graft occlusion. New transit time ultrasound based methods for graft-patency verification have been adopted in many centers during beating-heart and traditional bypass grafting. Although the results are very encouraging, correct interpretation of the flow findings may prove difficult if specific rules are not properly followed. Flow curves, pulsatility index, and flow values should always be considered simultaneously before revising a coronary graft. Measurements should also be always performed with and without a proximal coronary snare. This article summarizes the main features of flowmetry and provides some technical pitfalls and suggestions to achieve an adequate intraoperative flow measurement adopting the transit time method.

INTRODUCTION

The main aim of coronary artery bypass grafting (CABG) is to increase blood flow to ischemic myocardium. Although this procedure is successfully performed in more than several hundred thousand patients a year in the United States, graft flow measurements are rarely performed in most centers. It is assumed that grafts are patent at the end of the operation, especially if the patient has no hemodynamic demise and, if cardiopulmonary bypass (CPB) was used, separation from CPB was successful.

The need to measure coronary graft flows intraoperative has not been clearly defined. Electromagnetic flow meters were first used in the early 1960s (1, 2).

In the past decade, measurement of coronary graft flow has been almost abandoned due to limitations of the electromagnetic technique.1. The increasing popularity of CABG performed on a beating heart without CPB, with the recent introduction of ultrasound-based flow meters (Doppler and transit time flow measurement [TTFM]), has revived interest and concerns about intraoperative evaluation of graft patency. In this review article, the basis of intraoperative flow measurement in coronary surgery is reviewed with particular emphasis on modern technologies available for graft patency verification.

Electromagnetic, Doppler and TTFM Devices

Regardless of the type of flow measurement device used, general principles for measurement of coronary blood flow must be met. The measurement must be stable, reproducible, and representative of the real blood flow within the constructed graft. Flow probes should be user friendly and easy to calibrate. The recorded data should be stored in the flow meter for future analysis.

Electromagnetic devices measure the intensity of the electromagnetic field generated by the electrically charged red blood cells (iron bound to haemoglobin) that flow within the vessel. Actual blood flow value is derived from, and is directly proportional to, the intensity of the electromagnetic field generated. This technology has been abandoned due to the many sources of error that can be introduced during graft flow measurements. The probe must be placed perfectly perpendicular to the vessel and careful calibration should be obtained before and during each measurement. The measured values are influenced by the hematocrit and the thickness of the vessel wall. The recorded blood flow may be falsely increased when compared to the real blood flow in the vessel. Ultrasound technology has recently replaced the electromagnetic devices. It includes two different methods: the Doppler and TTFM. Although the Doppler method has

shown good reliability both in vivo and in vitro (3), the TTFM technology is the most accurate for intraoperative verification of coronary graft patency (4).

The transit-time technique offers many advantages: measurements are theoretically independent of internal or external vessel diameter, vessel shape, and Doppler angle; and it is insensitive to the alignment between probe and vessel. The probe does not have to be in direct contact with the vessel and calibration is not necessary. The recordings are stable and data storage and analysis are routinely done. Many of these features are not offered by the Doppler technology. For this reason, TTFM has become the most widely used device for accurate intraoperative interpretation of graft patency.

Principles of Transit Time Flow meters

The first transit time flow meter was described in 1962 (5) and was never used clinically because of technologic limitations. In 1978, Drost et al (6) presented the theoretical basis for volume flow measurement based on the transit time principle. Initial limitations had been eliminated and the flow meter became commercially available in 1983. The device is available with 2- to 32-mm flow probes. The flow probe consists of two small piezoelectric crystals, one upstream and one downstream, mounted on the same side of the vessel. Opposite to the crystals, there is a small metallic reflector. Each crystal produces a wide pulsed ultrasound beam covering the entire vessel width. The area of the transducers and the distance the beam has to travel between the two transducers are known.

Although different probes are available for a wide range of vessel sizes, the most frequently used in cardiac surgery is between 2 and 3.5 mm (frequency emitted, 3.7 MHz). The probe is connected to a computer that has more than 200 MB memory and is programmed with software in Microsoft Windows format. The necessary time for an ultrasound beam, emitted from the up-stream crystal, to arrive at the downstream crystal after being reflected, and for a signal from the downstream crystal to reach the upstream crystal, is measured. Since ultrasound travels faster if transmitted in the same direction as flow, a small time difference between the two beams is calculated as the transit time of flow. Thus, the flow is proportional to the transit time. All calculations are made automatically by the flowmeter and are displayed as millilitres per minute. The level of acoustical coupling is expressed by a colour-coded square and as a percentage of the optimal contact.

Measurements are not dependent on the angle between vessel and probe. The two crystals are mounted in a fixed position and, an increase in the angle between the upstream probe and the vessel, will always be compensated by a corresponding decrease of the angle between the downstream probe and the

vessel and vice versa. Homogenous distribution of flow within the vessel is not necessary because all flow components are detected across the vessel diameter by the wide ultrasound beam. As previously mentioned, measurements are also independent of the hematocrit level, heart rate, and thickness of the vessel wall. Flow curves, together with flow and pulsatile index (PI) values, are visualized in real time on a video screen. Up to four simultaneous flow measurements can be performed. A copy can be saved in the hard disk and can be printed through a parallel port.

Flow Curves and Pulsatile Index

To correctly interpret TTFM, flow curves, PI, and mean flow values should be evaluated simultaneously. In a patent coronary graft, the hemodynamics are similar to those physiologically observed in the coronary circulation: blood flow should be mainly diastolic with minimal systolic peaks taking place during the isovolumetric ventricular contraction (QRS complex) (Figure 1). To have a correct interpretation of blood flow patterns, curves should always be coupled with the ECG tracing to differentiate the systolic from the diastolic component.

The PI, expressed as an absolute number, is a good indicator of the blood flow pattern and, consequently, of the quality of the anastomosis. This number is obtained by dividing the difference between the maximum and the minimum flow by the value of the mean flow. In our experience, optimum PI should be between 1 and 5. The possibility of a technical error in the anastomosis increases for higher PI values (7). Mean flow is expressed as millilitres per minute; its value is not, per se, a good indicator of the quality of the anastomosis and is dependent

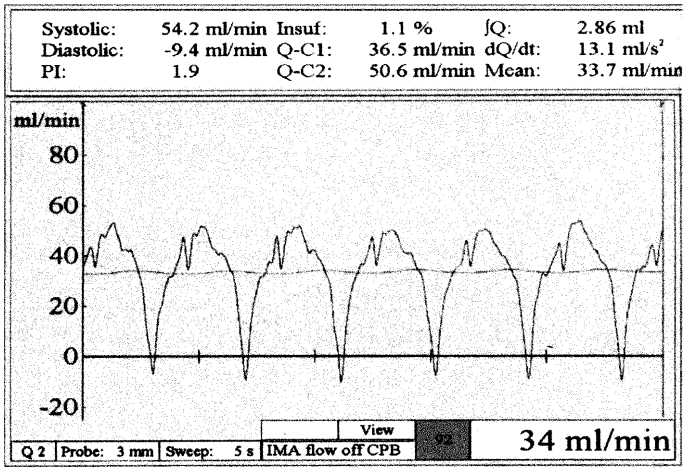

Figure 1. Normal appearing TTFM curve.

on the quality of the native coronary artery. Low flow values can be expected in fully patent anastomoses whenever the target territory has poor run-off (7).

Transit Time Flow meters in Cardiac Surgery: Technique and Pitfalls

By avoiding CPB in the construction of coronary grafts, surgeons have had to document graft patency intraoperatively. We adopted the transit time technology to depict patency of more then 1,000 coronary grafts performed without CPB (7).

In our experience, flow values and flow curves were obtained using the TTFM device (Medistim BF 2004; Medistim; Oslo, Norway) at the end of every single anastomosis. A standard technique of measurement has been developed to avoid erroneous results.

The TTFM probe is perfectly fitted around the graft. Different probe sizes are available to avoid distortion or compression of the graft. Skeletonization of a small segment of the mammary artery is necessary to reduce the quantity of tissue interposed between the vessel and the probe. No dissection is necessary for the venous grafts. Aqueous gel is used to improve probe contact. Transit time flow measurements have to be evaluated with and without proximal snaring of the native coronary artery to detect any possible imperfection localized at the toe of the anastomosis and to exclude flow competition from the native vessel. Before making any measurements, adequate de-airing of the grafts is performed using a 25 G needle. Adequate systemic blood pressure is maintained and traction on the pericardium is released to allow the heart to return to its anatomic position. Transit time flowmetry should be repeated before chest closure after protamine administration to confirm graft patency and to depict any possible graft kinking or compression. The TTFM findings are stored in the flowmeter hard disk with data concerning size and quality of the grafts and revascularized vessels.

Clinical Interpretation of Findings

A large series of comparative and validation studies have been performed in vitro and in vivo before accepting the clinical applicability of TTFM in vascular and cardiac surgery. Lundell and co-workers were the first to document the small variability and error of measurement of the transit time flowmeter (8).

Laustsen and associates validated the clinical use of TTFMs to depict blood flow in venous and arterial grafts after CABG (9). Comparison studies between TTFM and Doppler ultrasound methods have helped underline the superiority and increase the popularity of TTFM in cardiac surgery (4). We began using TTFM routinely in off-CPB coronary surgery in 1996. After 3 years of clinical experience, we believe that this technology is effective in the depiction of highly

stenotic coronary anastomoses. Data concerning the specificity and sensitivity of TTFM have never been published and, at the moment, the ability of TTFM to detect less than critical stenosis has not been clearly defined.

A neural network pattern recognition analysis of graft flow characteristics has been proposed by Cerrito and coworkers (10) to improve TTFM depiction of anastomotic errors. After a complex mathematical analysis of the flow curves, it is possible to detect stenoses causing a 50% or greater narrowing of the anastomoses. Less than critical stenoses cannot be detected with TTFM due to the fact that no modifications in the hemodynamic performances of the grafts happen at this level. Another limit of TTFM, which will be possibly solved with ever-increasing clinical experience, is the lack of standard or nominal curves and flow values for different types of grafts and revascularized vessels. Standardization of the TTFM findings is difficult due to large biologic variability between different subjects and within the same subject. Interpretation of flow curves and TTFM findings is still empirical and dependent on the surgeon's personal experience. Spence and associates (11) have tested the ability of 19 international surgeons to detect anastomotic errors by evaluating mean blood flow and flow waveform morphology. More than 70% of the surgeons accepted anastomoses with severe stenoses but all of them were able to detect highly stenotic anastomoses (>90% stenoses).

We believe the ability to correctly interpret TTFM findings needs to be acquired with clinical and experimental experience. Surgeons who have not been exposed to this technology cannot assign exact importance to the TTFM patterns. To improve the applicability of TTFM, flow patterns, PI values, flow values, and clinical findings (for example, ECG tracing, hemodynamic values) should always be evaluated simultaneously. Specific features should always be recognized in a flow curve. In patent grafts, flow curves should have a diastolic pattern with a small component of negative systolic flow. As previously mentioned, the flow in the coronary grafts follows the same hemodynamic rules as the flow in the native coronary arteries. During diastole, blood flows into the graft and is directed to the coronary artery; during systole, the coronary artery is compressed and retrograde blood flow is detected in the graft (Figure 1). If the anastomosis is stenotic, the flow curve becomes spiky and mainly systolic (Figure 2). In this situation the only flow through the graft is negative systolic flow since there is no perfusion of the coronary artery during diastole. The right coronary system follows different rules: a good quantity of blood flows in the right coronary during systole due to less compression of the epicardial vessels during right ventricular contraction. For this reason, whenever testing patent grafts to the right coronary system, a larger component of positive systolic flow

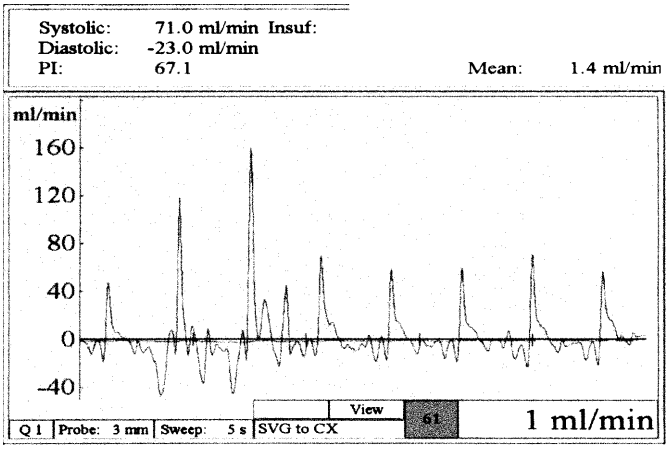

Figure 2. Spiked appearance of TTFM curve in a severely stenotic coronary graft.

may be recorded (7). Ironically, clinical experience has shown that absolute flow value per se is not a good indicator of the quality of the anastomosis and cannot justify graft revision. There are too many variables influencing absolute flow, including size of the graft and quality of the coronary artery revascularized. Moreover, coronary flow reserve can better delineate anastomotic imperfections than absolute flow. Walpoth and co-workers (12) documented that the quality of an anastomosis can be better defined by testing its dynamic ability to increase graft flow whenever myocardial oxygen demands are increased during infusion of adenosine. In our experience (7), PI values are good indicators of the quality of the anastomosis. High PI values are suggestive of anastomotic imperfections; therefore, the PI alone could justify coronary graft revision (7). Even though an absolute PI value has not been defined, we have empirically selected the limit of 5 on the basis of our clinical experience with TTFM. Di Giammarco and associates proposed a value of 2.5 as the limit PI above which an anastomosis should be revised. Again this value was derived from their clinical experience (13).

A standardized method of flow measurement should be used to minimize the errors of TTFM. Proximal snaring of the native coronary is important to obtain reliable TTFMs. Flow pattern remains unchanged when the coronary artery is proximally snared and increases in the unsnared artery. If lesions at the level of the toe of the anastomosis are present, a decrease in absolute flow will be recorded when the native coronary artery is snared proximal to the anastomosis.

Postoperative angiography is considered the gold standard in the evaluation of coronary graft patency. Findings with TTFM have often been compared with those of postoperative angiography. We believe a comparative study between postoperative angiography and intraoperative TTFM has limitations since

angiography provides a limited biplanar view of the coronary arteries and the coronary grafts, without providing specific information about the hemodynamic parameters of the anastomoses. Conflicting results between angiography and intraoperative TTFM have been reported (14).

TTFM is useful for the intraoperative detection of coronary graft stenoses, its ability to help predict midterm postoperative graft lesions needs to be better defined. Louagie and co-workers (15) reported that intraoperative hemodynamic assessment, via pulsed Doppler flowmeter, can have a satisfactory predictive value for midterm graft occlusion. On the contrary, the same hemodynamic parameters are useless in the prediction of midterm graft stenoses. This can be explained by the fact that midterm stenoses development is a dynamic process related to scar tissue formation and degeneration of the graft. For this reason, it cannot be detected at surgery. If the comparison between TTFM and angiography is difficult, encouraging results have been obtained when using other techniques of postoperative graft patency verification that, differently from angiography, can provide more precise information on hemodynamic characteristics of the grafts. Walpoth and associates (16) for example, have shown a significant correlation between intraoperative TTFMs and postoperative magnetic resonance imaging results.

CONCLUSION

Transit time flowmetry is a useful tool in the depiction of coronary graft imperfections intraoperative. As compared with angiography, this method is minimally invasive, easy to use, and provides real time information about the hemodynamic characteristics regarding constructed grafts. Compared to traditional flow meters, TTFM shows a higher standard of technology and reliability. Although it is evident that the sensitivity and specificity of TTFM remain to be understood (10, 11), correct interpretation of flow curves, mean flows, and PI values can reduce the number of undetected technical errors (7). These values should always be considered together with the clinical findings. Mean flow value is of minor importance when evaluating a coronary graft; on the contrary, PI values and flow patterns are good indicators of the quality of the anastomoses. Acceptable flow values with abnormal flow patterns and high PIs may underline highly stenotic lesions of the distal anastomoses (7). On the contrary, flows with good curve patterns may occur when the revascularized territory has poor run off (7). Even if interpretation of TTFM findings is still based on personal experience and empirical values, many researchers are focusing their attention on trying to

develop nominal TTFM curves and objective mathematical values to define the applicability of this new technology (10, 13). Regarding the ability of TTFM to help predict mid- and long-term patency rates, comparative studies with other diagnostic tools are necessary.

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Chapter 2

Flow Measurement in Coronary Surgery

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ABSTRACT

Background

Many of the modern less invasive approaches to coronary artery bypass grafting (CABG) are performed without the use of the heart lung machine and cardiac asystole. Even after the introduction of mechanical stabilizers, the ability to achieve a technically perfect anastomosis is less certain in beating heart bypass surgery. Our group has begun to assess the surgical results of beating heart CABG using Transit Time Flow Measurement (TTFM). Our experience indicates that a meticulous and controlled method of assessing the results of intraoperative flow measurements can improve the quality of information and increases the accuracy of diagnosing technical problems with newly constructed bypass grafts. For this reason, we developed a standard algorithm for using and interpreting intraoperative TTFM.

Methods

From January to August of 1998, 161 patients underwent off-pump CABG with a total of 323 distal anastomoses (2.0 grafts per patient). All completed grafts were tested intraoperative with TTFM and the decision to accept or revise any individual graft was based on a decision nomogram using key values readily available from the TTFM output.

Results

Thirty-two grafts (9.9%) were surgically revised based on unsatisfactory flow curves, the Pulsatile Index, or both. All revised grafts were found to have a significant technical error, such as an intimal flap, thrombus, conduit kinking, or dissection. There were no major complications, myocardial infarctions, or deaths in the entire series of patients.

Conclusions

Based on our favourable use of TTFM, we strongly recommend that patency of every graft be assessed whether the operation is performed off pump or on cardiopulmonary bypass. Guidelines for performing and interpreting TTFM ensure a high degree of confidence in the completed graft. The decision to revise a graft can be made based on simple parameters easily acquired from the TTFM device. Any concern about quality or quantity of flow should prompt immediate revision.

INTRODUCTION

Our group has established a new standard for performing coronary artery bypass grafting without the use of heart lung support in the majority of our current patient referral group (1). We have previously reported on the results of 505 patients undergoing transsternal multivessel off-pump coronary artery bypass (OPCAB) as compared to a historical control group of 2,869 patients operated with traditional heart-lung bypass and cardioplegia (1). Our initial results indicated that complications were fewer in the OPCAB group despite a greater number of redos, calcified ascending aortas, and immunocompromised patients when compared with the traditional group.

To ensure quality of the anastomosis in beating heart surgery, we have investigated the use of a specific flow-measurement device and a set of information parameters yielded by analysis of the flow curves. Transit time flow measurement (TTFM) is a new ultrasound based technology that improves the accuracy of graft flow measurement and yields real-time waveforms of graft flow (2). The use of the MediStim BF2004 transit-time flow meter has improved our surgical results by early detection of graft problems allowing immediate intraoperative revision.

Our experience with this technology in several hundred patients confirms our premise that off pump coronary revascularization can be performed safely with excellent intraoperative patency rates. This manuscript describes our intraoperative experience with TTFM in our most recent cohort of OPCAB patients.

MATERIALS AND METHODS

From January 1998 to August 1998, 161 patients underwent coronary revascularization without the use of the heart lung machine. A total of 323 distal anastomoses were created using saphenous vein and left internal mammary artery (LIMA) conduits, for a mean of 2.0 grafts per patient. There were 183 grafts to the anterior wall (left anterior descending and diagonal), 60 to the lateral wall (circumflex or marginal), 75 to the posterior wall (right coronary artery or posterior descending) and 5 to other minor coronary branches.

The MediStim Butterfly Model BF 2004 transit time flow meter (MediStim AS, Oslo, Norway) was used for assessment of every graft prior to closure of the chest. A standard algorithm for performance of the measurement, for quantitative analysis, and for waveform interpretation was developed and applied to each case.

SURGICAL TECHNIQUE

Once the target vessel was identified, a 4-0 pledgetted Prolene® suture is used to snare the coronary artery proximally. After 3 minutes of ischemic preconditioning, the snare was released and the coronary stabilizer put into place at the target site chosen for revascularization. After the arteriotomy was made, an intracoronary shunt (Cardiothoracic System, Cupertino, CA) was positioned into the vessel lumen and the anastomosis was completed using continuous 7-0 Prolene® suture. The stabilizer was then removed and TTFMs obtained with the snare on and off. Flow values and flow curves were recorded for every graft. All measurements were repeated again prior to chest closure.

RESULTS

We developed a standard algorithm for utilizing intra-operative TTFM data. Since normal flow measurement patterns have not been published, we revised the anastomosis if there was any doubt about its integrity.

The total number of revised grafts was 32 (9.9%): 17 LAD grafts, 7 circumflex or marginal grafts, 7 PDA grafts, and one to an acute marginal branch. At graft revision, six of the 32 explored grafts (18.8%) were found to be completely obstructed. Another nine grafts (28.1%) had minimal stenosis, 12 (37.5%) had an intimal flap or a clot in the native coronary. In five cases (15.6%), the conduit was kinked or a dissection of the LIMA was found.

All patients recovered without acute myocardial infarction. There were no major postoperative complications and no postoperative deaths. All patients are currently alive and symptom free at follow-up.

DISCUSSION

Flow assessment has been used in the past as a method of determining acute intraoperative graft failure. Foxworthy et al. published the classic paper on the decision to revise grafts based on intraoperative flow measurement (3). His group used an electromagnetic flow meter to assess every graft by performing maximal vasodilation and recruitment of maximal flow using intra-graft injections of 20 mg of papaverine. The average increase in post-papaverine flow was 115% (3). Grafts, which did not demonstrate at least a two-fold increase in electromagnetic flow value after papaverine injection, were subject to mechanical probing of the

anastomosis. Of the 32 grafts which were probed, 26 improved immediately (to 126% of baseline flow) indicating a minor but correctable problem with the distal anastomosis. If the flow still did not increase, then the grafts were revised.

Most devices used in past decades have been based on electromagnetics. These devices measure the deflection of the magnetic force created by the movement of the iron atoms in the hemoglobin complex. However, many variables affect the accuracy of electromagnetic flows.

Transit time flow measurement is based on the transit time principle. Lausten et al. verified improved accuracy with TTFM when compared with electromagnetic measurements (2). Other authors have documented the use of the TTFM and Doppler methods in cardiac surgery (4-7).

Our group has also developed a performance algorithm that tests the reactivity of the graft and the distal bed. The proximal snare also allows for detection of technical mistakes. For example, if a stenosis exists at the toe of the anastomosis, flow through the graft will be mainly retrograde and will decrease drastically whenever the proximal coronary snare is applied. If the native coronary has a non-critical lesion, absolute flow measurement may drop after the release of the snare due competition with native vessel flow.

Our practice is to perform TTFMs immediately after the anastomosis is completed and then again, several more times thereafter to detect spasm resulting from manipulation. TTFM readings should be made after removing the stabilizer and releasing all pericardial traction sutures since direct compression or distortion of the coronaries can result in false measurements. Close monitoring of the systemic pressure is also necessary when obtaining readings, especially when arterial grafts are used. Low systemic pressure and manipulation can cause spasm of the graft resulting in decreased absolute flow.

Competition between different grafts may also play a role in TTFM. Competitive flow from adjacent grafts supplying the same territory may affect the TTFM results. For this reason, whenever inadequate flow is measured, we test repeatedly while adjacent grafts are momentarily clamped to eliminate this effect. When venous grafts are used, measurement immediately before chest closure may reveal possible graft kinking.

The size of the probe used to measure flow is important. Only good contact with the flow probe can guarantee an accurate measurement. We utilize three different probe sizes for each case: 2, 2.5 and 3 millimeters. The flow probe should be applied so that the vessel lies within the sensing window and care should be taken not to compress the vessel. In addition, the probe should be exactly perpendicular to a straight, non-curved portion of the graft.

Turbulence will decrease the sensitivity of the measurement. For this reason, it is recommended not to place the probe close to a stenosis, side branch or curved segments of the vessel.

For a pedicled internal mammary artery graft, a section should be skeletonized so that the acoustic window of the probe fits exactly over the IMA to ensure optimal contact. An aqueous gel is used to decrease the space between the probe transducer and the vessel wall, thereby improving contact and reducing interference.

The importance of TTFM for evaluating coronary artery bypass grafts lies in the interpretation of the data. A low value of mean flow is not "per se" an indicator of an inadequate anastomosis. Grafts placed to small or diffusely diseased target vessels may yield low values even with a technically perfect anastomosis. This obligates the surgeon to understand the characteristics of the TTFM waveforms and the meaning of the derived values. When interpreting a TTFM curve, there are some crucial numerical values derived from the flow tracing which are displayed on the accompanying monitor. The mean flow (Q), expressed as millilitres per minute, and The Pulsatile Index (PI) expressed as an absolute number.

The Pulsatile index (PI) is a dynamic parameter obtained by dividing the difference between the maximum and minimum flow by the value of the mean flow. In our experience, the PI should be between one and five. The probability of a technical error in the anastomosis increases for higher PI values.

Understanding the flow curves is also essential to correctly interpreting the clinical significance of these numerical values. The TTFM curve is pulsatile with

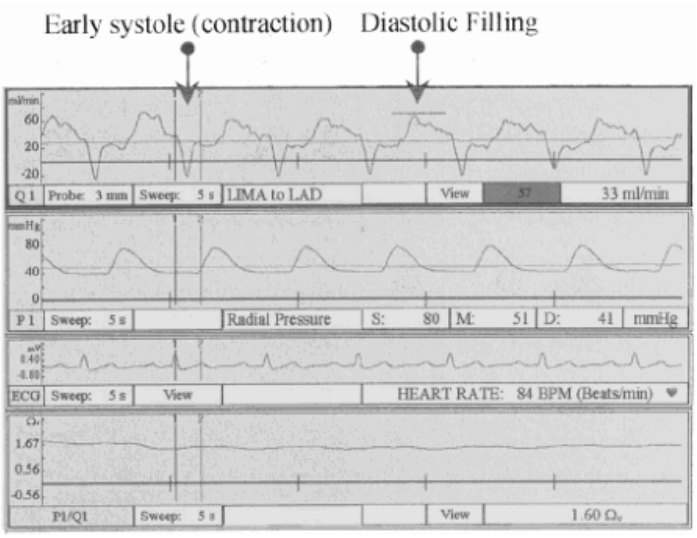

Figure 1: Normal appearing TTFM curve

a maximum, minimum and a mean flow value (Figure 1). The minimum flow is the early systolic negative peak normally followed by a large positive diastolic peak (diastolic filling). Typically, flow in a patent coronary graft occurs in diastole. Therefore, only variations from the standard flow curve, together with high PI values and low flow, justify revision.

For example, in Figure 2, the flow curve of a LIMA-LAD graft changes drastically after coronary snaring. Flow is reduced to almost zero, the PI increases, and the flow curve shows mainly systolic flow. As the proximal snare is reapplied, retrograde flow is eliminated unmasking a problem with the outflow in the graft. Exploration of the anastomosis revealed a stenosis at the toe.

In Figure 3, a saphenous - RCA graft has a flow of only 6ml/min with a PI of 29. The flow curve, with positive systolic peak, is suggestive of a technical

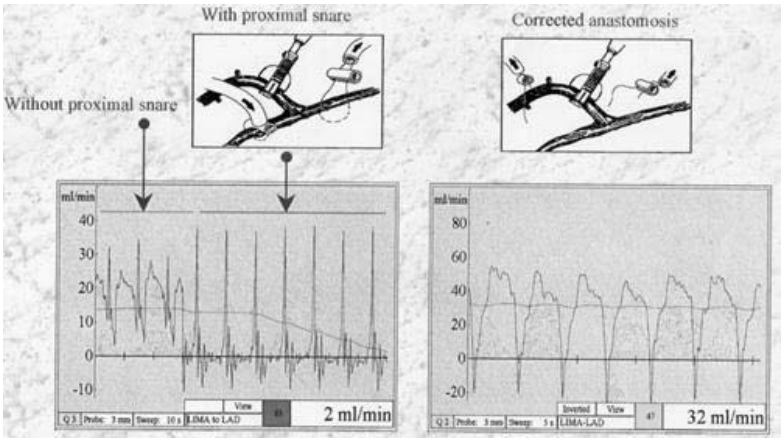

Figure 2: TTFM flow curve of LIMA to left anterior descending: note the mainly systolic flow. Revision of the graft revealed a stenosis at the toe of the anastomosis

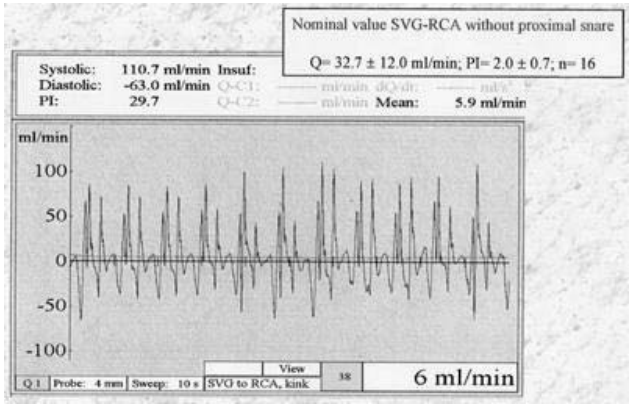

Figure 3: TTFM flow curve of a kinked SVG to the right coronary artery

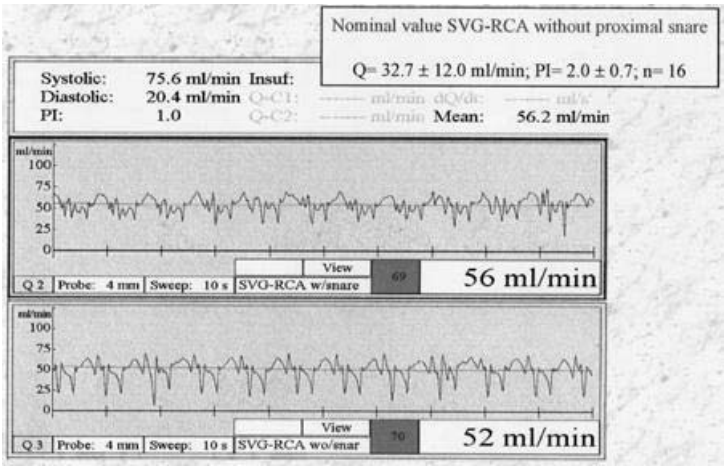

Figure 4: TTFM flow curve of the revised SVG to the right coronary artery

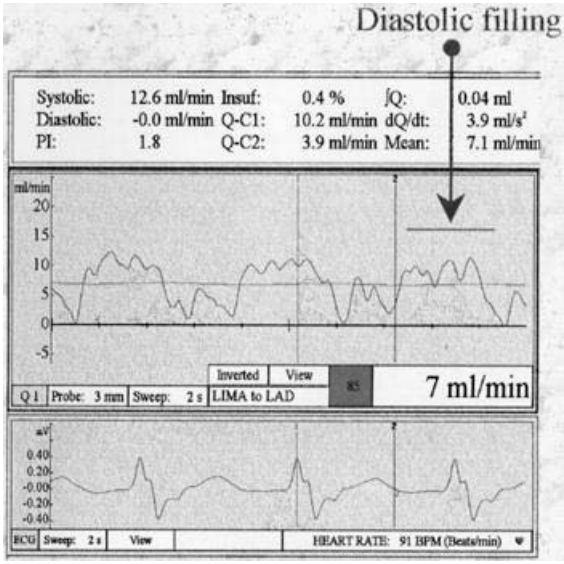

Figure 5: TTFM flow curve of a perfectly patent LIMA to the left anterior descending: note how the flow is only 7 ml/min but PI and curve shape are perfect. Lima and coronary were found to be very small in caliber

mistake. At re-exploration, the graft was found to be kinked. Figure 4 shows the curve after graft revision.

As noted above, sometimes low-flows are present despite a perfect anastomoses. Figure 5 shows a TTFM curve obtained from a LIMA - LAD graft where the mean flow is only seven ml/min but the PI and curve morphologies are perfect. This graft was not revised because both the mammary artery and the native coronary artery were very small in calibre.

In conclusion, we have routinely used TTFM in coronary artery bypass surgery to verify patency of every graft prior to chest closure. We have used the same flow equipment for hundreds of patients and developed a standard protocol for testing the completed graft with and without contribution of flow. Interpretation of the values obtained has allowed us to reach a decision whether or not to revise a graft. Based on our findings at revision, we believe this technology accurately diagnoses technical problems with a newly constructed bypass grafts. It should be used to assess every graft; even those created on the arrested heart with the assistance of the heart-lung machine.

In our experience, this device has proven to be very sensitive in detecting highly stenotic anastomoses. At this time, we can not make any comment about its ability to detect lower grade anastomotic stenosis. We believe that improvements in the technology of flow measurement will permit even more sensitive and specific flow-measurement devices. Further investigation and strict follow up studies are strongly encouraged by the present positive results.

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Chapter 3

Is intraoperative measurement of coronary blood flow a good predictor of graft patency?

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We read with interest Hirotani et al. manuscript (1) about intraoperative graft patency verification using transit time flow measurement (TTFM). The authors report their results with intraoperative TTFMs and postoperative angiography concluding that intraoperative coronary bypass flow is not, per se, a good predictor of graft stenosis.

We have been using TTFM technology since 1996 (2) to evaluate graft patency in more than 1200 patients. In our opinion strict protocols should be followed to correctly interpret TTFM findings.

1. Measurements should always be done with and without proximal occlusion of the revascularized coronary artery to detect any stenosis localized at the toe of the anastomosis and to exclude flow competition from the native vessel (2). High level of retrograde blood flow may exist in spite of stenosis at the toe of the anastomosis; in this case drastic reduction in absolute flow is observed after proximal snaring of the coronary artery (2). On the contrary, low flow status may be detected in perfectly patent anastomoses, whenever competition is present from less than critically stenosed coronary arteries. In this case, after placement of proximal snare, an increase in absolute graft flow can be observed (2).

2. Graft patency evaluation on the only basis of absolute flow value should be discouraged. Blood flow is directly proportional to blood pressure and inversely proportional to vascular resistance (Q = P/R, Q = Blood flow, P = Blood pressure, R = vascular resistance). Vascular resistance is the real limit to blood flow and is dependent on many variables including blood viscosity, length of the vascular conduits, and the fourth power of the vessel's radius ($R = 8\eta L/\pi r^4$, R = vascular resistance, η = blood viscosity, L = conduit length, r = vessel's radius). For this reason, absolute blood flow is not a good predictor of anastomotic quality because high vascular resistances may exist in spite of fully patent anastomoses.

3. To correctly address TTFM findings, flow curves, pulsatile index (PI) and mean flow values should be evaluated simultaneously. The curves are coupled with the EKG tracing to correctly differentiate systolic from the diastolic flow. In a patent coronary graft, the hemodynamics are similar to those physiologically observed in the coronary circulation: blood flows mainly during diastole with minimal systolic peaks taking place during the isovolumetric ventricular contraction (QRS complex).

The PI, expressed as an absolute number, is a good indicator of the flow pattern and, consequently, of the quality of the anastomosis. This number is obtained by dividing the difference between the maximum and the minimum flow by the value of the mean flow. In our experience, the PI should be between 1 and 5. The possibility of a technical error in the anastomosis increases for higher PI values (2, 3).

In conclusion we agree that mean graft flow, being very dependent by the quality of the revascularized coronary artery, is not per se a good indicator of the quality of the anastomosis. On the contrary, TTFM technology may be very useful if mean flow values are interpreted together with TTF curves and PI values. Although there is still necessity to define the sensitivity of TTFM in detecting less then critical stenosis, correct and simultaneous interpretation of flow curves, mean flows, and PI values is crucial to reduce the number of undetected technical errors.

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Chapter 4

Graft revision after transit time flow measurement in off-pump coronary artery bypass grafting

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ABSTRACT

Objective

To determine whether coronary graft patency can be predicted by transit time flow measurement (TTFM).

Methods

From May 1 1997 to December 31 1998, TTFM was prospectively evaluated in 409 patients undergoing coronary artery bypass grafting (CABG) without cardiopulmonary bypass (CPB). All grafts (1145) were tested with TTFM.

Results

Thirty-seven out of 1145 grafts (3.2%) were revised in 33 patients (7.6%). In six cases (18.1%) use of CPB was necessary during revision due to hemodynamic instability. The remaining patients underwent revision off-pump. Thirty-four grafts (91.9%) were revised for both low flow and abnormal flow curve patterns. Findings at revision included: thrombosis of the anastomosis (n . 6), stenosis at the toe or heel of the anastomosis (n . 8), coronary flap or dissection (n . 5), dissection of the internal mammary artery (n . 5), graft kinking (n . 4), flap at proximal anastomosis (n . 1), coronary stenosis distal to the graft (n . 3), and no findings (n . 2). After revision all flow values and flow patterns improved. Although three additional grafts (8.1%) were revised for low flow (7 ml/min) despite normal flow patterns, there were no findings at revision and flow values and curves remained unchanged after revision. Postoperatively, one patient developed a stroke (3%), one had an acute myocardial infarction (MI) (3%), one had a sternal wound infection (3%), and one required prolonged ventilatory support (3%).

Conclusion

Evaluation of TTFM is valuable in determining the status of a coronary graft after CABG. Correct interpretation of flow patterns allows for correction of abnormalities prior to chest closure.

INTRODUCTION

The increasing popularity of coronary artery bypass grafting (CABG) performed on a beating heart without cardiopulmonary bypass (CPB), has raised interests and concerns about intraoperative evaluation of graft patency. In the past, a wide variety of flow measurement techniques have been used to assess intraoperative the quality of the anastomoses after traditional CABG performed under CPB conditions (1,2).

Transit time flow measurement (TTFM) has recently been introduced as an effective and reliable mean for intraoperative evaluation of coronary grafts. This technology allows for flow determination independently of vessel size, shape and Doppler angle used (3). Exact interpretation of transit time flow patterns is essential to correctly use this technology in both off-CPB and traditional CABG (4,5). The objective of this study was to assess the clinical applicability of TTFM in detecting anastomotic imperfections following myocardial revascularization in off-CPB coronary artery surgery.

MATERIALS AND PATIENTS

From May 1997 to December 1998, TTFMs were evaluated in 409 patients undergoing off-CPB coronary artery surgery via median sternotomy. A total of 1145 grafts were tested with TTFM.

SURGICAL TECHNIQUE

After median sternotomy and conduit harvesting, the pericardium was opened and pericardial stay sutures were placed. Exposure of the different coronary branches was obtained placing the `single' suture in the oblique sinus of the pericardium (6). Coronary stabilization was achieved with the CTS stabilizer (CTS, Cupertino, CA). Systematically proximal snaring (4-0 pledgetted suture) and intracoronary shunting of the involved coronary artery branches were used.

The distal anastomoses were performed with 7-0 prolene running suture. The proximal anastomoses were performed with 6-0 prolene running suture on a partially excluded ascending aorta.

TTFM TECHNIQUE

At the end of every single anastomosis, flow values and flow curves were obtained using the TTFM device (MediStim BF 2004, MediStim, Oslo, Norway).

The TTFM probe was perfectly fitted around the graft. Different probe sizes were available to avoid distortion or compression of the graft. Skeletonization of a small segment of the mammary artery was necessary to reduce the quantity of tissue interposed between the vessel and the probe.

Aqueous gel was used to improve probe contact. TTFM was evaluated both with and without proximal snaring of the native coronary artery to detect any possible imperfection localized at the toe of the anastomosis and to exclude flow competition from the native vessel.

Before making any measurement, adequate de-airing of the grafts was performed, adequate systemic blood pressure was maintained, traction on the pericardium was released and the stabilizer was removed from the epicardial surface to allow for the heart to return to its anatomical position. TTFM was repeated before chest closure to confirm graft patency and to detect any possible graft kinking or compression.

CURVE INTERPRETATION

During our clinical experience we developed a progressive expertise in TTFM findings interpretation. To correctly address the TTFM findings, flow curves, pulsatile index (PI) and mean flow values are evaluated. The curves should always be coupled with the EKG tracing to correctly differentiate the systolic from the diastolic flow. In a patent coronary graft, the hemodynamics are similar to those physiologically observed in the coronary circulation: blood flows mainly during diastole with minimal systolic peaks taking place during the isovolumetric ventricular contraction (QRS complex) (Fig. 1).

The PI, expressed as an absolute number, is a good indicator of the flow pattern and, consequently, of the quality of the anastomosis. This number is obtained by dividing the difference between the maximum and the minimum flow by the value of the mean flow. In our experience, the PI should be included between 1 and 5. The possibility of a technical error in the anastomosis increases for higher PI values. The mean flow is expressed as ml/min and, being very dependent by the quality of the revascularized coronary artery, is not a good indicator of the quality of the anastomosis.

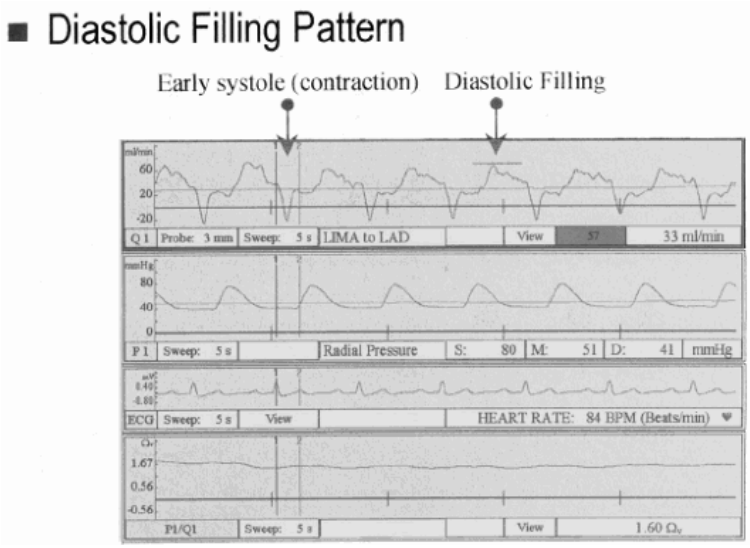

Figure 1: Normal TTFM curve

Mean flow values should always be interpreted together with TTF curves and PI values.

RESULTS

Forty-one grafts (41/1145) were revised in 33 patients. In three patients, four flow curves and flow values were not properly stored in the TTFM device hardware and for this reason have not been included in this study.

A total of 37 grafts are included: 18 to the left anterior descending coronary (LAD) and diagonal branches, ten to the circumflex system and nine to the right coronary artery system (RCA) (Table 1).

A total of six patients (18.1%) underwent graft revision on CPB. TTFM findings before revision are summarized in Table 1.

Curve patterns, flow and PI values remained unchanged after topical use of vasodilators (papaverine and nitrates). Twenty-nine grafts (78.37%) were revised for abnormal (systolic) flow patterns, high PIs and low flow values. In five cases (13.51%), despite abnormal flow curves (systolic spikes) and high PIs, flow values were on average greater than 15 ml/min. Findings at revision of these 34 grafts included: thrombosis of the anastomosis (six patients), stenosis at the toe or heel of the anastomosis (eight patients), intimal flap or dissection in the native coronary artery (five patients), dissection of the internal mammary artery (five patients), graft kinking (four patients), flap at proximal anastomosis (one

Table 1: TTFM findings in 37 grafts before revision.

Graft	% Coronary stenoses	Size coronary (mm)	Mean flow w/wo snare (ml/min)	PI w/wo snare	Resistance w/wo snare (Ω)	Flow pattern
SVG ⇒ RCA	*90*	*1.5*	*12/12*	*49/49*	*7.08/7.08*	*Systolic*
LIMA ⇒ LAD	100	2	5/5	6.6/6	12/12	Systolic
SVG ⇒ RCA	70	2.5	3/3	55/50	25.6/25.6	Systolic
SVG ⇒ D	85	2.0	6/12	10.8/4.2	9/7.83	Systolic
LIMA ⇒ LAD	90	2.5	0/1	7/7	60/60	Systolic
SVG ⇒ RCA	**100**	**1.5**	**5/5**	**0/3.3**	**11/11**	**Diastolic**
LIMA ⇒ LAD	85	2	0/4	4.2/3.2	80/23.24	Systolic
LIMA ⇒ LAD	*90*	*2.5*	*8/19*	*4.5/1*	*10.25/4.31*	*Systolic*
LIMA ⇒ D	90	2	12/7	3/3	6.5/11.42	Systolic
RIMA ⇒ RCA	100	2.5	0/15	48/4.3	62/3.86	Systolic
SVG ⇒ CX	50	1.5	0/1	12.7/12.6	51/51	Systolic
SVG ⇒ OM	90	2.0	0/0	45.7/45.7	83/83	Systolic
LIMA ⇒ LAD	90	1.5	1/1	34.6/34.6	87/87	Systolic
SVG ⇒ CX	90	1.5	0/0	22.1/22.1	67/67	Systolic
LIMA ⇒ LAD	**85**	**1.5**	**10/6**	**4.3/4.6**	**9.3/13.5**	**Diastolic**
SVG ⇒ RCA	80	2.0	0/14	10.4/2	73/5.7	Systolic
LIMA ⇒ LAD	90	2.0	1/4	14/4.9	69/17.5	Systolic
SVG ⇒ RCA	*95*	*2.0*	*13/13*	*8.2/8.2*	*7.3/7.3*	*Systolic*
LIMA ⇒ LAD	100	1.5	6/12	5.8/3.5	11.83/6.16	Systolic
LIMA ⇒ LAD	80	2.0	6/5	10/10	68/70	Systolic
SVG ⇒ OM	80	2.5	3/1	13.9/22	21.5/71	Systolic
SVG ⇒ OM2	90	2	0/10	225/6.5	70/7	Systolic
SVG ⇒ RCA	100	1.0	3/5	12/12	25.3/15.2	Systolic
SVG ⇒ D	90	1.5	0/0	52.8/52.8	67/67	Systolic
SVG ⇒ OM2	100	2.5	6/6	11.7/11.7	9/9	Systolic
SVG ⇒ LAD	90	1.5	0/11	58.4/2	86/8.3	Systolic
LIMA ⇒ LAD	**50**	**1.5**	**7/7**	**1.3/1.3**	**16.57/16.57**	**Diastolic**
LIMA ⇒ LAD	90	2.0	2/13	30.9/4.3	34/5.38	Systolic
SVG ⇒ LAD	60	1.5	0/0	265/265	89/89	Systolic
SVG ⇒ CX	60	1.5	1/1	67.1/67.1	57/57	Systolic
SVG ⇒ RCA	70	2.0	11/11	10/10	60/60	Systolic
SVG ⇒ OM1	*75*	*2.0*	*9/12*	*33.5/5*	*6.5/4.9*	*Systolic*
SVG ⇒ D	75	2.0	0/0	70.5/11	74/74	Systolic
SVG ⇒ RCA	95	2.5	8/4	14/14	8/16.25	Systolic
SVG ⇒ OM2	100	1.5	0/2	16/10	100/50	Systolic
SVG ⇒ OM1	*90*	*2.5*	*15/20*	*15/6.5*	*5.3/4.5*	*Systolic*
LIMA ⇒ LAD	90	2.5	0-1/0	60/60	78/78	Systolic

Bold characters indicate grafts revised on the basis of low flow values despite normal flow patterns. Italic characters indicate grafts revised on the basis of abnormal flow patterns despite flow values greater than 15 ml/min on average.
LIMA, left internal mammary artery; SVG, saphenous vein graft; RIMA, right mammary artery; LAD, left anterior descending; D, diagonal; RCA, right coronary artery; CX, circumflex coronary artery; OM, obtuse marginal.

patient), coronary stenosis distal to the graft (three patients) and no findings (two patients). After revision, all flow patterns improved (diastolic flows) and mean flow values increased from a mean value of 3.85±4.63 to 32.47±28.59 ml/min with proximal snare (P<0.0001) and from 6.58±6.00 to 36.29±26.91 ml/min without snare (P<0.0001). PI values also improved from 38.45 ± 56.56 to 3.03 ±1.6 with snare and from 24.44±46.51 to 2.80±1.68 without snare (P<0.0001). TTFM findings after revision are summarized in Table 2. In three additional grafts (8.1%) revision was performed on the basis of low mean flow values (7.3 ±2.51 ml/min with snare and 6±1 ml/min without snare) despite normal flow curves (diastolic) and PI values (1.86±2.20 with and 3.06 ±1.66 without snare). There were no findings at revision and curves, flow and PI values remained unchanged after revision (Tables 1 and 2). Postoperatively one patient developed a stroke (3%), one had an acute myocardial infarction (AMI) (3%), one required reoperation for bleeding (3%), one had a sternal wound infection and one

Table 2: TTFM findings in 37 grafts after revision

Graft	% Coronary stenoses	Size coronary (mm)	Mean flow w/wo snare (ml/min)	PI w/wo snare	Resistance w/wo snare (Ω)	Flow pattern
SVG ⇒ RCA	*90*	*1.5*	*25/25*	*3/3*	*4/4*	*Diastolic*
LIMA ⇒ LAD	100	2	41/41	1.5/1.5	1.41/1.41	Diastolic
SVG ⇒ RCA	70	2.5	10/10	8.7/8.7	10/10	Diastolic
SVG ⇒ D	85	2.0	21/21	2.5/2.5	2.85/2.85	Diastolic
LIMA ⇒ LAD	90	2.5	31/34	2.8/1.7	2/1.91	Diastolic
SVG ⇒ RCA	100	1.5	5/5	2/1	10/10	Diastolic
LIMA ⇒ LAD	85	2	11/11	1.9/1.9	7.2/7.2	Diastolic
LIMA ⇒ LAD	*90*	*2.5*	*35/35*	*1.2/1.2*	*2.28/2.28*	*Diastolic*
LIMA ⇒ D	90	2	14/31	1.8/1.3	5.8/2.5	Diastolic
RIMA ⇒ RCA	100	2.5	4/47	1/0.8	1.4/1.2	Diastolic
SVG ⇒ CX	50	1.5	22/49	3.1/2.1	2.9/1	Diastolic
SVG ⇒ OM	90	2.0	23/24	5/5	2.69/2.69	Diastolic
LIMA ⇒ LAD	90	1.5	150/150	2.3/2.3	0.53/0.53	Diastolic
SVG ⇒ CX	90	1.5	85/85	2.2/2.2	0.98/0.098	Diastolic
LIMA ⇒ LAD	85	1.5	10/5	5/5	9/13	Diastolic
SVG ⇒ RCA	80	2.0	15/22	2/1.8	4.33/2.9	Diastolic
LIMA ⇒ LAD	90	2.0	23/19	1.8/3.9	3.3/4	Diastolic
SVG ⇒ RCA	*95*	*2.0*	*19/19*	*4/4*	*4/4*	*Diastolic*
LIMA ⇒ LAD	100	1.5	28/49	5.1/3.5	2.6/1.5	Diastolic
LIMA ⇒ LAD	80	2.0	24/35	2.9/1	2.9/1.9	Diastolic
SVG ⇒ OM	80	2.5	64/64	4.1/2.9	0.9/1	Diastolic
SVG ⇒ OM2	90	2	18/14	3.6/5.4	3/6	Diastolic
SVG ⇒ RCA	100	1.0	86/63	1.8/0.7	0.8/1.18	Diastolic
SVG ⇒ D	90	1.5	6/6	4.6/4	11.16/11.16	Diastolic
SVG ⇒ OM2	100	2.5	31/32	6.2/6	1.74/1.74	Diastolic
SVG ⇒ LAD	90	1.5	9/19	1.8/1.9	7.4/3.5	Diastolic
LIMA ⇒ LAD	50	1.5	8/6	3.4/2.6	10.3/14	Diastolic
LIMA ⇒ LAD	90	2.0	22/31	3.5/2.7	3.5/2	Diastolic
SVG ⇒ LAD	60	1.5	31/31	1.6/1	1.83/1.83	Diastolic
SVG ⇒ CX	60	1.5	15/15	3.3/3.3	3.8/3.8	Diastolic
SVG ⇒ RCA	70	2.0	52/56	4/3.2	1.36/1.25	Diastolic
SVG ⇒ OM1	*75*	*2.0*	*19/19*	*3/2.9*	*3.15/3.15*	*Diastolic*
SVG ⇒ D	75	2.0	28/20	3/2.5	3/ 4.2	Diastolic
SVG ⇒ RCA	95	2.5	50/54	4.5/4	2/2	Diastolic
SVG ⇒ OM2	100	1.5	12/20	1.5/1	5/5	Diastolic
*SVG*OM2*	*90*	*2.5*	*40/50*	*2/3*	*3/2.7*	*Diastolic*
LIMA ⇒ LAD	90	2.5	40/33	2/2.3	2/2.4	Diastolic

LIMA, left internal mammary artery; SVG, saphenous vein graft; RIMA, right mammary artery; LAD, left anterior descending; D, diagonal; RCA, right coronary artery; CX circumflex coronary artery; OM, obtuse marginal.

required prolonged ventilatory support (3%). All patients were discharged after a mean hospital stay of 8.15 days.

DISCUSSION

Several techniques have been used in the past to test coronary graft flow intraoperative: electromagnetic flow meters, initially adopted in coronary surgery, have been recently replaced by ultrasonic technology (Doppler and TTFM). Many authors have demonstrated the superiority of TTFM over Doppler systems in direct real time detection of flow independently of vessel diameter and Doppler angle (2,3).

Increasing interest in intraoperative evaluation of graft flows has followed the advent of CABG without CPB. Intraoperative flow measurements together with post-operative angiographic follow-up are important methods aimed at

documenting the feasibility of this operation. We began using TTFM routinely in off CPB coronary surgery since 1996. After 3 years of clinical experience we believe that this technology is effective in detecting highly stenotic coronary anastomoses. The sensitivity of TTFM in detecting less than critical stenoses remains to be defined. Cerrito et al. (7) indicated that neural network pattern recognition analysis of graft flow characteristics, can improve detection of anastomotic errors with intra-operative TTFM. After a complex mathematical analysis of the flow curves is possible to detect stenoses causing a 50% or greater narrowing of the anastomoses. It is evident that less than critical stenoses can not be detected by TTFM due to the fact that no modifications in the hemodynamic performances of the grafts happen at this level. At the present, standard or nominal curves and flow values for different type of grafts and revascularized vessels have not been described and the variability between different subjects and within subjects is extremely large.

In an interesting survey, Spence et al. (8) tested the ability of 19 international surgeons to detect anastomotic errors by evaluating mean flow and flow waveforms. More than 70% of the surgeons accepted anastomoses with severe stenoses but, all of them, were able to detect highly stenotic anastomoses (.90% stenosis).

It is important to emphasize the fact that the ability to correctly interpret TTFM findings is slowly acquired with clinical and experimental experience.

Even if we understand there is a limit in TTFM findings interpretation, our clinical experience with more than 1000 grafts tested, has showed that early detection of stenotic grafts can be achieved by the surgeons simultaneous evaluation of flow patterns, PI values, flow values and clinical findings (i.e. EKG tracing, hemodynamic values). Flow curves in patent grafts have a mainly diastolic pattern with a small component of negative systolic flow. The diastolic flow is the actual flow that at every diastole flows from the graft in to the coronary through the anastomosis, the systolic component is retrograde flow that cannot flow in to the anastomosis during systole and goes backwards in to the graft (Fig. 1). In the case of stenotic anastomosis the flow curve becomes spiky and mainly systolic (Fig. 2): in this situation the main flow through the graft is systolic and there is minimal perfusion of the anastomosis during diastole. Even if these rules apply generally to all vessels, we have noticed some differences whenever testing grafts anastomosed to the right coronary system. A good component of blood flow in to the right coronary takes place during systole simply due to a minor compression of the epicardial vessels during right ventricular contraction. For this reason, a larger component of systolic positive flow can be observed in patent anastomoses to the RCA. As mentioned, we do not have nominal flow and PI values to suggest

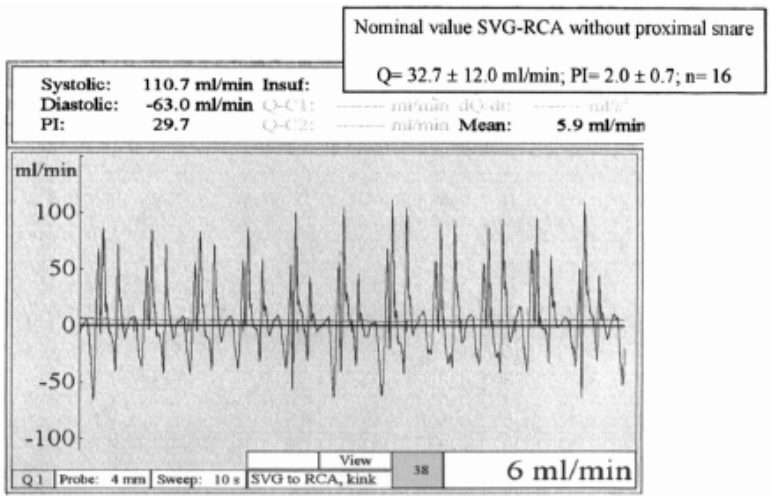

Figure 2: TTF curve in a severely stenotic saphenous vein graft to the RCA.

for a correct interpretation of TTFM findings and our statements are based on the simple visual assessment of flow curve morphology and clinical findings. Di Giammarco et al. (9) have analyzed the differences in TTFM patterns in different coronary grafts but, at present, no standard values have been reported. We are convinced that flow value per se is not a good indicator of the quality of the anastomosis and can not justify graft revision: absolute flow is influenced by too many variables including type and size of the graft, and quality of the coronary artery distal territory. In our experience graft revision was erroneously performed in three cases only on the basis of low flow values despite satisfactory flow patterns and low PI values: at surgical inspection no anastomotic lesions were found and the flow values remained unchanged after revision (Tables 1 and 2). Use of vasodilating agents (i.e. papaverine and nitro-glycerine) did not improve the flow values and the small calibre of the revascularized coronary arteries (,1.5 mm) was responsible for our findings. Coronary flow reserve can help in correctly diagnose anastomotic imperfections and, as described by Walpoth et al. (10), the quality of the anastomosis can be tested by recording the modifications of flow during infusion of adenosine. We do not have experience with calculation of flow reserve but we believe that a more precise detection of anastomotic imperfections with TTFM could be achieved by testing the dynamic ability of the anastomoses to increase the blood flow whenever the oxygen requests of the myocardium are increased. If mean flow values are not good predictors of grafts' quality, on the contrary PI values are, per se, very suggestive of the actual status of the anastomoses. As mentioned in the results, we correctly revised five grafts on the basis of abnormal flow curves and high PI values (22.04 ±21.17 with snare

and 13.94 ± 19.77 without snare) despite flow was on average higher than 15 ml/min. At surgical inspection all five anastomoses resulted to be severely stenotic and after revision flow patterns and PIs were improved (2.64 ±1.07 with snare and 2.82±1.01 without snare) (Tables 1 and 2).

To our knowledge, an absolute PI value has never been officially proposed and we empirically decided the limit of 5 on the basis of our clinical experience. Di Giammarco et al.(9) proposed a value of 2.5 as the limit PI above which an anastomosis should be revised but, again, this value seems to be derived by personal clinical experience. Flow curves, PI and mean flow values should always be evaluated with and without occlusion of the native coronary arteries: proximal snaring of the native coronary is, in our opinion, important in order to achieve a reliable interpretation of TTFM findings. The shape of the curve should remain unchanged when snaring the coronary proximally and an increase in absolute flow should be recorded if competition from the native coronary was present with the unsnared coronary. The proximal snare will also permit to detect lesions at the level of the toe of the anastomosis: in this situation whenever the coronary is snared the absolute flow will drastically decrease documenting lack of ante-grade flow through the anastomosis. Verification of intraoperative TTFM findings can be obtained with immediate postoperative angiographic studies. Even if we do not have a systematic angiographic follow up for our revised grafts, we believe our immediate postoperative clinical results being satisfactory and somehow confirming intraoperative TTFM findings. Angiography, per se, gives a limited bidimensional view of the coronary arteries and the coronary grafts without giving any specific information about the hemodynamic parameters of the anastomoses; for this reason a comparative study between postoperative angiography and intraoperative TTFM may result difficult. In reoperative CABG for example, we found conflicting results when comparing preoperative angiography and intraoperative TTFM; in one particular case angiographic documentation of anastomotic sub-occlusion of an old saphenous graft, was not confirmed during surgical revision and intraoperative TTFM.

In an interesting study, Louagie et al. (11) reported that intraoperative hemodynamic assessment, via pulsed Doppler flowmeter, can have a satisfactory predictive value for midterm graft occlusion, on the contrary the same hemodynamic parameters are useless for prediction of midterm graft stenosis. Together with Dr Louagie we feel that midterm stenosis development is a dynamic process related to scar tissue formation and degeneration of the graft and, for this reason, can not be detected at the time of the procedure. TTFM has also been compared with other techniques of postoperative graft patency verification that, differently from angiography, can give more precise information about the hemodynamic

characteristics of the grafts. In a series of 22 patients, Walpoth et al. (12) have shown a significant correlation between intraoperative TTFM and post-operative magnetic resonance findings of the internal mammary artery grafts.

In conclusion we may say that there are certainly some limits in the interpretation of TTFMs findings and there is still necessity to define the sensitivity of TTFM in detecting less then critical stenosis (7, 8). Correct interpretation of flow curves, mean flows and PI values are crucial in reducing the number of undetected technical errors and in decreasing the number of grafts erroneously revised. The mean flow value per se is not a good indicator of the quality of the anastomosis.

Acceptable flow values with abnormal flow patterns and high PIs may underline highly stenotic lesions of the anastomoses (five cases in our experience). On the contrary, we observed low flow conditions with good flow curves in three anastomoses which, at revision, resulted in fully patent anastomoses. This situation may occur whenever the revascularized territory has poor run off.

TTFM is reliable in detecting technical errors after CABG without CPB. Graft revision should be promptly performed whenever flow curves, mean flows, and PI values are abnormal. In this situation, revision of the distal anastomoses leads to improvement in flow patterns. Postoperative outcome can be improved by a meticulous use and understanding of TTFM in patients undergoing coronary artery surgery with and without CPB.

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APPENDIX A. CONFERENCE DISCUSSION

Dr. A. Royse (Victoria, Australia): You certainly have a very large series. I think you have shown us fairly well from your data that a high PI value and abnormal flow curves was correlated with a critical conduit of anastomotic stenosis, but what you haven't shown us is what is the denominator?

How many of those who had a normal or slightly abnormal flow curve actually had a critical stenosis but you missed it or you didn't revise it? In other words, you are only telling us of the critical stenoses that you actually revised, not how many theoretically there were in those that you didn't revise.

My question is, have you done any other tests such, as, perhaps angiography to try and establish if there is a critical stenosis in those who you didn't revise?

Dr. D'Ancona: No, we didn't make any angiographic study. I outlined in the conclusion, we really are not able to say how critical should be the stenosis to be detected by the TTFM. Dr Paul Spence's group in Louisville, Kentucky did make some experimental settings showing that TTFM is able to detect stenosis that at angiography result higher than 50%.

Dr. J. Melo (Carnaxide, Portugal): When we measurements low flows should we take precautions like a late angiography?

Dr. D'Ancona: In our experience, if we are sure that the size of the vessel and the territory revascularized were very poor, we are not really very much concerned when we have low flows if we have good curves and good PI values, so we don't do anything, and as a matter of fact, we didn't have any clinical postoperative implication using this strategy. So I think you shouldn't be worried about any angiographical study in those patients. This is our personal opinion.

Chapter 5

Coronary grafts flow and cardiac pacing modalities: how to improve perioperative myocardial perfusion

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ABSTRACT

Objective

Aim of this study was to investigate modifications of coronary grafts flow during different pacing modalities after CABG.

Materials and Methods

Two separate prospective studies were conducted in patients undergoing CABG and requiring intraoperative epicardial pacing. In a first study (22 patients) coronary grafts flows were measured during dual chamber pacing (DDD) and during ventricular pacing (VVI). In a second study (10 patients) flows were measured during DDD pacing at different atrio-ventricular (A-V) delay periods. A-V delay was adjusted in 25 ms increments from 25 to 250 ms and flow measurements were performed for each A-V delay increment. A transit time flowmeter was used for the measurements.

Results

An average of 3.4 grafts/patient were performed. In the first study, average coronary graft flow was 47.4 ± 20.8 ml/min during DDD pacing and 41.8 ± 18.2 ml/min during VVI pacing (P = 0.0004): Furthermore average systolic pressure was 94.3 ± 10.1 mmHg during DDD pacing and 89.6 ± 12.2 mmHg during VVV pacing (P = 0.0007): No significant differences in diastolic pressure were recorded during the two different pacing modalities. In the second study, maximal flows were achieved during DDD pacing with an A-V delay of 175 ms (54 ± 9.6 ml/min) and minimal flows were detected at 25 ms A-V delay (38.1 ± 4.7 ml/min) (P = ns). No significant differences in systolic or diastolic blood pressure were noticed during the different A-V delays.

Conclusion

Grafts flowmetry provides an extra tool to direct supportive measures such as cardiac pacing after CABG. DDD mode with A-V delay around 175 ms. should be preferred to allow for maximal myocardial perfusion via the grafts.

INTRODUCTION

The main aim of coronary artery bypass grafting (CABG) is to increase blood flow to ischemic myocardium. Although this procedure is successfully performed in more than several hundred thousand patients per year in Europe, intraoperative graft patency verification is still considered optional in most of the cardiac surgery centers. Grafts are assumed to be patent at the end of the operation, especially if the patient has no hemodynamic compromise and if weaning from cardiopulmonary bypass (CPB) is successful. After an initial attempt to expand graft flowmetry in standard cardiac surgery practice, in the early 1960s measurement of coronary graft flow has been almost abandoned due to the many limitations of the obsolete electromagnetic flowmeters adopted at that time (1)

The recent popularization of off-pump CABG, together with the amelioration of the technology available for accurate graft flow measurement, have revived interests and concerns about the focal importance of intraoperative graft patency verification and documentation (2). The introduction of ultrasound-based flow meters such as Doppler and Transit Time Flow Measurement (TTFM) systems, is presently giving a tremendous scientific and technological impact in the field of rheology and flow measurement.

In our experience intraoperative graft patency verification, if properly performed, may not only inform the surgeon about the status of the newly constructed coronary anastomoses, but could also guide him in modifying his perioperative conduct and strategy to achieve an ideal hemodynamic performance and, consequently, a maximal myocardial perfusion through the bypass conduits (3).

In the present manuscript we summarize our experience with intraoperative cardiac pacing and simultaneous coronary graft flow measurement trying to identify which are the pacing strategies that allow for an optimal coronary graft rheology.

MATERIAL AND METHODS

Over a one-year period, two separate prospective studies were conducted at the Cork University Hospital in order to evaluate coronary grafts flow modifications in patients requiring epicardial pacing following primary CABG.

Patients were enrolled following preoperative informed consent.

All patients were operated on CPB and cardiac arrest was achieved via antegrade intermittent crystalloid cold cardioplegia. Distal anastomoses were

performed with 7-0 polypropilene running sutures. Proximal anastomoses were constructed on partial aortic clamping with 5-0 polypropylene running sutures.

After aortic declamping, epicardial pacing was initiated due to nodal rhythm, atrio-ventricular dissociation, or sinus bradycardia.

Two epicardial atrial and two ventricular pacing wires were placed in each patient.

In a first study including 22 patients, coronary grafts flows were measured after weaning from CPB initially during dual chamber pacing (DDD) and secondly during ventricular pacing (VVI).

In a second study including 10 patients, flows were measured during DDD pacing at different atrio-ventricular (A-V) delay periods. A-V delay was adjusted in 25 milliseconds increments from 25 to 250 ms and flow measurements were performed for each A-V delay increment.

Although cardiac indexes were not routinely recorded, flow in the new pacing modality was detected only after allowing two minutes of hemodynamic stabilization aiming at systolic arterial blood pressure of 100 mmHg and diastolic of 60 mmHg to standardize measurements. Measurements were performed twice per each graft in the same pacing modality and averages were calculated.

A TTFM device was used to test the grafts. Flow probes have a size ranging from 2.5 to 3 mm and can be easily placed around the constructed grafts. A small amount of aqueous gel is placed between the probe and the conduit to increase the contact. The probe consists of two small piezoelectric crystals, one upstream and one downstream, mounted on the same side of the vessel. Opposite to the crystals, there is a small metallic reflector. Each crystal produces a wide pulsed ultrasound beam covering the entire vessel width. Both the amount of time necessary for an ultrasound beam emitted from the upstream crystal to arrive at the downstream crystal after being reflected, and for a signal from the down-stream crystal to reach the upstream crystal are measured. Since ultrasound travels faster if transmitted in the same direction as flow, a small time difference between the two beams is calculated as the transit time of flow and thus, the actual flow is proportional to the transit time (5). All calculations are made automatically by the flow meter and are displayed as ml/min.

Flow findings were recorded together with hemodynamic values. No pulsatility indexes were recorded. Data were stored in a database and differences were statistically tested with the paired Student t-test (DDD-VVI and A-V delay study), and with the one-way ANOVA test (A-V delay study).

Differences in mean flows between arterial and venous conduits at different pacing modalities, correlations between mean flow changes and conduits size, flow variations for grafts to different myocardial areas and after use of different

myocardial protection techniques were not investigated in the present study and are object of analysis in two further ongoing larger studies.

RESULTS

Study 1

An average of 3.4 grafts/patient were performed. All 22 patients received a LIMA graft to the LAD. No further arterial grafts were adopted. Average coronary graft flow as measured in the 22 patients included in the study was 47.4 ± 20.8 ml/min during DDD pacing and 41.8 ± 18.2 ml/min during VVI pacing (P = 0.0004). Furthermore average systolic pressure was 94.3 ± 10.1 mmHg during DDD pacing and 89.6 ± 12.2 mmHg during VVV pacing (P = 0.0007): No significant differences in diastolic pressure were recorded during the 2 different pacing modalities

Study 2

An average of 3.4 grafts/patient were performed. All 10 patients received a LIMA graft to the LAD. No further arterial grafts were adopted. Although maximal coronary grafts flows were achieved during DDD pacing with an A-V delay of 175 ms (mean 54 ± 9.6 ml/min) and minimal flows were detected at 25 ms A-V delay (mean 38.1 ± 4.7 ml/min), no statistically significant differences were reported (P = ns). Furthermore, no significant differences in systolic or diastolic blood pressure were noticed during the different A-V delays. Mean flow values as recorded for each patient at different A-V delays are reported in Fig. 1.

All patients involved in study 1 and 2 remained hemodynamically stable during the procedure, and upon transfer to the ICU. No perioperative AMIs were reported.

No further mortality or morbidity were noticed. No angiographic studies were conducted.

DISCUSSION

Intraoperative graft patency verification should be considered as a precious technology to include in the armamentarium already available to the modern cardiac surgeon.

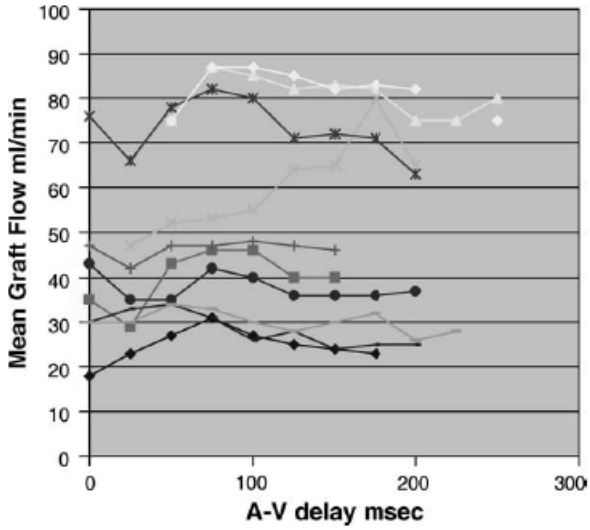

Figure 1: Mean grafts flows in 10 patients at different A-V delays.

Unfortunately scepticism and misinformation persist in the surgical community and the large majority of cardiac surgeons are still reliant on the tactile sense of their fingertips to evaluate quality and flow of their grafting (6).

Although performed in a limited group of patients, our study has emphasized the importance of intraoperative flow measurement not only in testing patency of coronary anastomosis but also in correctly guiding perioperative management (i.e. cardiac pacing) to achieve ideal hemodynamics and consequently maximal grafts flows.

Electrical conduction disturbances may frequently occur after CABG as a result of mechanical problems or ischemic/reperfusion injury. To optimize hemodynamics, epicardial pacing may be required following CABG. Bicameral pacing has been proved to be the most physiological pacing mode (7). Although it has been demonstrated that A-V sequential pacing may increase atrial priming of the left ventricular end diastolic pressure and consequently allow for an increase in cardiac output up to 25% (8), benefits in terms of increased bypass grafts performance have never been investigated.

As shown in our first study, improvement in systemic hemodynamics during DDD versus VVV pacing does also permit to achieve optimal myocardial perfusion via the newly constructed grafts. Increment in graft flow averages 6 ml/min and can arrive to a maximum of 20 ml/min.

On the basis of these findings, DDD mode should be preferred in patients requiring pacing immediately after CABG in order to allow for maximal reperfusion of the previously ischemic myocardium via the grafts.

Moreover, an ideal or optimal A-V delay during perioperative DDD pacing has never been proposed. In our second study we have tried to define the most appropriate A-V delay by using conduit flow as a hemodynamic index in patients requiring sequential pacing post CABG.

Interestingly, although systemic hemodynamics do not seem to be influenced by the A-V delay value, coronary grafts flows achieve an optimal level at 175 ms. of A-V delay and a minimum level towards 25 ms. of A-V delay. Although these findings are limited to a small number of patients and differences did not achieve statistical significance, it could be suggested that, in patients requiring DDD pacing, maximal coronary grafts flow may be obtained when maintaining an A-V delay in the 175 ms range.

As already emphasized, the importance of intraoperative coronary grafts flows findings is continuously increasing as a result of the technological improvements in the flow measurement technology. The introduction of ultrasound-based systems has revolutionized the flow measurement field. The term ultrasound has a generic definition that includes two different methods: Doppler and TTFM. The two systems rely on different properties of the ultrasound waves and, although the Doppler methods have shown good reliability both in vivo and in vitro (4), the TTFM technology offers many important advantages and is the most accurate system for intraoperative verification of coronary graft patency (9–11). In the present studies we have adopted a TTFM device whose principles of functioning have been already described above. In our experience, the TTFM device is very easy to use and requires no more than 30 s per measurement. No complications resulted from the use of this flowmeter device. The flowmeter provides not only an absolute value expressed as ml/min but gives also a flow curve that summarizes the variations of graft flow during the different phases of the cardiac cycle. Because coronary graft flow is mainly diastolic, it is important to adopt an adequate modality of pacing that could allow for good diastolic filling and pressure without compromising the systolic performance.

CONCLUSION

Intraoperative graft patency verification and coronary grafts flow detection should be used to testify for a successful intraoperative myocardial revascularization and to guide a safe perioperative hemodynamic performance. Graft flow

findings are not solely an anastomosis status indicator, but also a useful index for the patient hemodynamic condition. Appropriate intraoperative evaluation of coronary grafts flows may provide an extra tool to correctly direct supportive measures such as cardiac pacing modalities after CABG.

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Chapter 6

Preoperative Angiography and Intraoperative Transit Time Flow Measurement to Detect Coronary Graft Patency in Reoperations: An Integrated Approach

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ABSTRACT

Coronary angiography is the gold standard for preoperative diagnosis of coronary artery disease. In reoperative coronary artery surgery the physiologic significance of suspect lesions by angiography can be confirmed by direct intraoperative measurement of blood flow in the old grafts; such interpretation can prevent unnecessary graft revisions.

INTRODUCTION

Coronary angiography provides a two-dimensional image of epicardial vessels and coronary grafts and remains the "gold standard" for the diagnosis of native coronary artery disease and graft stenosis. Methods of intraoperative detection of graft flow (eg, transit time flow measurement or TTFM) provide additional dynamic physiologic information regarding flow in coronary grafts including absolute graft flow, diastolic flow pattern, and coronary flow reserve. In reoperations, this information may be useful in patients with questionable graft lesions observed by pre-operative coronary angiography. We herein describe a case in which the clinical and anatomic significance of what was viewed as a critical angiographic lesion in a vein graft was questioned by intraoperative TTFM.

CASE-REPORT

A 73-year-old woman with a history positive for coronary artery disease, previous anterior myocardial infarction, unstable angina (CCS IV), and congestive heart failure (CHF), presented with non-Q wave myocardial infarction. Coronary angiography demonstrated depressed left ventricular function (ejection fraction 25%) with critical three-vessel coronary artery disease. She underwent coronary artery bypass grafting (CABG) without cardiopulmonary bypass (CPB) using the left internal mammary artery to the left anterior descending (LAD), and separate saphenous vein grafting of the right and circumflex coronary arteries. Graft flows were measured intraoperatively via transit time flow measurement (TTFM) and were satisfactory. She had an uneventful post-operative course and was discharged home.

She remained asymptomatic and had good functional recovery at 3 and 6 months follow-up. She was readmitted 9 months later for an episode of sudden cardiac death. An electrophysiologic study was performed and an internal cardioverter defibrillator was implanted for sustained ventricular tachycardia. Angiography documented sub-occlusion of the saphenous graft to the right coronary artery (Figure 1) with patent grafts to the LAD and circumflex arteries. Via lower ministernotomy, the saphenous vein graft to the right coronary artery (RCA) was identified and a 3 mm TTFM probe was positioned around it and excellent flow values and curves were recorded documenting patency of this graft (Figure 2). The graft was temporarily clamped, and after the coronary distal to the anastomosis was opened, good antegrade flow was noticed whenever the clamp on the vein graft was released. Although an anatomic lesion was not found

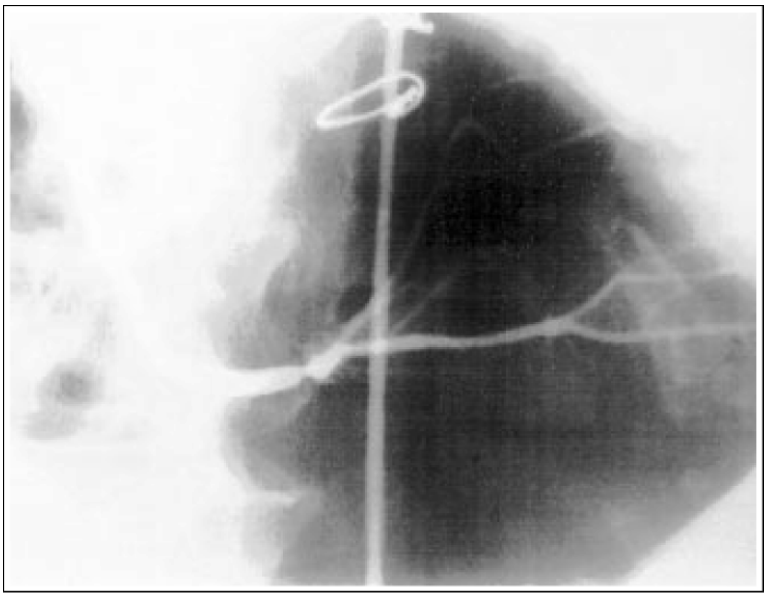

Figure 1. Angiography showing subocclusion of right coronary graft.

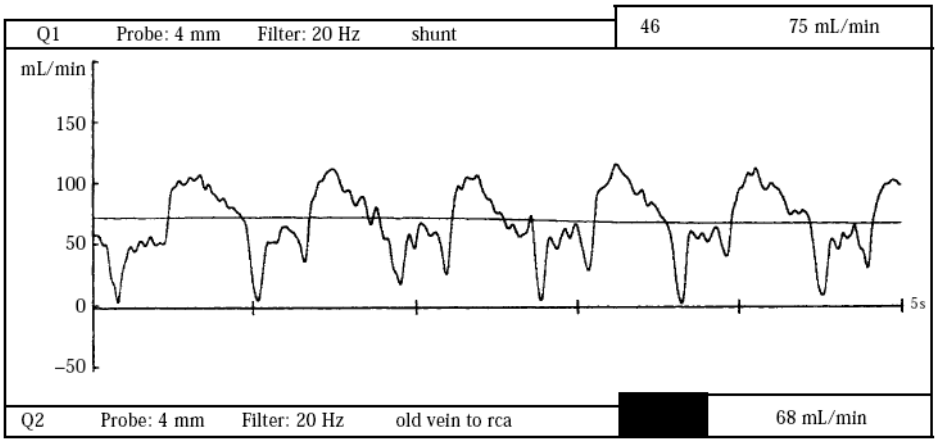

Figure 2. TTFM findings of old right coronary graft.

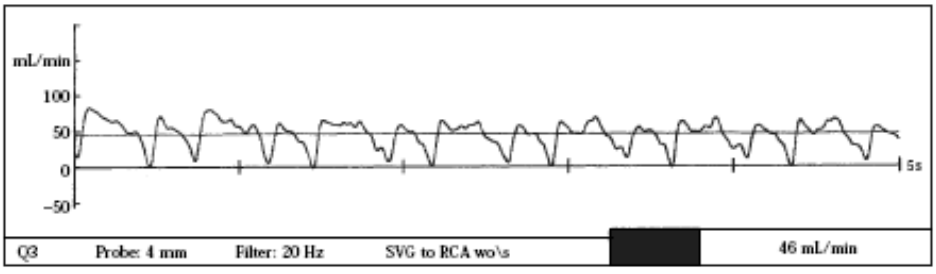

Figure 3. TTFM findings of new right coronary graft.

to explain the angiographic stenosis, a new saphenous graft was anastomosed to the distal RCA on the beating heart; proximal anastomosis was performed to the lateral wall of the old RCA graft. TTFM was obtained and flow curves were satisfactory; interestingly, absolute flow in the new graft was lower than that recorded in the old graft (Figure 3). The operation was completed and recovery was uneventful with discharge home on the fourth postoperative day.

DISCUSSION

Although coronary angiography is the "gold standard" for the evaluation of coronary artery stenosis, its interpretation can occasionally be misleading (1). As in this case, coronary angiography can falsely diagnose coronary graft stenosis, resulting in an unnecessary operative intervention. Angiography gives a limited biplanar view of the coronary bed without a real measurement of the blood flow; on the contrary there are other methods that can be used to gain hemodynamic data about native coronary and coronary grafts. Intracoronary translesional flow velocity measurements using the Doppler flow wire (2) for example, provide pre-stenotic and post-stenotic flow values, aiding in the discrimination of physiologically significant coronary stenoses. Less accurate techniques include phase difference magnetic resonance flow (3), which is a non-invasive method of assessing physiologically significant coronary artery stenosis.

In redo coronary surgery, intraoperative TTFM can be used to gain physiologic information about flow in all grafts, especially when their degree of stenosis is suspect and in situations where the above mentioned diagnostic modalities are not available preoperatively. Intraoperative TTFM to document graft patency after CABG has recently been introduced. This technology is ultrasound based and offers many advantages when compared to the traditional methods of intraoperative flow measurement, ie, electromagnetic and Doppler. TTFM findings are independent of hematocrit level, Doppler angle, and size of the graft tested; the flow values recorded result from a real-time direct measurement and are not derived from mathematical calculations. Together with mean flow values, flow patterns, pulsatile index, and vascular resistance values can also be assessed by TTFM. We have used this technology to detect patency in more than 1,000 anastomoses performed off CPB, systematically revising grafts with abnormal TTFM patterns (4). Graft patency is always tested with and without proximal occlusion of the revascularized coronary in order to exclude competitive flow from the native vessels and to assess patency at both toe and heel of the anastomoses.

On the basis of our clinical experience, we believe TTFM is a good modality that can reliably interpret the functional status of coronary anastomoses. In experimental studies TTFM has shown a good sensitivity, and lesions that at angiography appeared equal to or greater than 50% were easily detected by correct interpretation of TTFM findings (5).

To our knowledge this is the first report of graft patency documented by intraoperative TTFM after being incorrectly interpreted as critically stenosed by angiography. Surgical strategy is normally directed by angiographic findings, and for this reason we decided to perform a new bypass distal to the old one despite satisfactory TTFM findings. We believe that unnecessary revision of patent grafts can be avoided by integrating dynamic intraoperative studies, i.e., TTFM, with preoperative angiographic studies; with this integrated approach patency of old grafts, in reoperative coronary surgery, can be confirmed and assessed by direct intraoperative evaluation of graft hemodynamics.

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Chapter 7

Heparin Dose, Transfusion Rates, and Intraoperative Graft Patency in Minimally Invasive Direct Coronary Artery Bypass

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ABSTRACT

Background

Many investigators have demonstrated the short-term and midterm efficacy of minimally invasive direct coronary artery bypass (MIDCAB). However, the influence of heparin dosing during MIDCAB on postoperative and immediate graft patency is less well defined. This report outlines our experience with MIDCAB employing a variety of heparinization protocols.

Methods

The traditional MIDCAB approach was used in 152 patients who underwent single-vessel off-pump coronary artery bypass. Before the left internal mammary artery was divided, a 150-U/kg bolus of heparin sodium was given to 76 patients (group 1), and 300 U/kg was given to another 76 patients (group 2). Additional heparin was given during the procedures to maintain an activated clotting time of greater than 300 seconds for group 1 and greater than 400 seconds for group 2.

Results

On average, patients in group 1 required more boluses of heparin during treatment than patients in group 2. A larger standard deviation from the mean was observed for the activated clotting time in group 1 at any time during treatment than for patients in group 2. The number of revised grafts was smaller in group 2 (1/76, 1.3%) than in group 1 (4/76, 5.2%). All of these revisions revealed thrombus at the site of anastomosis. In addition, noncoronary thrombotic complications were seen in 5 patients in group 1, and none were seen in group 2.

Conclusion

Coronary artery surgery without cardiopulmonary bypass does not trigger the systemic inflammatory response, but surgical tissue trauma remains a constant. The preserved hemostasis theoretically may lead to a procoagulant state. This study demonstrates that insufficient anticoagulation therapy can lead to intracoronary thrombosis following MIDCAB as well as increased noncoronary thrombotic complications.

INTRODUCTION

Coronary artery bypass grafting (CABG) without cardiopulmonary bypass (CPB) has been popularized as an alternative to conventional myocardial revascularization in the treatment of coronary artery disease [1]. Long-term studies of off-pump CABG (OPCAB) are pending; shortterm and midterm efficacy of both minimally invasive direct coronary artery bypass (MIDCAB) and OPCAB have been demonstrated by many investigators [2-5]. Technical refinements have improved hemodynamics, target vessel exposure, and mechanical epicardial stabilization, enabling both MIDCAB and OPCAB to be performed by the vast majority of cardiac surgeons. Despite these enabling technologies, hemorrhagic complications and the need for allogeneic transfusions are still major problems after MIDCAB and OPCAB [6,7]. Investigators have demonstrated not only reduced bleeding following MIDCAB and OPCAB but also reduced requirements in the postoperative period for transfusions of packed red blood cells, fresh frozen plasma, and platelet-rich plasma [8-10]. However, the influence of heparin dosing during MIDCAB and OPCAB on postoperative bleeding and immediate graft patency is less well defined [11]. The present report outlines our experience with MIDCAB employing two different anticoagulation regimes.

MATERIALS AND METHODS

From May 1999 to July 2001, 152 patients underwent single vessel OPCAB using the traditional MIDCAB approach as described by Calafiore and colleagues. All patients requiring MIDCAB during this period were included in this series except patients who underwent a redo procedure and patients who were taking platelet glycoprotein IIb/IIIa inhibitors or clopidogrel at the time of the operation. This series also excluded 53 patients who underwent single-vessel OPCAB via the endoscopic atraumatic coronary artery bypass procedure, which used the AESOP robotic system (Computer Motion, Goleta, CA, USA) to harvest the left internal mammary artery (LIMA) via minimal access techniques [12]. The clinical characteristics of the MIDCAB patients are summarized in Table 1. A standard MIDCAB incision (8 cm) was used in these 152 patients. Three patients (3/152, 2%) required rib resection to enable complete harvesting of the LIMA. Before the left internal mammary artery was divided, a 150-U/kg bolus of heparin sodium was given to 76 patients (group 1), and 300 U/kg was given to another 76 patients (group 2), with the patients assigned at random to groups by medical record number. Additional heparin was given during the procedure to

maintain an activated clotting time (ACT) greater than 300 seconds for group 1 or greater than 400 seconds for group 2. A mechanical stabilizer (CardioThoracic Systems, Cupertino, CA, USA) was used for stabilization of the left anterior descending coronary artery target. A humidified, sterile, carbon dioxide blower was used to clear the surgical field of blood from the arteriotomy (Medtronic DLP, Grand Rapids, MI, USA). The coronary target was occluded proximally with a pledgetted 4-0 polypropylene (Prolene) snare in all cases unless the native left anterior descending coronary was occluded proximally. All targets were shunted locally via intracoronary shunts (CardioThoracic Systems) during creation of the anastomosis. Intraoperative graft patency was verified in all cases with the transit time flow measurement technique and the Medi-Stim Butterfly Flowmeter (Model BF2004; Medi-Stim AS, Oslo, Norway), as described by D'Ancona and colleagues [13]. All shed blood was recycled with a Cell Saver (Continuous AutoTransfusion System; Fresenius, Schweinfurt, Germany). Systemic heparinization was reversed completely with protamine in all patients. All patients were administered aspirin before surgery and in the intensive care unit the day following surgery.

RESULTS

There was no operative or 30-day mortality in this series of MIDCAB patients. Postoperative myocardial infarctions as assessed by cardiac enzyme levels (creatine phosphokinase and troponin) or electrocardiogram occurred in 2 patients, and none were transmural. One myocardial infarction occurred in group 1, and another occurred in group 2. Overall, there were no neurologic complications in these patients. The average length of stay in the intensive care unit was 24 hours for group 1 and 26 hours for group 2, and the total postoperative length of stay was 3.8 days for group 1 and 4.3 days for group 2 (Table 2). There were no differences in age, sex, or elective/urgent status between the groups. Preoperative risk factors (stroke, hypertension, previous myocardial infarction, diabetes, and congestive heart failure) were identical in the two groups (Table 1). Following harvest of the LIMA, group 1 patients received 150 U/kg of heparin as a bolus, and group 2 patients received 300 U/kg of heparin as a bolus. Group 1 patients received both a smaller bolus of heparin and a smaller total heparin dose (28,000 U) to maintain ACT levels above 300 seconds during the procedure. This value is lower than the total heparin dose (32,000 U, bolus and maintenance) required to maintain the a CT above 400 seconds for group 2 patients during the MIDCAB procedure. On average, patients in group 1 required more boluses of heparin (5000 units)

Table 1. Patient Demographics

	Group 1 (n = 76)	Group 2 (n = 76)
Age, y	64 ± 10	68 ± 10
Urgent	44%	48%
Left ventricular ejection fraction	51% ± 6%	48% ± 5%
Risk factors, n*	30 (40%)	34 (45%)

*Risk factors assessed include previous stroke, hypertension, previous myocardial infarction, and congestive heart failure.

Table 2. Postoperative Data

	Group 1 (n = 76)	Group 2 (n = 76)
Extubation (<4 h)	68%	64%
Intensive care unit stay, h	24	26
Transfusion, n	26 (34%)	21 (28%)
Packed red blood cells, units	1.4	1.2
Hospitalization, d	3.8 ± 1	4.3 ± 1
Observed mortality	0%	0%
Expected mortality	2.4%	2.8%

during the procedure than patients in group 2 (2.8 versus 1.5; $P < .05$). A larger standard deviation from the mean value for ACT was observed for patients in group 1 at any time during the procedure than for patients in group 2 (95 seconds versus 55 seconds). Thus, the ACT was more variable in group 1 than in group 2 at any time during the MIDCAB procedure. This observation remained true at the end of the procedure before reversal with protamine, and therefore the mean dose of protamine required to reverse the heparin therapy and to obtain the baseline values of ACT at the end of grafting was slightly higher (1.3 times) for patients in group 1 than for patients in group 2. The number of revised grafts was smaller in group 2 (1/76, 1.3%) than in group 1 (4/76, 5.2%; $P < .05$). All of these revisions revealed thrombus at the site of anastomosis without any other technical problems (eg, dissection, "back-walling," conduit failure, and so on). The mean volume of shed blood harvested by the Cell Saver was 800 mL for group 1 and 650 mL for group 2. Blood transfusion was required for 34% of the patients in group 1 and 28% of the patients in group 2. On average, patients in group 1 who required transfusion received 1.4 units of packed red blood cells (range, 1-3 units), and patients in group 2 who required transfusion received 1.2 units of

Table 3. Postoperative Complications

	Group 1 (n = 76), n	Group 2 (n = 76), n
Mortality	0 (0%)	0 (0%)
Respiratory insufficiency	3 (3.9%)	2 (1.6%)
Renal insufficiency	1 (1.3%)	0 (0%)
Wound infection	1 (1.3%)	1 (1.3%)
Bleeding with reexploration	1 (1.3%)	0 (0%)
Myocardial infarction	1 (1.3%)	1 (1.3%)
Neurologic complications	0 (0%)	0 (1.3%)
Noncoronary thrombosis	5 (6.6%)	0 (0%)

Table 4. Respiratory Insufficiency

	Group 1, n	Group 2, n
Total	3	2
Atelectasis	2	1
Pulmonary embolism	1	0
Pneumonia	0	1

Table 5. Noncoronary Thrombotic Complications*

	Group 1, n	Group 2, n
Iliofemoral DVT	2 (2.6%)	0 (0%)
Pulmonary embolism	1 (1.3%)	0 (0%)
Upper extremity DVT	2 (2.6%)	0 (0%)

*DVT indicates deep vein thrombosis.

packed red blood cells (range, 1-2 units) (Table 2). There were no differences in the frequencies of transfusions of fresh frozen plasma or platelets between the groups, because the frequencies of transfusions for these products were very small (less than 5%). Nine patients (6%) developed postoperative complications (Table 3) within the first 30 days of surgery. These complications included respiratory insufficiency (5 patients), renal insufficiency (1 patient), superficial wound infection (2 patients), bleeding requiring reexploration (1 patient), nontransmural myocardial infarction (2 patients), and noncoronary thrombotic complications (5 patients). Table 4 shows that respiratory insufficiency was due to atelectasis (3 patients), pulmonary embolism (1 patient), and pneumonia (1 patient). Of

the entire study group, 3 patients (3/152, 2%) were readmitted during the first 30 days after discharge. Two patients (group 1) had deep vein thrombosis requiring anticoagulation therapy, and 1 patient experienced a pulmonary embolism. Non-coronary thrombotic complications were seen in 5 patients in group 1, and none were seen in group 2 (Table 5). Postoperative atrial fibrillation rates were nearly identical in the two groups (15% for group 1 and 18% for group 2).

COMMENT

Surgical coronary revascularization using CPB remains an important determinant of morbidity, which includes bleeding, thromboembolism, and temporary or permanent organ dysfunction [14-16]. Avoidance of CPB has recently emerged as an effective strategy to further reduce the complications encountered during single-vessel CABG, especially in patients with major preoperative risk factors who may benefit to a greater extent [17]. Significant improvements in technology and technique have rendered it possible to perform MIDCAB in a large proportion of the patients with single-vessel disease requiring surgical revascularization and have resulted in excellent angiographic patency rates [10]. Although postoperative bleeding following OPCAB and MIDCAB is reduced compared with CABG using CPB, questions and concerns have arisen about the need, type, and amount of antiplatelet therapy before and after OPCAB and about the amount of heparinization required to perform these procedures safely [11]. A recent study performed by our group has shown that the practice pattern of cardiac surgeons with regard to the use of both antiplatelet therapy and heparinization for MIDCAB and OPCAB is highly variable [11]. Unlike conventional surgery on CPB, OPCAB surgery does not trigger the systemic inflammatory response; however, surgical tissue trauma remains a constant between the two techniques. The preserved hemostasis theoretically achieved by using the MIDCAB or OPCAB technique may lead to a procoagulant state, as has been reported for major general surgery. On the contrary, whenever hemostasis is impaired, as occurs during CABG with CPB, the chances of microvascular thrombosis are reduced. As a consequence, it is reasonable to conclude that the risk of anastomotic thrombosis unrelated to technical mistakes should be greater in MIDCAB and OPCAB patients. In our experience, anastomotic thrombosis has been diagnosed more frequently during MIDCAB/OPCAB than during CABG using CPB [13]. The current study demonstrates this fact and provides further support for the practice of maintaining high ACT levels (exceeding 400 seconds) during MIDCAB. Higher ACT levels were achieved

in group 2 patients, and the number of revised grafts was smaller (1/76, 1.3%) than in group 1 (4/76, 5.2%). All of these revisions revealed thrombus at the site of anastomosis without other technical problems (eg, dissection, back-walling, conduit failure, and so forth). The higher dose of protamine required to reverse the heparin effect in group 1 cannot alone account for the 4-fold increase in graft thrombus formation compared with patients in group 2. Intraoperative graft flow measurements are very useful in diagnosing anastomotic thrombosis following CABG. Surgeons who do not use any method of graft patency verification may not be aware of the actual graft patency rates at the end of the MIDCAB procedure [18]. The current study demonstrates that insufficient anticoagulation therapy can lead to increased intracoronary thrombosis following MIDCAB. Mariani and colleagues [19] have reported intracoronary thrombosis and pulmonary embolism in OPCAB. They tested the procoagulant activity in a series of patients undergoing OPCAB. Prothrombin F1+2, factor VII, and fibrinolysis degradation products were sampled to test inherent coagulation activity. Procoagulant activity as represented by prothrombin F1+2 levels increased significantly 24 hours after surgery. A depletion of the coagulation factors in the extrinsic pathway was indicated by a significant decrease in factor VII levels 24 hours after surgery. Fibrinolysis was also activated, as indicated by an increase in the level of degradation products at postoperative day 1. Our current study leads one to believe that a procoagulant effect in MIDCAB can be reduced intraoperatively by maintaining higher ACT levels. It is surmised that the further procoagulant activity of MIDCAB and OPCAB at 24 hours following surgery, as described by Mariani and colleagues, may be attenuated by an aggressive anticoagulation protocol during surgical coronary revascularization without CPB. Pulmonary embolism may have been underdiagnosed in our patients, and we were able to confirm pulmonary embolism for only 1 patient in this series of 152 patients who underwent MIDCAB. This embolism occurred in a female patient with a previous history of deep vein thrombosis who was given a bolus with full-dose heparin (group 2). Two patients in group 1 had femoral deep vein thrombosis and were readmitted within 30 days of discharge, and 2 other patients in group 1 had upper extremity deep vein thrombosis that was treated with outpatient anticoagulation therapy. These observations are further corroborative evidence to suggest that proper anticoagulation therapy may be beneficial in attenuating the procoagulant state associated with coronary revascularization without CPB. This study supports the basic science work presented by Mariani and colleagues [19]. Despite the smaller dose in the heparin bolus and the smaller total heparin dose used during MIDCAB in group 1, patients in this group shed more blood than the patients in group 2 whose anticoagulation therapy

consisted of a full heparin dose (800 mL versus 650 mL). The higher rate of bleeding resulted in a higher frequency of transfusions in group 1 patients. As this study has demonstrated, a larger bolus of heparin during the harvesting of the LIMA conduit enables a higher baseline ACT (exceeding 400 seconds) and reduces the need for excessive bolus administrations of heparin. Also, this practice avoids a larger standard deviation from a mean value for a therapeutic ACT. Such swings in ACT values may create a prothrombotic state and may explain in part the increased frequency of graft thrombosis following MIDCAB and the larger amounts of blood shed despite a smaller total dose of heparin for a given MIDCAB procedure. ACT levels were more variable in group 1 than in group 2 at any time during the MIDCAB procedure. This observation remained true at the end of the procedure, i.e., before reversal with protamine. Thus, the mean dose of protamine required to reverse heparin therapy and to obtain baseline values of ACT at the end of grafting was slightly higher in group 1 patients than in the patients of group 2. Protamine dosing at the termination of the MIDCAB procedure may also be another important factor in the rates of graft thrombosis and transfusion needs following MIDCAB. A larger study investigating this variable in beating heart coronary artery surgery is in progress. The improved intraoperative patency rates documented by transit time flow measurements and reduced transfusion rates in MIDCAB cases treated with the full heparinization protocols presented here are encouraging. These data are clear evidence that careful surgical technique, enabling stabilization technologies, and meticulous blood recovery techniques using Cell Saver permit reproducible and precise construction of coronary bypass anastomoses on the beating heart. However, only a large, prospective, randomized longitudinal comparison of graft patency using angiographic techniques after MIDCAB and OPCAB procedures can validate the safety, efficacy, and superiority of full-dose heparinization during beating heart coronary artery bypass surgery.

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Chapter 8

Epicardial coronary artery doppler: validation in the animal model

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ABSTRACT

Aim of the study was to validate a newly-designed epicardial coronary artery Doppler probe and test its detection of changes in coronary blood flow velocity.

Left anterior descending (LAD) coronary blood flow and flow-velocity were evaluated in 4 pigs with a pericoronary transit time flow (TTF) probe and a newly-designed epicardial Doppler micro-probe.

Four consecutive measurements were taken for each of the following condition: basal, partial stenosis, occlusion, and reperfusion of the LAD.

Mean TTF value (ml/min) was 23.2±6.6 in basal condition, 16.2±5.7 after partial LAD stenosis, 0.1±0.3 during LAD occlusion, and 67.4±23.3 at reperfusion ($p<0.001$). Similar patterns were recorded in terms of Doppler velocity (cm/sec) with values of 4.0±1.9 in basal condition, 3.5±2.3 after partial LAD stenosis, 0.5±1.4 during LAD occlusion, and 11.1±5.5 at reperfusion ($p<0.001$).

No significant differences in both TTF and Doppler velocity were detected between basal condition and partial LAD stenosis (p=ns).

Epicardial coronary arterial Doppler represents a valuable tool to detect coronary arterial flow velocity in basal condition. Although changes in flow velocity are easily recorded after coronary occlusion and reperfusion, modifications after partial coronary stenosis are not clearly defined.

INTRODUCTION

On selection of appropriate coronary targets and assessment of coronary anastomosis quality (1, 2) some authors have dedicated their researches to epicardial coronary Doppler performed with custom-made probes in both porcine models and in the ex-vivo human beating heart (3-5). Although this technology could be routinely adopted in the operating room, the lack of specifically-designed micro-probes and paucity of comparative studies with other functional evaluation means such as transit time flow-measurement (TTFM), have limited a wider application of epicoronary Doppler.

Differently from the existing tools for intraoperative coronary anastomoses evaluation, and thanks to modern micro-probes designing, Doppler technology will provide both functional and anatomical information on the target vessel, the graft used for revascularization, and the newly constructed anastomosis.

We herein report our initial experience, in a porcine model, with a newly-designed epicardial coronary Doppler micro-probe (X-plore®, MediStim, Oslo, Norway) and discuss the possible future applications of this technology.

MATERIALS AND METHODS

Four adult pigs (50 kg) were sedated with ketamine (30 mg kg^{-1}i.m.), anaesthetized with thiopental (10 mg kg^{-1}i.v.), intubated and ventilated. Anaesthesia was maintained with midazolam (2 mg kg^{-1}+ 1 mg kg^{-1} h^{-1}i.v.) and fentanyl (10 µg kg^{-1} h^{-1}i.v.).

Animals were treated in compliance with the current ethical regulations on animal experimentation.

Median sternotomy and pericardiotomy were performed.

The left anterior descending (LAD) coronary artery was isolated and a pericoronary snare placed proximally around the vessel. LAD absolute flow (ml/min) and flow velocity (cm/sec) values were simultaneously measured using respectively a 2-mm pericoronary TTFM probe (Transonic Systems Inc.®, Ithaca, New York, USA) and a newly-designed epi-coronary Doppler probe (X-plore®, MediStim, Oslo, Norway). The Doppler probe used has a 7,5Mhz -3 by 6 mm unfocused crystal.

The Doppler probe is connected to a flowmeter device (Veri-Q, MediStim, Oslo, Norway) for data measuring and storage.

The device applies a pulsed Doppler, allowing the user to control the depth from where the velocity should be measured.

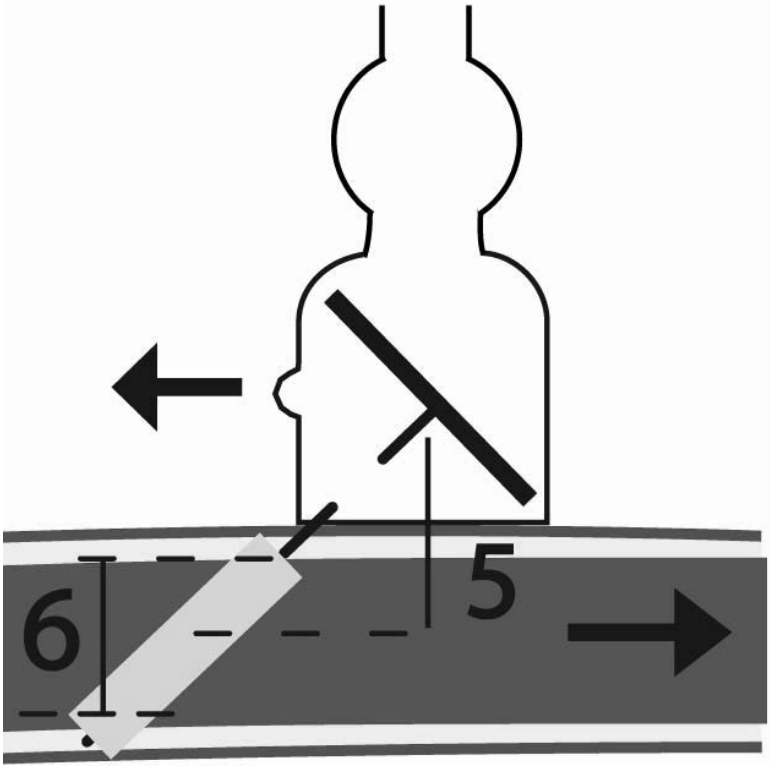

Figure 1: 7.5 MhZ X-plore® Doppler probe. Note the 45˚ orientation of the unfocused crystal and the default 6mm sample volume and 5mm at the center of the probe.

Additionally, sample volume is adjustable and selected as a range around the depth setting. The default settings are a depth of 5 mm, and a volume of 6 mm.

These settings allow for sampling flow velocities at depths ranging 2 to 8 mm from the probe surface. The Veri-Q will display the Doppler spectrum at the default 5 seconds sweep rate as soon as a probe is connected. The probe crystal is arranged in a 45° angle when the probe is held perpendicularly to the vessel.

The velocity scales are compensated for the same 45° angle (Fig. 1-2).

The TTF probe was placed immediately distally to the snare and the epicoronary Doppler probe placed more distally on the LAD and away from the point of stenosis to avoid extreme velocity peaks secondary to a condition of vorticosity.

Adequate contact between probe and vessel was achieved by means of aqueous gel. Simultaneous measurements of TTF and Doppler flow velocity were recorded during 4 different phases: in basal condition, after creating a stenosis of the LAD with the proximal snare, during coronary occlusion, and during coronary reperfusion.

Figure 2: Suction type epicardial coronary Doppler probe

Four consecutive measurements were recorded during each phase of the experiment. Similarly, invasive blood pressure (BP), heart rate (HR), and left ventricular end diastolic pressure (LVEDP) were recorded.

Data were stored and analyzed. Data were expressed in terms of means ± standard deviation. ANOVA was used in the analysis to evaluate significant differences in TTF, Doppler flow velocity, BP, HR, and LVEDP between the four different stages of the experiment (basal, partial stenosis of LAD, occlusion LAD, and reperfusion). Whenever significant differences between the groups were reported, multiple range testing was adopted within coupled groups. Pearson's correlation coefficient was calculated to test relationship between coronary flow and coronary flow velocity values.

Statistical significance was stated for P values < than 0.05.

All experiments were performed and funded by the Erasmus University Hospital in Rotterdam, NL.

At the end of the experiments, the animals were used for other investigations and eventually sacrificed in the operating room.

RESULTS

Blood pressure, heart rate, and left ventricular end diastolic pressure were recorded during the four different phases of the experiment (table 1) and no statistically significant differences were detected.

There were statistically significant differences when comparing TTFM and Doppler flow velocity measurements during the four stages of the experiment. Doppler Velocity in cm/sec was 4.0±1.9 in basal condition, 3.5±2.2 during partial coronary stenosis, 0.50±1.4 at occlusion, and 11.0±5.5 during reperfusion (p<0.0001) (Table 2). Similarly, TTF in ml/min was 23.1±6.6 in basal condition, 16.2±5.7 during partial coronary stenosis, 0.0±0.2 at occlusion, and 67.4±23.2 during reperfusion (p<0.0001) (Table2).

Furthermore, no differences were found within groups, in TTF and Doppler flow velocity within the basal condition and partial LAD stenosis (p=ns).

A strong correlation was found between mean coronary flow and mean Doppler velocity values (P coefficient 0.99; p<0.001) (Figure 3).

Table 1: Hemodynamic values during the 4 experimental phases

	BP mmHg	HR bpm	LVEDP mmHg
Baseline	69.1±8.7	98.8±19.7	**22.1±24.5**
Partial Coronary Stenosis	64.1±2.0	86.9±23.5	**31.2±28.4**
Coronary Occlusion	64.2±6.0	87.8±24.6	**20.8±22.6**
Reperfusion	64.9±8.6	88.4±25.0	**23.5±25.5**
P-value	0.2	0.4	0.8

Table 2: Coronary blood flow and blood velocity values during the four different experimental phases

	Mean TT Flow (cc/min)		Mean Doppler Flow Velocity (cm/sec)
Baseline	23.2±6.6*		4.0±1.9*
Partial Coronary Stenosis	16.2±5.7*		3.5±2.2*
Coronary Occlusion	0.1±0.2		0.50±1.4
Reperfusion	67.4±23.2		11.0±5.5
P-value	<0.0001 * ns	<0.0001 * ns	

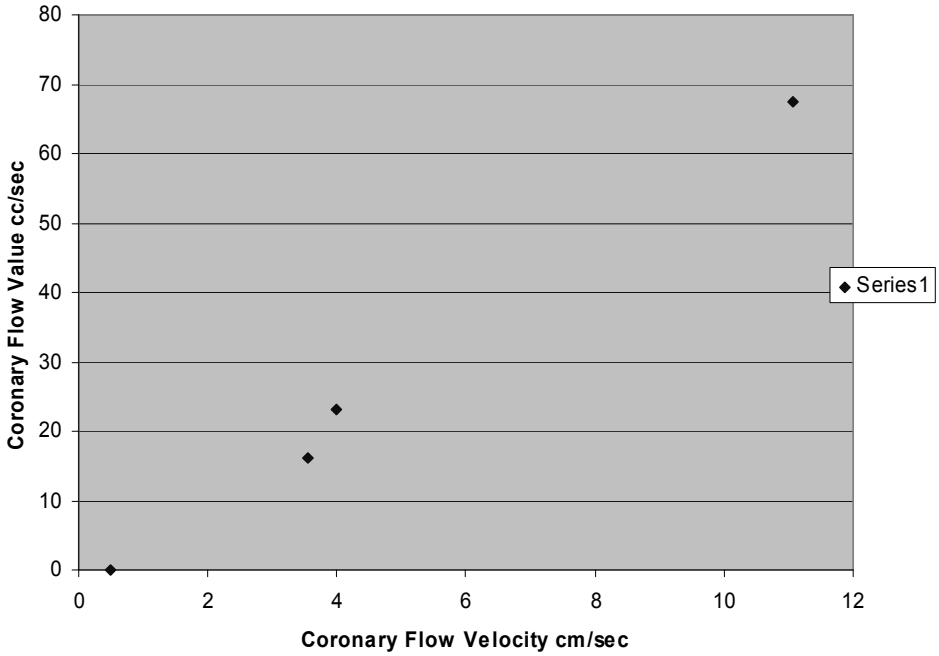

Figure 3: Correlation between mean coronary blood flow and velocity during the four different experimental phases

DISCUSSION

The current referral pattern for coronary artery bypass grafting (CABG) has changed including patients with more complex coronary pathology and anatomy, and associated comorbidities. In the light of this, there has been a revived interest in methods for intraoperative coronary graft patency verification and coronary target selection. Although TTF has been widely demonstrated as a sensitive tool for intraoperative quality assessment of newly constructed grafts (6-9), its application cannot be extended to the evaluation of coronary targets due to limitations intrinsic to transit time technology. Transit time probes are formed by two piezoelectric crystals and one metal reflector placed on the opposite side of the probe itself. The vessel under evaluation is placed within the probe and interposed between the crystals and the reflector. For this reason, accurate dissection of the vessel is required before applying the TTFM probe.

Differently from TTFM probes, Doppler epi-coronary probes are formed by a single crystal and do not require dissecting and encircling the target artery under study and, therefore, are more easily applicable to test the status of the native coronaries and their blood flow before and after the revascularization has been performed.

In this regard, Doppler technology has recently resurged as a valuable intraoperative armamentarium to help cardiac surgeons select adequate coronary targets for revascularization and depicting both anatomical and functional features of newly constructed anastomosis.

Potential applications of a custom-made 13 Mhz epicardial coronary Doppler probe were previously investigated demonstrating its ability to successfully visualize and assess coronary arteries and anastomoses on all sides of the heart in both the animal model and ex-vivo in humans (4).

Moreover, micro-probe Doppler has allowed for safe graft vessel harvesting (left internal mammary artery) and for selection of optimal anastomotic target sites (5).

Although the X-plore® probe technical features are based on the same specifications of the most commonly available Doppler probes with a similar frequency – i.e., a center frequency of 7.5 Mhz and a wide bandwidth of +/– 30% –, some small adaptations have been performed:

1) The angle of incidence between ultrasound and blood flow direction is crucial for accurate measurement of velocity. Standard Doppler probes must be angled correctly by the operator, while the X-plore® probe has an inbuilt angle of 45° allowing the probe to be placed perpendicularly to the vessel.
2) In the X-plore® probe a rectangular 3 by 6 mm crystal has been used allowing the ultrasound beam to cover the full cross section of the vessel. Differently, standard probes have round crystals with a focused beam that measures only part of the vessel's cross section.
3) The above mentioned two features allow for a direct placement of the X-plore® probe on the coronary vessel with minimal wall compression.
4) Lastly, the X-plore® probe has been adapted with a suction system to stabilize the device on the myocardium avoiding Doppler noise caused by heart movements.

In our analysis the X-plore® probe seemed to immediately detect adequate Doppler signals. Eventual disturbances in the signal wave were automatically filtered by the system.

A more advanced model of this micro-probe includes a suction system that maintains the probe on top of the vessel in order to reduce any signal disturbance (Fig.2).

In basal condition, Doppler velocity values were easily obtained and showed consistence during the four consecutive measurements. Interestingly, both flow velocity, as detected by the epicardial Doppler probe, and absolute flow values,

as detected by the pericoronary TTF probe, failed to show significant change after partial snaring of the LAD, confirming the fact that changes in coronary rheology may not occur until levels of vessel sub-occlusion are achieved.

As demonstrated in the occlusion phase of the experiment, zero flow velocity may be easily detected with epicardial coronary Doppler technology and represents a total coronary occlusion situation. Furthermore, in the reperfusion phase, the Doppler micro-probe detected brisk increases in blood flow velocity documenting the occurrence of significant increases in coronary absolute flow values. To translate these findings clinically, if epicardial coronary Doppler technology is used as a sole means to record flow velocity, some valuable conclusions may be deducted concerning the coronary status, location, and the successful reperfusion after graft anastomosis.

Despite the initial indication for the X-plore® probe to identify intra-myocardial coronary targets we believe its application should be enlarged.

When searching for intramuscular vessels, the surgeon places the probe in the approximate area of the vessel, and listens for the audible Doppler signal. The operator should select an appropriate volume setting that enables the surgeon to hear the signal, and possibly help differentiate arterial flow (pulsatile waveform as in figure 4) or venous flow (continuous flow) from acoustic disturbances related to probe movements.

When looking for a stenosis, the surgeon first needs to measure a normal, patent segment of the vessel. When a stable curve is displayed, the operator

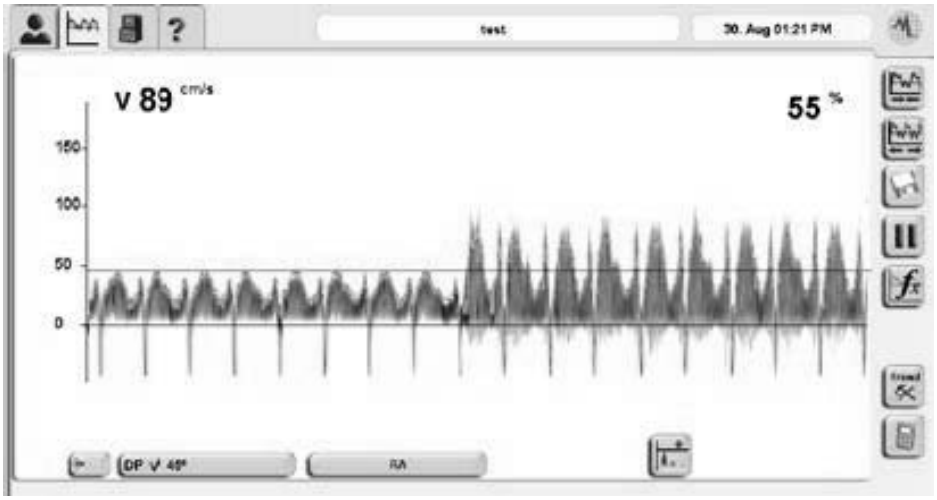

Figure 4: Coronary flow velocity as measured by epicoronary X-plore® Doppler probe: on the left side of the panel the velocity is measured before the stenosis; on the right, the flow velocity immediately at the level of the stenosis where vorticosity is increased and peak velocity is 55% higher than the reference value.

should memorize the finding in the Veri-Q system. The system will display a reference line, demonstrating the recorded reference peak velocity. When the surgeon repositions the probe on the target vessel, the measured peak velocity will be compared with the reference line. The system will display the change in peak velocity as a percent of stenosis (Figure 4).

The velocity scale may also need to be modified when the probe is above a narrow stenosis, causing the peak velocity to increase by four times (Figure 3).

As the probe is moved further down the stenosis, the velocity will go back down again and become much lower than the reference value.

Epicardial Doppler technology could also be applied in dubious situations to distinguish between arterial and venous coronary branches and guide adequate anastomotic targeting.

As demonstrated in our study, reperfusion after coronary revascularization may be easily detected with Doppler devices. In this context, we suggest using a combined approach by associating peri-graft TTF measurements and epicardial coronary Doppler to record simultaneously coronary graft absolute flow and coronary flow velocity. As previously described, TTF measurements may show faulty values if proximal coronary snaring is not applied in the experimental setting (9). As a matter of fact, almost normal TTF findings are documented in some cases where a stenosis at the toe of the anastomosis is present together with a perfectly patent anastomotic heel. In this particular situation, the absolute values as detected with the perivascular TTF probe are representative of the sole flow going towards the proximal part of the coronary. In a similar situation, the proximal snaring would imply significant reduction of the TTF values and document the anastomotic failure. Snare omission may be obviated by the routine use of epicardial coronary Doppler and documentation of flow velocity direction and its increase proximally and distally to the anastomosis. In addition, improvements in coronary perfusion may be selectively and specifically identified even in sequential grafts where measurement of TTF values at the level of the main graft may not be fully representative of the status of the different sequential anastomosis.

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Chapter 9

Intraoperative validation of a new system for invasive continuous cardiac output measurement

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Objective

Although bolus thermodilution technique for cardiac output (CO) measurement has widespread acceptance, new systems are currently available. We evaluated a continuous CO system (TruCCOMS, Aortech International, Inc) that operates on the thermal conservation principle and we compared it with the reference standard transit time flow measurement (TTFM).

Materials and Methods

Nine consecutive cardiac surgery patients were evaluated. After general anesthesia and intubation, a TruCCOMS catheter was percutaneously placed in the pulmonary artery (PA).

After median sternotomy and pericardiotomy, a TTFM probe was placed around the main PA. Right ventricular (RV) CO measurements were recorded with both the TruCCOMS and TTFM at different times: before cardiopulmonary bypass (CPB) (T0), during weaning from CPB (T1), and prior to sternal closure (T2). Data analysis included paired student t-test, Pearson correlation test, and Bland-Altman plotting.

Results

TruCCOMS CO values were significantly lower at T0 (TruCCOMS 4.0±1.0 vs. TTFM 4.5±1.0 L/min; $p<0.0001$) and T1 (TruCCOMS 3.6±0.5 vs. TTFM 4.2±0.7 L/min; $p<0.0001$), and comparable at T2 (TruCCOMS 4.5±0.7 vs. TTFM 4.6±0.8 L/min; $p=0.4$).

Pearson test showed a significant correlation between TruCCOMS and TTFM CO measurements ($RT0=0.9$, $RT1=0.8$, $RT2=0.6$; $p<0.0001$).

Bland-Altmann plotting showed a bias of -0.53±0.43 L (-12%) at T0, -0.64±0.43 L (-14.5%) at T1, and -0.1±0.66 L (-0.8%) at T2.

Conclusion

Although TruCCOMS may significantly underestimate CO, measurement trends correlate with TTFM. For this reason, a negative trend in RV output should trigger more specific diagnostic procedures.

INTRODUCTION

The recent change in the referral pattern for cardiac procedures has increased the number of patients with complex comorbidity profiles that are evaluated for surgical intervention.

In a similar context, perioperative anesthesia monitoring of cardiac function should guarantee appropriate continuous hemodynamic surveillance particularly in patients with compromised ventricular function.

Although at the present stage the "gold standard" for continuous cardiac output (CCO) monitoring is based upon the heat thermodilution technique, some limitations of this method should be emphasized. In fact, the main disadvantage of the current CCO systems is that measurement are not recorded as "real time" beat-to-beat values but are the result of averaging sample values actually taken at scheduled time intervals (approximately every minute).

In this study we have evaluated the performance of a CCO intrapulmonary catheter (truCCOMS system, Aortech Critical Care, Scotland, UK), that works on the principle of energy conservation and gives real time continuous measurements. We focused primarily on the right ventricular CCO monitoring performed with an intrapulmonary catheter and, as a reference method, we used a peri-pulmonary artery transit time flow probe (TTF) (Veri-Q, Medistim, Oslo, Norway) during different phases of cardiac surgery procedures.

MATERIALS AND METHODS

After signing a written consent, 9 consecutive patients undergoing cardiac surgery were included in this prospective study.

In the operating room, in addition to continuous EKG, pulse oximetry, and noninvasive blood pressure monitoring, a 20-G radial artery catheter was placed under local anesthesia. General anesthesia was induced with midazolam (0.1 mg/kg), fentanyl (0.01 mg/kg), and propofol (1mg/kg). Myorelaxation was achieved with cisatracurium (0.2 mg/kg). After tracheal intubation, anesthesia was maintained with sevoflurane 1-2% (propofol 5 mg/kg/hr during cardiopulmonary by-pass).

Additional fentanyl and cisatracurium were administered, when necessary.

After tracheal intubation, the lungs were mechanically ventilated with a mixture of oxygen and air. A right internal jugular introducer (AVA HF Triple Lumen, Edwards Lifesciences, LLC) plus a TRUCCOMS pulmonary artery catheter

were placed and correct positioning at the bifurcation of the main pulmonary trunk (with the tip of the catheter pointing towards the right pulmonary artery) was confirmed with trans-esophageal echocardiography (TEE). The TruCCO catheter allowed for routine monitoring of central venous pressures (proximal port) and pulmonary artery pressures (distal port) that were measured with a standard invasive pressure monitoring set (Edwards Lifesciences). Data were shown on the operating room monitor.

The TruCCO pulmonary catheter was also connected to a separete TruCCO monitor, which recorded CO measured with the CCO system. The measurement of the CCO is based on the principle of thermodynamic heat transfer. This catheter includes a thermistor and a heat transfer device cooled by the circulating blood. The thermistor measures the blood temperature and the heat transfer device maintains its temperature 1°C above blood temperature. The CO is continuously calculated from the amount of energy required to maintain that temperature gradient at a constant level.

TEE was performed as part of our standard monitoring during cardiac surgery.

After median sternotomy and pericardial opening, a TTF probe was placed around the main pulmonary artery. We deliberately decided to use TTF as reference method as this technology gives a real time, continuous, and true evaluation of cardiovascular rheology that includes blood flow, flow curve (systolic and diastolic), and pulsatility index (Maximal flow-Minimal flow/Mean Flow) [1].

TTFM probes work on the transit-time principle. The probe is placed around the vessel, generating a uniform ultrasound field across the vessel lumen. Ultrasound pulses are transmitted from two separate piezoelectric crystals located on the same side of the probe (and so of the vessel). On the opposite side of the probe, and at the same distance from the 2 crystals, there is a reflector. Ultrasound beams cross the vessel and are reflected back to the crystals. The time spent by the ultrasound wave to go from one crystal across the vessel and then to be reflected (by the reflector on the opposite side of the probe) and reach the other crystal, is called transit time. Ultrasound waves that travel upstream the flow will travel slower than those going downstream. The difference in transit time between the pulse going upstream and the one going downstream is proportional to the volume of flow passing through the probe ($Q \approx t2 - t1$).

TTFMs remain stable independently by the measurement angle (position of the probe on the vessel), blood temperature, and hematocrit level.

During the different stages of the operation, a total of 9 CO measurements were simultaneously recorded with both the TruCCOMS and TTFM at scheduled times. Three measurements were taken before initiation of cardiopulmonary

bypass (CPB) (T0), 3 during weaning from CPB (T1), and 3 before sternal closure after achieving normothermia, discontinuing CPB, and administering protamine (T2).

To guarantee a steady hemodynamic state, heart and great vessels manipulation was avoided while taking the measurements. Furthermore, measurements were taken only whenever a stable systemic blood pressure trace was achieved and while maintaining stable perfusion flows during CPB. To reduce artifacts on the TruCCO monitor, electric cautering was discontinued during the measurements. Furthermore, close body temperature monitoring was adopted to maintain normothermia during the different phases of the operation (including while on CPB) and to guarantee for stable TruCCO catheter readings. Data were recorded and analyzed. Normality was tested by means of Wilk-Shapiro test. Paired student t-test was used to compare measurements taken with the TruCCOMS and TTFM. Pearson correlation test was used to evaluate correlation between measurements taken with the two methods. Moreover, correlation of changes from one time point to the other was tested to evaluate concordance in time. ANOVA was used to test for reproducibility of measurements in short time intervals per patient. Bland-Altman plotting test was used to calculate the bias between the TruCCOMS and the reference measurement (TTF). A p-value<0.05 was considered statistically significant. Data are presented as mean ± standard deviation.

RESULTS

At T0 (before starting CPB) TruCCOMS average values were significantly lower (TruCCOMS 4.0±1.0 vs. TTFM 4.5±1.0 L/min; p<0.0001). Similarly, while weaning off-CPB (T1), TruCCOMS underestimated the CCO reference value (TruCCOMS 3.6±0.5 vs. TTFM 4.2±0.7 L/min; p<0.0001).

At T2, CCO values were comparable (TruCCOMS 4.5±0.7 vs. TTFM 4.6±0.8 L/min; p=0.4).

Pearson test showed a significant correlation between TruCCOMS and TTFM CO measurements at the 3 different time stages (RT0=0.9, RT1=0.8, RT2=0.6; p<0.0001).

Correlation was also present when comparing the differences of the measurements taken at the different time points (T0, T1, T2) with the TruCCOMS and TTFM (RT0-T1=0.9, RT1-T2=0.8, RT0-T2=0.9; p<0.0001).

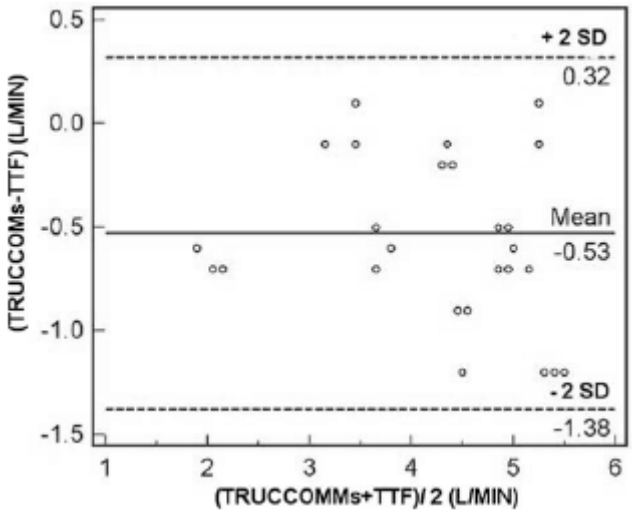

Figure 1: Bland Altman diagram of cardiac output (CO) measurements with TruCCOMS compared to Transit Time Flow (TTF) at T0 (prior to cannulation).

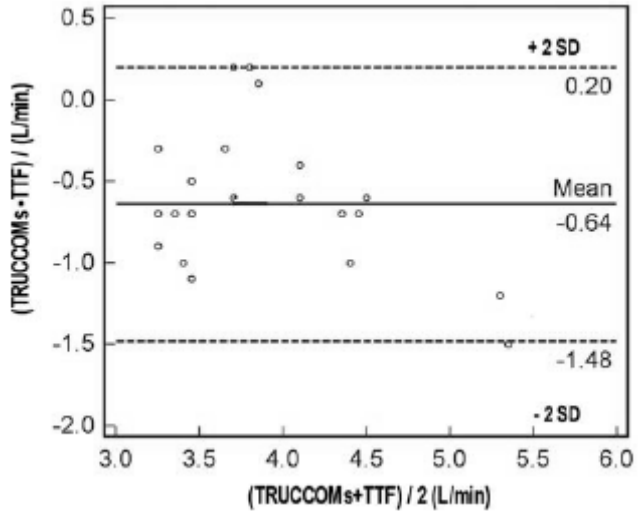

Figure 2: Bland Altman diagram of cardiac output (CO) measurements with TruCCOMS compared to Transit Time Flow (TTF) at T1 (during weaning from cardio-pulmonary bypass).

Per each patient we tested reproducibility of measurements taken with TruCCOMS at T0, T1, and T2. ANOVA confirmed that, per each of the 9 patients, TruCCOMS measurements were reproducible and values taken in the same patient within short time frames were not significantly different ($p>0.05$).

Bland-Altmann plotting showed a bias of -0.53±0.43 L (-12%) at T0, -0.64±0.43 L (-14.5%) at T1, and -0.1±0.66 L (-0.8%) at T2. Precision was 0.43 at T0, 0.43

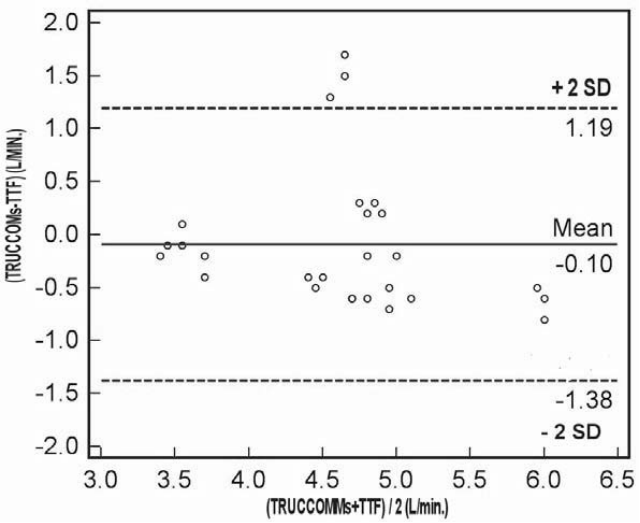

Figure 3: Bland Altman diagram of cardiac output (CO) measurements with TruCCOMS compared to Transit Time Flow (TTF) at T2 (prior to sternal closure)

at T1, and 0.66 at T2. Lower limits of agreement were -1.40 (-31.7%) at T0, -1.50 (-32.5%) at T1, and -1.41 (-31.9%) at T2. Upper limits of agreement were 0.34 (7.6%) at T0, 0.21 (3.5%) at T2, and 1.2 (30.3%) at T2 (Fig. 1-2-3). Those limits defined 95% confidence intervals for T0, T1, and T2.

DISCUSSION

Adequate CO measurement acquires major importance when dealing with patients with impaired ventricular function.

Many authors have compared bolus with automatic thermodilution CO measurement methods, concluding that the latter ones provide accurate values [2-5].

The TruCCO system is based on the principle of thermodynamic heat transfer and, despite offering the advantage of continuous monitoring, its accuracy when compared to the standard thermodilution methods remains controversial.

Leather et al. have compared TruCCO measurements with triplicate cold bolus thermodilution as the standard reference in a cardiac surgery setting. They concluded that TruCCO underestimates CO at higher values and overestimates low COs. Most importantly, TruCCO failed to accurately detect CO drug-induced changes (dobutamine) [6].

To our knowledge, TruCCOMS has been compared to other continuous CO techniques only in a limited number of studies.

Padua et al. have evaluated in 16 cardiac surgery patients the performance of TRUCCOMS, pulsion continuous CO (PiCCO), and echocardiography using traditional thermodilution as standard method of reference (7). Within the 3 methods, TRUCCOMS showed the lowest mean difference (bias) with the standard reference [7].

As previously suggested by Thierry et al. [8], we used peri-vascular TTF as reference standard for CO evaluation. We believe the "gold standard" for CO measurement should be a method providing a more direct and real time blood flow monitoring unbiased by sudden variations in hemodynamics, hematocrit, and/or blood temperature that may take place in the clinical context. TTF technology fully responds to such requirements and its accuracy has been already tested in even more complex rheological conditions such as those often encountered within the coronary anatomy [1].

Thierry et al. highlighted how continuous CO measurement by means of the TruCCO catheter was in agreement with continuous CO measurement using a peri-aortic TTF probe, and with bolus CO measurement with the conventional pulmonary artery catheter. In the operating room, the coefficient of correlation between CO measured by the TTF probe and the TruCCO system was 0.79 and the bias was +0.11 l/min (i.e., TruCCO slightly under-estimated CO). In the intensive care unit the coefficient of correlation between CO measured by thermodilution and the TruCCO system was 0.56 and the bias was 0.07 l/min [8].

In our experimental set-up, we decided to compare TruCCO values with those obtained with the TTF probe placed around the pulmonary artery as we were interested in specifically evaluating variations in right ventricular function at baseline conditions and during weaning from CPB. We designed this experiment based on the fact that in our clinical experience continuous evaluation of residual right ventricular output by means of intrapulmonary catheters becomes very crucial and cumbersome in patients placed on different forms of complex ventricular assistance (either extracorporeal membrane oxygenator or simple left ventricular assist devices).

Our findings are somewhat in agreement with those obtained by Thierry et al. as we also noticed a considerable statistical correlation between TruCCO and TTF measurements during the three phases of the experiment. Correlation persisted when comparing the differences of the measurements taken with TruCCO and TTFM at the different time points. In this context, we may conclude that the TruCCO system gives an indication of the hemodynamic trends in different clinical conditions.

More specifically, we noted that a significant underestimation of CO may result by TruCCO, particularly in conditions of sudden hemodynamic or blood temperature variations such as those observed in the initial phases of heart surgery, after sternotomy and pericardial opening, during heart manipulation for cannulation, and while weaning the patient off CPB. In the latter condition, for example, TruCCO has an average negative bias of 640 ml. that accounts for up to 14.5% of the total CO.

Once the hemodynamic status and the patient temperature have been stabilized at the end of the procedure, TruCCO readings are comparable to TTF probe ones with a negative bias of only 100ccs.

We suggest that, for this reason, TruCCOMS should have a more appropriate applicability in the ICU continuous CO monitoring rather than in the intraoperative settings where clinical conditions may undergo sudden changes.

Moreover, TruCCO catheter position within the pulmonary vasculature may, theoretically, further influence the readings. Although we did not specifically investigate the differences in CO measurements when moving the catheter within different pulmonary artery branches, we may state that positioning at the level of the main pulmonary trunk bifurcation gives stable and reproducible measurements.

In our experience, TruCCOMS may easily detect variations in CO, although exact quantification of CO in the clinical setting remains a limit.

In a meta-analysis of studies using bias and precision statistics to compare CO measurement techniques, Critcheley et al. have shown that a new technique of CO monitoring should rely on limits of agreement between the new and reference technique of up to ± 30% [9]. Those limits were proposed by the Authors after an attempt analysis of the literature where thermodilution was taken as the reference method against which compare new methods of CO monitoring. In our analysis we achieved limits of agreement slightly higher (-32.5% lowest of the lower limits and 30.3% highest of the upper limits) than those proposed by Critcheley. We should emphasize that we took a much more sensitive technique (TTFM) as reference method and, for this reason, an extrapolation of ± 30% limits, suggested when using thermodilution as reference, may be inappropriate.

In this context, we could argue that more emphasis should be placed on the device's reliability in reporting trends in CO than in defining its absolute values.

For this reason, a negative trend in ventricular output should trigger performance of more specific diagnostic procedures such as echocardiography.

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Chapter 10

Use of nitinol-U clips and flow characteristics of LIMA-LAD anastomoses

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ABSTRACT

The aim of this study was to compare flow characteristics of LIMA-LAD anastomoses constructed using two different techniques. Thirty patients underwent MIDCAB using either simple continuous suture (20) or separate nitinol U-clips (10). Intraoperative transit time flow measurements were recorded. Preoperative variables were similar in the two groups. Anastomosis time was significantly higher in the U-clipped group (9.9 ± 1.5 min. vs.11.4± 1.5 min; P= 0.016). Average flow value in the 20 continuous suture LIMA-LAD anastomoses was 26.7 ± 8.8 ml/min versus 36.3 ± 10.6 ml/min in the 10 U-clipped grafts (P=0.014). Pulsatility Index value was significantly lower in the U-clipped group (3.1 ± 0.9 vs. 1.8 ± 0.3, P=0.0001) and diastolic flow index was significantly higher (0.7 ± 0.04 vs. 0.8 ± 0.03, P=0.046). Perioperative results were similar in the two groups (P = ns). No mortality was reported. Postoperative trans-thoracic Doppler confirmed patency of the LIMA in all 30 patients. At short-term clinical follow-up (60 ± 4 days), all patients were in CCSI. Nitinol U-clips can be used to construct LIMA-LAD anastomoses on the beating heart. Flow dynamics of these anastomoses are superior to those of grafts constructed using continuous suture technique. Particularly, total flow is higher and diastolic flow may reach values of 80% of the total measured flow.

INTRODUCTION

The present technique in constructing vascular anastomoses with continuous sutures as described by Alexis Carrel at the beginning of the 20th century [1] has been proven to be reproducible and effective in millions of patients operated upon for both vascular and cardiac surgery procedures. Although satisfactory long-term results have been achieved when using this technique in conventional coronary artery bypass grafting (CABG) surgery, imperative questions regarding technical factors that may directly influence anastomotic patency rates and operative outcomes remain uninvestigated. In this regard differences between continuous and interrupted suture technique as applied to CABG have been poorly investigated. The limited number of studies showing definite advantage of the interrupted suture technique [2,3,4,5] has contributed to a broader adoption of the easier and faster continuous suture technique. On the other hand, the recent introduction and popularization of minimally invasive and endoscopic robotically enhanced coronary surgery [6] has refocused attention on new technologies that may ease construction of coronary anastomoses maintaining good operative results. Many different surgical devices have been investigated and among them, the coalescent U-clip (Coalescent Surgical. Inc. Sunnyvale, CA) has been safely adopted in animal and human studies [7, 8]. This device reproduces the theoretical advantages of the interrupted sutures anastomoses technique in a self-closing stitch that does not need to be manually tied. Although short-term angiographic patency rates of coronary anastomoses constructed with U-clips have been already addressed [7, 8], limited information is available concerning the blood flow patterns in U-clipped coronary artery grafts [8].

Furthermore, differences in graft flow characteristics of U-clipped versus conventionally sutured coronary anastomoses have never been investigated.

In this manuscript we report our results in a prospective comparison between intraoperative transit time flow measurement (TTFM) findings of conventionally constructed (continuous polypropylene suture) versus Uclipped left internal mammary artery (LIMA) to the left anterior descending (LAD) coronary artery anastomoses.

PATIENTS AND METHODS

Between October 2001 and May 2002, 30 patients were enrolled in this study at the Buffalo General Hospital. Minimally invasive direct coronary artery bypass grafting (MIDCAB) was performed in all 30 patients. Twenty consecutive procedures using continuous suture were done followed by 10 consecutive procedures

using U-clip. Assignment to one of the two groups was mainly done on the basis of U-clip availability. All operations were performed by the same surgeon. The selection criteria used were: requirement for a single vessel LIMA-LAD anastomosis approachable by MIDCAB, and LAD diameter > 1.75 mm. Patients with calcified, intramural, and < 1.75 mm LAD were excluded from the study. These are the criteria that we normally apply to MIDCAB patients. Use of U-clip technique did not add any further exclusion criterion to the study. LIMA was harvested through a left anterior small thoracotomy in the 4th intercostal space, and the anterior pericardium was opened to expose the LAD. Coronary stabilization was achieved by means of pressure type stabilizer. A 1.75-mm shunt was routinely used and allowed for satisfactory hemostasis. Anastomosis of the LIMA to the LAD was performed in 20 (66.6%) patients on the beating heart using a traditional technique with 7-0 polypropylene simple running suture. In 10 patients (33.3%) LIMA to LAD anastomoses were performed on the beating heart using nitinol U-clip single armed sutures (Coalescent Surgical, Inc, Sunnyvale, CA). The clip is made of titanium and nickel and has shape-memory properties. The clip is maintained in its U-shape configuration and is connected to a flexible wire with a releasing mechanism in between. The 3-cm long wire has a needle at its other extremity. The needle is passed through the graft and the coronary as in conventional suturing. When the two tissues are properly approximated and the U-clip is placed in the desired position, the clip is deployed by compressing the 1-mm-long release mechanism located between the wire and the clip. At this point, the released clip returns to its original shape as a closed ring connecting the LIMA to the LAD. At the end of each anastomosis intraoperative graft patency verification was performed by means of transit time technology (Medistim, Oslo, Norway). Measurements were performed with the proximal snare applied in order to exclude any possible competition of flow from the native coronary artery. Flow curves, total flow, pulsatility index (PI) (Maximum Flow-Minimum Flow/Mean Flow), and diastolic index values (mean diastolic/mean total flow) were recorded for each graft after protamine infusion. Cost of continuous suture was approximately $60 (one continuous suture + one additional, in case of placement of hemostatic sutures at $30 each), while the cost of U-clip sutures was $165 (11 U-clips at $15 each). Demographic and perioperative data were prospectively collected for the two groups (continuous suture vs. U-clip) and statistically compared. Differences between variables were considered significant with a two-tailed P value <0.05. Continuous variables were compared using the unpaired t-test. Discrete variables were compared by using the chi-square test or the Fisher's exact test. Welch t-test was used instead of the unpaired t-test when differences between standard deviations were significant.

RESULTS

Demographic and preoperative data were comparable in the two groups (Table 1). Average LAD occlusion time was similar in the two groups (11.1 ±1.9 min continuous suture vs.12.0 ± 1.6 min U-clipped; P = ns). Average anastomosis time was significantly higher in the U-clipped group (9.9 ± 1.5 min continuous suture vs.11.4 ± 1.5 min U-clipped; P = 0.016). An average of 11 ± 2 clips were used in the U-clipped group. No anastomosis in the U-clipped group was converted to a continuous suture technique. No conversion to full sternotomy or to cardiopulmonary bypass (CPB) was necessary in the two groups. Intraoperative

TTFM data were compared in the two groups. Although all recorded flow curves appeared to have a diastolic flow pattern, statistically significant differences in the absolute flow, PI, and diastolic index flow values were reported. Data from all three parameters were normally distributed according to the method of Kolmogorov and Smirnov. Average flow value in the 20 LIMA-LAD anastomosed with continuous suture technique was 26.7 ± 8.8 ml/min versus 36.3 ± 10.6 ml/min in the 10 U-clipped grafts (P = 0.014). PI value was significantly lower in the U-clipped group (3.1 ± 0.9 continuous suture vs. 1.8 ± 0.3 U-clipped, P =

Table 1. Preoperative and perioperative data in 30 patients undergoing LIMA-LAD anastomosis (20 continuous suture vs. 10 U-clip)

	Cont. suture (20)	U-clipped (10)	*P*
Age	64 ± 6.7	63.7 ± 4.6	NS
Male	17 (85%)	8 (80%)	NS
LVEF > 40%	20 (100%)	10 (100%)	NS
Diabetes	7(35%)	3 (30%)	NS
Previous CVA	0%	0%	
Previous AMI	4 (20%)	2 (20%)	NS
Intubation time (h)	0.8 ± 1.5	0.6 ± 1.4	NS
Unit blood transfused	0.7 ± 1.2	0.4 ± 0.8	NS
Troponin-I (ng/ml)	0.12 ± 0.32	0.18 ± 0.13	NS
Bleeding revision	1 (5%)	0	NS
AMI	0	0	
CVA	0	0	
Hospitalization (days)	4.7 ± 0.8	4.7 ± 0.7	NS
Mortality	0	0	

0.0001). Standard deviations between the two groups for PI were found to be extremely statistically significant (P<0.0006) using the unpaired t-test. Thus the Welch t-test was conducted, yielding a P value of 0.0001. Diastolic flow index was significantly higher in the U-clipped group (0.7 ±0.04 continuous suture vs. 0.8 ± 0.03 U-clipped, P=0.046). Perioperative data are reported in Table 1.

Postoperative trans-thoracic Doppler confirmed patency of the LIMA with diastolic flow pattern in all 30 patients. At clinical follow-up (60 ± 4 days) all patients were free from angina and EKG stress tests performed 1 month after surgery did not show signs of myocardial ischemia.

DISCUSSION

More than three decades have passed since the basic techniques adopted for CABG were firstly described [9,10,11]. Although many changes and advancements have been introduced through the years to improve outcomes of the operation, considerable issues regarding physiological and technical factors involved in the construction of coronary anastomoses remain unanswered. In this regard only a limited number of comparative studies have objectively addressed differences between anastomoses constructed with continuous or interrupted suture technique [2,3,4].

Using cast models, Young et al. [2] reproduced the internal configuration of saphenous vein to coronary artery anastomoses and examined the effects of different technical factors. The authors observed that, although the external appearance of the anastomosis was not a reliable indicator of its internal configuration, interrupted suturing consistently produced an internal configuration of the anastomosis with minimal deformities [2]. Shioi et al. [4] investigated the internal configurations of sequential anastomosis constructed with interrupted and continuous suturing technique. Interrupted sutures produced a larger anastomosed area for the incised length than other suture techniques. Furthermore, fine suturing spacing appeared to be less critical when interrupted sutures were used and an average of six to eight sutures per side appeared to produce well formed anastomoses. In a more recent experimental study, Baumgartner et al. [3] compared the effects of continuous vs. interrupted polypropylene (stiff) and polybutester (compliant) sutures on the luminal dimension and compliance of vascular anastomoses. End-to-end anastomoses constructed with continuous polypropylene, continuous polybutester, and interrupted sutures had respectively cross-sectional areas of 70%, 90%, and 107% of that of the native coronary (P< 0.05). The authors concluded that interrupted suture line should be used

when constructing end-to-end anastomoses in small vessels. In spite of the theoretical superiority of the interrupted sutures technique, construction of vascular anastomoses with continuous simple sutures has increasingly gained popularity and has become standard practice in coronary surgery thanks to its advantages in terms of ease and speed of use. The recent popularization of minimally invasive coronary surgery and particularly the introduction of endoscopic robotically enhanced CABG [6] has focused interests in rethinking the technique of vascular anastomoses construction. In an attempt at eliminating long suture handling and knot tying, that may became a real challenge especially during endoscopic surgery, and with the aim of speeding anastomosis construction on the beating heart, many alternative ingenious techniques and technologies have been proposed [7,8,12,13,14,15]. Use of non-penetrating titanium clips to construct coronary anastomoses has been proposed by Nataf et al. [12]. Successful application of the clip requires eversion of the coronary and graft tissues and cannot be easily performed with calcified vessels [12]. A one-shot anastomotic clip device has been proposed by Heijmen et al. Accurate removal of the periadventitial tissue of the LITA should be performed to allow for appropriate release of the clips [13]. Gundry et al. [14] and Buijsrogge et al. [15] have successfully used biologic adhesives to construct coronary anastomoses in animal models. The nitinol U-clip device has been successfully used to perform vascular anastomosis in animal [7] and human [8] studies. Hill et al. successfully created right internal mammary to coronary anastomosis on the beating heart and repaired carotid arteriotomies in 13 consecutive calves. Patency was confirmed at angiography and neointimal resurfacing of the anastomoses was found at histopathologic evaluation [6]. More recently, Ono et al. reported successful U-clip construction of LIMA-LAD anastomoses in 14 patients operated upon with or without CPB [7]. In the present study we focused our attention on the comparison between intraoperative TTFM findings of LIMA-LAD grafts performed with continuous suture versus interrupted U-clips. Although physiological and anatomical differences between anastomoses constructed with interrupted versus continuous sutures have been partially addressed [2,3,4], functional studies investigating differences in coronary graft flow characteristics are lacking. TTFM findings in the present study confirm that U-clipped anastomoses on the beating heart can be safely performed, considerably improving flow dynamics of the newly constructed grafts when compared to the traditional single continuous suture technique. Performances of U-clipped anastomoses in terms of flow dynamics are satisfactory and diastolic flow averages 80% of the total flow value (diastolic flow index 0.8 ± 0.03). On the other hand, although continuous single suturing technique for LIMA-LAD anastomoses construction has also demonstrated

satisfactory clinical results, its flow dynamics are significantly different when compared to the U-clip technique. Total flow value is significantly less when using the continuous suturing technique (26.7 ± 8.8 ml/min continuous suture vs. 36.3 ± 10.6 ml/min U-clip, P = 0.014) and more importantly the percentage of diastolic flow is significantly lower (0.7 ± 0.04 continuous suture vs. 0.8 ± 0.03 U-clip, P= 0.046). As confirmation of the superior hemodynamic performance of the U-clip group, mean PI value was significantly lower than in the continuous suture anastomoses (3.1 ±0.9 continuous suture vs. 1.8 ± 0.3 U-clip, P =0.0001).

CONCLUSION

Superior hemodynamic performances of the U-clipped anastomoses have been reported in our study with a particular emphasis on the superior values of total diastolic flow and diastolic flow ratio. Although these findings are interesting and confirm at least the theoretical advantages offered by separated suture over continuous suture anastomoses, there has not been any clear difference in clinical outcome when using U-clips. Lack of angiographic controls and adequate mid-term follow-up are present limitations that will be specifically addressed in the future developments of this study.

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Chapter 11

Intraoperative Graft Patency Verification: Should You Trust Your Fingertips?

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The main aim of coronary artery bypass grafting (CABG) is to increase blood flow to ischemic myocardium. Although this procedure is successfully performed in more than several hundred thousand patients per year in the United States, intraoperative graft patency verification is still considered optional in most centers. Grafts are assumed to be patent at the end of the operation, especially if the patient has no hemodynamic compromise and, if cardiopulmonary bypass (CPB) was used, that weaning from it is successful.

In the last decade, measurement of coronary graft flow has been almost abandoned due to the many limitations of this obsolete electromagnetic technique (1). The increasing popularity of CABG performed on the beating heart without CPB, together with the introduction and improvement of ultrasound-based flow meters such as Doppler and Transit Time Flow Measurement (TTFM; MediStim, Oslo, Norway), has revived some interests and concerns about the importance of intraoperative documentation of graft patency (2). Despite the tremendous improvements offered by the new technology in the field of rheology and flow measurement, a large number of cardiac surgeons are still very sceptical and often misinformed about the applicability and limitations of modern flow meters.

A recent survey conducted on a limited sample of 100 cardiac surgeons and sponsored by an internationally known medical company (Genzyme Surgical Products, Cambridge, MA), has shown some interesting findings about the current graft patency verification practice in the United States. The majority (68.1%) of those interviewed stated that manual palpation of the grafts is their current method to detect graft patency after CABG. More than 70% of the surgeons included had never used a flow meter in their practice. When questioned about the reasons for not using a graft patency verification system, most of the surgeons interviewed answered that flow meters are often difficult to use, interpretation of the findings are unclear, and revision rate is low enough that graft patency verification seems unnecessary. Although most of the surgeons declared that a flow meter is not routinely necessary, interestingly 86% of them stated that it is important to have a system available in the operating room if, in some selected cases, it is necessary. More than 20% of those interviewed recognized the compelling importance of intraoperative graft patency verification. More than 60% of the surgeons recognized the applicability of this technology in both off-pump and on-pump procedures. Thirty-seven percent of those interviewed stated that this technology is only applicable during off-pump procedures because, on pump, the chance of anastomotic mistakes is very low.

The surgeons were then questioned about the action that they would have taken in case of abnormal findings during intraoperative coronary graft-flow measurements. More than 50% of those interviewed stated they would revise the grafts in question. The remaining would either wait or use another method of graft patency verification. When asked about their normal graft revision rate during CABG, 88% of the surgeons declared an error rate of 4% or less with an average rate of 3.1%. The majority of the surgeons stated that poor native vessels were the most common cause of graft revision.

Finally, surgeons placed a dollar value on the ability to accurately measure graft patency intraoperative. In U.S. dollars, the responses ranged from $0 to $1,000. Although this questionnaire was limited to a small number of surgeons, the findings are very interesting and probably applicable to all cardiac surgeons in the United States.

We began our experience with intraoperative graft patency verification in 1996 to document the feasibility of off-pump CABG. To date, more than 800 patients who have had off-pump surgeries have been tested using intraoperative TTFM and we feel very confident with the features offered by TTFM technology. We understand that graft testing with syringes, fingertips, and direct probing of the anastomoses seem to be more immediate than interpreting a flow curve, but this is not always the case. We believe the information given by flow meters may be misleading, especially when the operator does not fully understand the advantages and limitations of the present technology. Often the manufacturers are more interested in selling their product than clarifying its real applicability. Surgeons prefer, for this reason, to rely on their "accurate" tactile sense.

When choosing a flow meter, special features should be evaluated. The measurement must be stable, reproducible, and representative of the real flow within the constructed graft. Flow probes should be user friendly and easy to calibrate. The recorded data should be stored in the flow meter for future analysis and included in the patients' charts for documentation. Much of the scepticism about intraoperative graft patency verification is also based on failure of the electromagnetic technology. Electromagnetic devices measure the intensity of the electromagnetic field generated by the electrically charged red cells (iron bound to hemoglobin) that flow within a vessel. Actual blood flow value is derived from, and is directly proportional to, the intensity of the electromagnetic field generated. This technology has been abandoned and has been recently replaced by ultrasound devices.

The term ultrasound has a generic definition that includes two different methods: Doppler and TTFM. The two systems rely on different properties of the ultrasound waves and, although the Doppler methods have shown good

reliability both in vivo and in vitro (3), the TTFM technology offers many important advantages and is the most accurate system for intraoperative verification of coronary graft patency (4-6). TTFM measurements are theoretically independent of internal or external vessel diameter, vessel shape, and Doppler angle. TTFM is also insensitive to the alignment between probe and vessel. The probe does not have to be in direct contact with the vessel and calibration is not necessary. The recordings are stable and data storage and analysis are routinely done. Many of these features are not offered by Doppler technology.

The TTFM device is very easy to use and requires no more than 30 seconds per measurement. Flow-probe size varies from 2 to 32 mm and the size of the flow probes used most frequently in cardiac surgery ranges between 2 and 3.5 mm. The flow probe consists of two small piezoelectric crystals, one upstream and one downstream, mounted on the same side of the vessel. Opposite to the crystals, there is a small metallic reflector. Each crystal produces a wide pulsed ultrasound beam covering the entire vessel width. The probe is connected to a computer that has more than 200 MB of memory and is programmed with software in Microsoft WINDOWS format. Both the amount of time necessary for an ultrasound beam emitted from the upstream crystal to arrive at the downstream crystal after being reflected, and for a signal from the down-stream crystal to reach the upstream crystal are measured. Since ultrasound travels faster if transmitted in the same direction as flow, a small time difference between the two beams is calculated as the transit time of flow and thus, the actual flow is proportional to the transit time. All calculations are made automatically by the flow meter and are displayed, as ml/min. Measurements are not dependent on the angle between vessel and probe. The two crystals are mounted in a fixed position. An increase in the angle between the upstream probe and the vessel will always be compensated by a corresponding decrease of the angle between the downstream probe and the vessel and vice versa. As mentioned above, measurements are also independent of hematocrit level, heart rate, and thickness of the vessel wall. Flow curves, together with flow and Pulsatile Index (PI) values, are visualized in real time on a video screen, can be saved in the hard drive, and can be printed through a parallel port.

Correct interpretation of TTFM findings may be difficult if this technology is not routinely applied and if established protocols and rules for flow measurement are not followed. The flow meter is not a magical device that can be forgotten in the operating room only to provide an exact answer whenever we have doubts about the quality of the anastomosis. The operator should interpret flow curves and, although most of the TTFM findings have an immediate interpretation, there is a learning curve for the more difficult cases. Confidence

with the flowmeter increases with the number of cases in which this technology is applied. For TTFM to be correctly interpreted, flow curves, PI, and mean flow values should all be evaluated simultaneously. In a patent coronary graft, the hemodynamics are similar to those physiologically observed in the coronary circulation: blood flow should be mainly diastolic with minimal systolic peaks taking place during the isovolumetric ventricular con-traction (QRS complex). To correctly interpret flow patterns, curves should always be coupled with the ECG tracing to differentiate the systolic from the diastolic component. The PI is a good indicator of the flow pattern and, consequently, of the quality of the anastomosis. This number is obtained by dividing the difference between the maximum and the minimum flow by the value of the mean flow. In our experience, the PI value should be between 1 and 5; the possibility of a technical error in the anastomosis increases for higher PI values (6, 7). Mean flow is expressed as mL/min and its value is not necessarily a good indicator of the quality of the anastomosis. Mean flow is very dependent on the quality of the native coronary artery and low flow values can be expected in fully patent anastomoses (6) whenever the target territory has poor run-off.

We believe that intraoperative graft patency verification should be routinely adopted in all cases and not exclusively in patients operated on without CPB. Today, the modern techniques of exposure and stabilization of the different coronary artery branches can, in the majority of the off-CPB cases, provide very stable conditions and excellent surgical exposure comparable to the cases using CPB. In spite of that, surgical mistakes are still possible and, most of the time, difficult to admit. Our revision rate off-CPB has recently decreased from 8% to 4% and, in most of the cases, a technical error was found at revision (6). Flow abnormalities related to poor quality of the revascularized territory may be easily detected if a standard technique of measurement is correctly adopted. The TTFM probe should be perfectly fitted around the graft. Skeletonization of a small segment of the mammary artery is necessary to reduce the quantity of tissue interposed between the vessel and the probe. Aqueous gel is used to improve probe contact. TTFM has to be evaluated both with and without proximal snaring of the native coronary artery to detect any possible imperfection localized at the toe of the anastomosis and to exclude flow competition from the native vessel. Before making any measurements, adequate de-airing of the grafts is performed using a 25-gauge needle. Adequate systemic blood pressure is maintained and traction on the pericardium is released to allow the heart to return to its anatomical position. TTFM should be repeated before chest closure and after protamine administration to confirm graft patency and to detect any possible graft kinking or compression. We believe that prompt graft revision may very

well be necessary whenever abnormalities in flow curves and values are found. Although it is very hard to admit technical mistakes, most of the time errors are not visually detectable, at least while performing the anastomosis. It is also true that this technology has been proven effective in detecting highly stenotic coronary anastomoses, and that data concerning the specificity and sensitivity of TTFM have never been published. A neural network pattern recognition analysis of graft-flow characteristics has been proposed by Cerrito et al. (8) to improve TTFM detection of anastomotic errors. After a complex mathematical analysis of the flow curves, it is possible to detect stenoses that causes 50% or greater narrowing of the anastomoses. Less than critical stenoses cannot be detected by TTFM because no modifications in the hemodynamic performances of the grafts occur at this level.

Another limit of TTFM that will be possibly solved with increasing clinical experience is the lack of standard or nominal curves and flow values for different types of grafts and revascularized vessels. Standardization of the TTFM findings is difficult due to large biological variability between different subjects, as well as within the same subject. Interpretation of flow curves and TTFM findings is still empirical and is dependent on the surgeon's personal experience. Jaber et al. (9) have tested the ability of 19 international surgeons to detect anastomotic errors by evaluating mean flow and flow wave-form morphology. We believe that the ability to correctly interpret TTFM findings develops with clinical and experimental experience and, for this reason, surgeons who have not been exposed to this type of technology cannot easily give it the proper level of importance. Flow patterns, PI values, flow values, and clinical findings (i.e., ECG tracing, hemodynamic values) should always be evaluated simultaneously to improve the applicability of TTFM. Absolute flow value does not necessarily reflect anastomosis quality because there are too many variables influencing absolute flow, including size of the graft and quality of the revascularized coronary artery. Instead, coronary flow reserve can better help to correctly diagnose anastomotic imperfections. Walpoth et al. (10) have documented that quality of the anastomosis can be better defined by testing its dynamic ability to increase graft flow whenever myocardial oxygen requests are increased during infusion of adenosine. PI values are good indicators of the quality of the anastomoses. In our experience, high PI values are suggestive of anastomotic imperfections and the high PI values alone could justify coronary graft revision (6,7). Even though an absolute PI value has not been defined, we have empirically selected the limit of 5 based on our clinical experience with TTFM.

Di Giammarco et al. (11) proposed a value, derived from their clinical experience, of 2.5 as the limit of the PI value above which an anastomosis should be revised (11). Finally, the price for this technology cannot be defined with economical parameters. Even if interpretation of graft flows is still based on personal experience and empirical values, these are not good excuses for avoiding intraoperative graft patency verification. The flow meter should be used routinely as a surgical armamentarium to improve patient care and surgical results independently by the surgical technique adopted. Ability to interpret flow data will improve with use of the flow meter. Surgeons should not feel questioned or intimidated by the possible negative judgments of the flow meter. We understand the financial limitations imposed by hospital administrators but we believe that, in the future, surgeons that do not routinely adopt methods of intraoperative graft patency verification may be legally prosecuted in cases of perioperative complications. The use of fingertips to detect coronary graft patency after CABG will be seen, in years to come, in the same way as using the bare ear to detect paravalvular leaks after valve replacement.

ACKNOWLEDGMENTS

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Chapter 12

Intraoperative graft patency verification in coronary surgery: Modern diagnostic tools

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ABSTRACT

Nowadays medical procedures require a quality control method, and this is especially true for complex procedures such as heart operations. Various intraoperative tools are currently available to test coronary graft patency during coronary bypass grafting.

A distinction should be made between imaging techniques and flow assessment devices. Both methods have clear limitations, and we should consider using the two different technologies simultaneously. This paper reviews the means currently available to intraoperative test and document the status of newly constructed coronary anastomoses.

INTRODUCTION

The standard of care in modern medicine is supported by many quality control tools and intraoperative graft patency testing after coronary surgery can be proposed, in this context, as part of the operation documenting the success of the procedure itself.

The aim of coronary artery bypass grafting (CABG) is to increase blood flow to ischemic myocardium. This statement acquires further impact if we realize that 5-20% of all grafts performed fail before discharge from the hospital and up to 30% before 1 year (1, 2) without any objective evidence that these grafts were actually patent in the operating room.

Many of these early failures are probably secondary to technical issues that could be promptly solved if adequately diagnosed intraoperatively.

Although there are no data available in literature documenting the actual utilization rate of intraoperative coronary graft patency verification tools, a survey conducted on a limited sample of cardiac surgeons has shown some interesting figures (3). The majority (68.1%) of those interviewed stated that manual palpation of the grafts is their current method to detect graft patency after CABG; 70% of the surgeons included had never used an intraoperative graft patency verification tool in their practice. Most of the surgeons interviewed thought that graft flow meters are often difficult to use, interpretation of the findings is unclear, and revision rates are low enough that graft patency verification seems unnecessary. Although the majority declared that a flowmeter is not routinely necessary, 86% of them interestingly stated that it is important to have a system available in the operating room (3).

Being complementary to percutaneous coronary intervention, cardiac surgery has lost its supremacy in the treatment of coronary artery disease, and cardiac surgeons should concentrate on how to optimize the quality of care they are providing.

This paper reviews the methods that are currently available to intraoperative test and document the status of newly constructed coronary anastomoses.

A clear distinction is made between imaging techniques and flow assessment devices.

IMAGING TECHNIQUES

Standard Angiography

Although coronary angiography is a purely anatomical evaluation of native vessels, constructed bypass grafts, and anastomoses, for historical, economic, and logistical reasons it is considered "the gold standard" and the benchmark which every new method of investigation of graft patency should be compared with.

Angiographic images however, have little value in testing the hemodynamic function of the coronary grafts. No information is obtained concerning the flow reserve and flow response to stress. *A*ngiography is ***per se*** only a bi-dimensional representation without any direct functional information.

Intraoperative coronary angiography has logistic limitations that have prevented most surgeons from its routine adoption to test coronary graft patency.

Integration of high-end digital angiographic imaging equipment in the operating room may offer several opportunities (4). In addition to allowing a hybrid approach to coronary disease, on-table assessment of graft patency can be performed with cardiac catheter lab quality images. Intraoperative angiograms should be performed after sternal closure as chest closure may cause graft distortion.

Using fixed angiographic equipment in a hybrid operating theater, Hol and colleagues have reported an intraoperative graft failure rate of 4.2% (5). A team from the catheter lab performed the on-table angiography ensuring acquisition of high image quality, maintenance of low complication rate, and limitation of procedural time (30 extra minutes) (5).

Although many technical improvements have been introduced such as pulsed fluoroscopic systems with dynamic acquisition, the extra budgetary and personnel demands have limited broad application of conventional angiography in the operating room. With the advent of combined open surgical and catheter based procedures the availability of angiographic systems in the operating room will possibly increase in the very next future. This will eventually offer a broader spectrum of treatments in case of early detection of graft malfunction. Possibly, with the device available in the operating room, angiography should be anticipated before sternal closure and performed immediately after weaning off cardiopulmonary bypass. Prompt graft revision (either on or off-cardiopulmonary bypass) should be performed whenever necessary and possible. Alternatively, percutaneous intervention could be suggested for particularly complicated cases where further prolongation of the operative time could lead to deleterious complications.

Thermal Coronary Angiography

Thermal coronary angiography (TCA) is a promising imaging modality that could be routinely applied for quality control purposes in coronary surgery. TCA works on the principle of temperature difference between the myocardium and the coronary arteries by injecting either cold or warm cardioplegia inside the newly constructed coronary grafts (or by letting the patient's own blood flow through a pedicled mammary artery).

When the temperature of the coronary artery is higher than the myocardium's, images are white; vice versa, when the solution injected in the coronaries is colder than the myocardium, images are black.

Thermal imaging created by infrared technology provides real-time and easy-to-interpret coronary angiographies and graft flow measurements (derived by thermo dilution method).

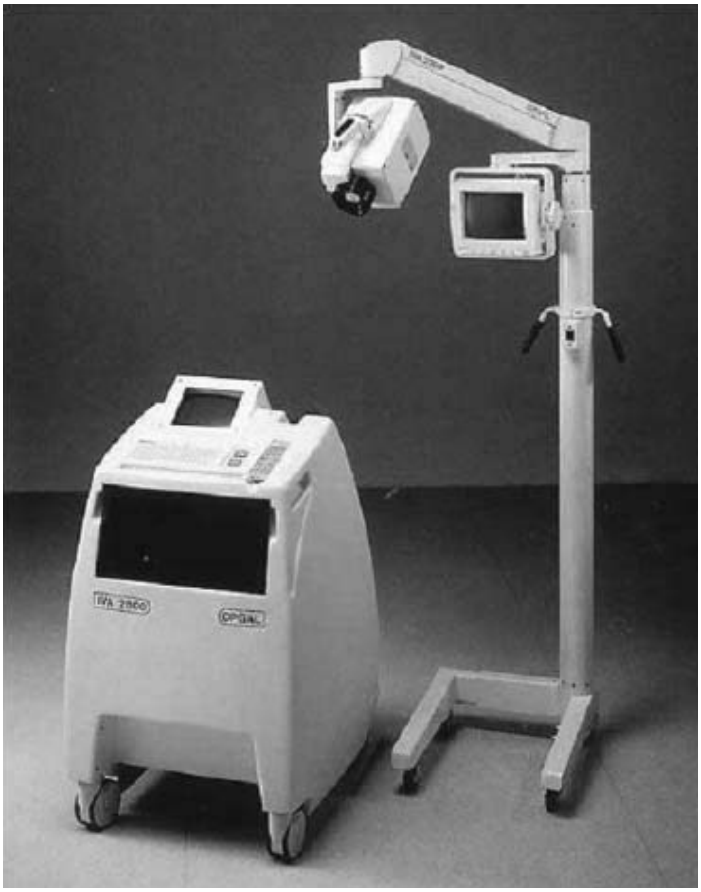

Figure 1: Thermal coronary angiography device consists of two mobile parts.
The camera can be placed over the heart while the console is placed anywhere in the operating room.

The TCA device consists of two mobile parts, namely a camera and a console. The console contains a video recorder, a video printer, a monitor, a wired remote control and an image-processing unit. The camera unit contains an infrared imager, a video camera and a monitor on a post for the surgeon's view (Fig. 1). The camera unit is easily placed over the heart from the anesthesia side and it can be easily pointed at the area of interest by the surgeon using sterile handles. The console can be placed anywhere in the operating room. The coronary arteries, either on the front or the back of the heart, can be visualized

Reports on TCA date back to the late 1980's (6). More recently, Falk and co-workers applied TCA to visualize a total of 693 vein grafts. In 9.4% of the measurements, TCA failed to produce usable images. In the remaining 628 grafts, TCA revealed intraoperative patency in 98.8%. (7).

In a more recent and larger experience, Sonmez et al. investigated 4105 bypass grafts in 1401 patients. TCA guided the decision to perform some changes in the surgical strategy in 23 patients (adding another graft, or performing coronary endarterectomy) (8).

Furthermore, Iwahashi and colleagues compared the findings of immediate postoperative standard angiography with a new generation intraoperative TCA

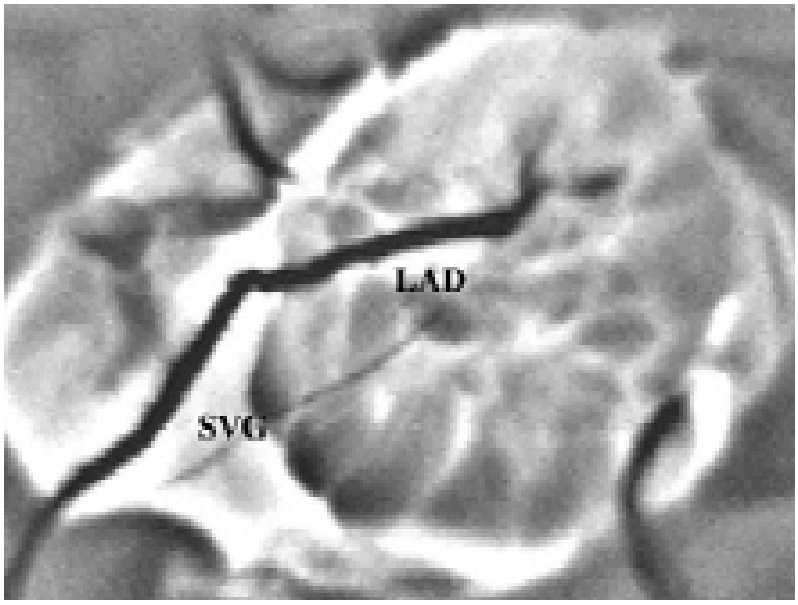

Figure 2: Saphenous vein grafting (SVG) to the left anterior descending (LAD) coronary artery as visualized by intraoperative new generation thermal coronary angiography.
This picture was published in Iwahashi H, Tashiro T, Morishige N, et al. New method of thermal coronary angiography for intraoperative patency control in off-pump and on-pump coronary artery bypass grafting.Ann Thorac Surg 84(5):1504-7, 2007

(9). The graft patency rate as assessed with TCA was 96.3%. By contrast, the postoperative patency rate for standard contrasted angiography was 95.3%. Temperature differences of only 0.1°C between the injectant and the epi-myocardium were necessary to obtain high contrast imaging (fig. 2).

As technology improves, TCA may allow for measuring blood flow and obtaining imaging information simultaneously.

Intraoperative Fluorescence Imaging

Intraoperative fluorescence imaging is a vascular imaging technique based on the fluorescent properties of indocyanine green (ICG) dye. After intravenous injection, ICG binds to plasma proteins and, when illuminated with a laser light (near infrared), it emits light with a wavelength of 830 nm. This fluorescence is captured on a charged couple device video camera. Practically, the camera is positioned 30 cm above the heart. At completion of the distal anastomosis, 1 cc of dye can be injected either in the ascending aorta or in the central venous pressure catheter (if the operation is performed off-cardiopulmonary bypass) or directly into the oxygenator in on-pump surgery.

Immediately after intravenous dye injection (or after a 5-second delay if the dye is injected into the oxygenator), the laser power is activated. Images are recorded on the computer and the appearance of fluorescent ICG dye passing inside bypass grafts and perfusing the coronary tree confirms graft patency (fig. 3). The procedure takes approximately 3 minutes per graft.

First experience with intraoperative fluorescence imaging in coronary surgery was reported by Rubens et al. in 2002 (10). To date, at least 5 major centers have

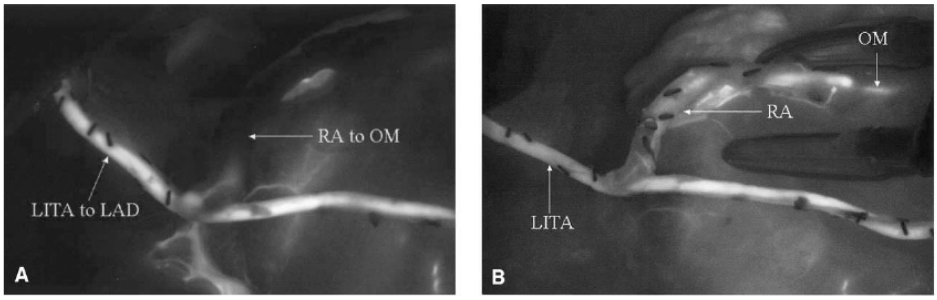

Figure 3: A, The image shows in situ left internal thoracic artery (LITA) graft to the left anterior descending (LAD) artery. A composite radial artery (RA) graft from the LITA is anastomosed to the obtuse marginal (OM) artery. As fluorescence is not seen within the RA, a technical problem is suspected and the anastomosis is revised. B, This image was taken after revision of the LITA-to-RA anastomosis. Fluorescence is now seen in the RA and OM coronary artery.
This picture was published in Balacumaraswami L, Abu-Omar Y, Anastasiadis K, Choudhary B, Pigott D, Yeong SK, Taggart DP.Does off-pump total arterial grafting increase the incidence of intraoperative graft failure?J Thorac Cardiovasc Surg. 2004 Aug;128(2):238-44.

reported their experience with this technology and over 1,400 coronary grafts have been investigated (11).

Results are very much consistent showing an overall graft revision rate of 1.7% in approximately 5% of patients.

Furthermore, Desai et al. (12) have very recently evaluated, in a prospective randomized study, sensitivity and specificity of intraoperative coronary fluorescence imaging to detect grafts that at postoperative standard angiography had resulted to be abnormal (>50% stenosis) or occluded. The sensitivity and specificity of indocyanine green angiography to detect stenosis or occlusion greater than 50% was 83.3% and 100%, respectively (12).

Although this technique has promising features, some limitations have to be outlined.

As any purely anatomical study, fluorescence imaging does not produce precise measurements of flow in patent grafts but gives a rather semi-quantitative and monoplane assessment of graft patency.

Furthermore, in conditions where the native flow creates competition, fluorescence imaging may lead to erroneous interpretation of the graft status. In this situation, snaring of the native coronary proximally to the anastomosis may clarify dubious findings.

Another limitation is that as a result of limited tissue penetration and image acquisition from directly above the anastomoses, fluorescence imaging cannot provide precise details on anastomotic quality and mainly detects fluorescing contrast distribution within the grafts and the coronary tree.

Moreover, the laser light source may detect only a portion of the graft and, whenever an abnormality (a compression, twist or bend) occurs in the graft in a point far away from the laser light source, the finding may be erroneously interpreted as a graft stenosis on a still image capture.

Finally it may be argued that, to standardize the findings of this technique and to optimize its diagnostic potential, the indocyanine dye should be injected only once the heart is completely reperfused, the effects of cardioplegia are completely resolved, and the cardiopulmonary bypass has been weaned off. Although at present there is no scientific evidence, it seems reasonable to state that grafts flow dynamics should be tested in physiologic conditions such as those achieved in a full beating heart and with pulsatile arterial pressure.

FLOWMETRY

Differently from imaging tools, flow measuring devices give us the possibilities to intraoperative detect the flow dynamics of newly constructed coronary grafts.

The functional status of a vascular anastomosis is an indicator of the different anatomical parameters of graft, anastomosis, and revascularized territory.

Although flow meters can provide us with a good representation of how a coronary graft performs and responds to the blood requirements of the revascularized myocardial territory, correct interpretation of flow measurement findings requires a good knowledge of the different variables involved in coronary rheology.

At present, ultrasound based flow meters are those most commonly used as intraoperative diagnostic tools during coronary surgery. Among the ultrasound flow meters, we should make a distinction between transit time and Doppler based flow meters.

Transit Time Flow Measurement (TTFM)

TTFM probes work on the transit-time principle. The probe is placed around the vessel, generating a uniform ultrasound field across the vessel lumen. Ultrasound pulses are transmitted from two separate piezoelectric crystals located on the same side of the probe (and so of the vessel). On the opposite side of the probe, and at the same distance from the 2 crystals, there is a reflector. Ultrasound beams cross the vessel and are reflected back to the crystals. The time spent by the ultrasound wave to go from one crystal across the vessel and then to be reflected (by the reflector on the opposite side of the probe) and reach the other crystal, is called transit time. Ultrasound waves that travel upstream the flow will travel slower than those going downstream. The difference in transit time between the pulse going upstream and the one going downstream is proportional to the volume of flow passing through the probe ($Q \approx t2 - t1$) (Fig.4).

A range of different probes are available for vessel diameters from 1.5 mm up to 35 mm. Probes are connected to a computerized systems that allows for flow curve and flow parameters recording, printing, and retrieval (Fig.5).

TTFM has been recently popularized with the resurgence of beating heart coronary surgery (13). Many authors have tried to interpret intraoperative TTFM findings and their sensitivity and specificity.

In summary, TTFM findings include: mean flow value, flow curve pattern, and pulsatility index. Mean flow depends on many factors, including mean arterial pressure and graft-coronary resistance. The value of vascular resistance is summarized in the formula $R = 8\eta L/\pi r^4$ where η refers to blood viscosity, L to

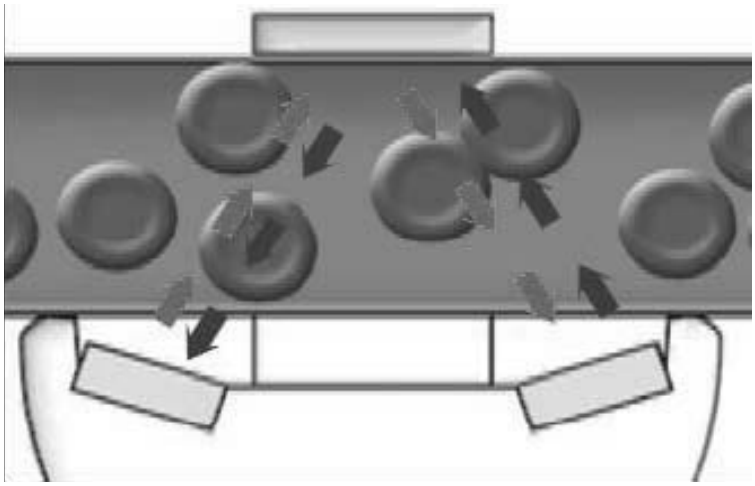

Figure 4: Transit Time Principle: Ultrasound pulses are transmitted from two separate piezoelectric crystals located on the same side of the probe. Ultrasound beams cross the vessel and are reflected back to the crystals. The time spent by the ultrasound wave to go from one crystal across the vessel and then reach the other crystal, is called transit time. The difference in transit time between the pulse going upstream and the one going downstream is proportional to the volume of flow passing through the probe ($Q \approx t2 - t1$).

Figure 5: New generation transit time flow measurement device

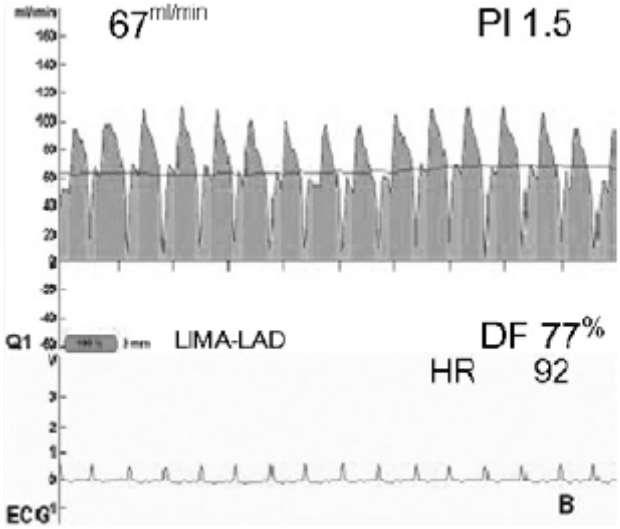

Figure 6: Transit-time Flow Curve

graft length, and r to the radius of the graft. From this mathematical approximation, it is quite clear that the quantity of flow may change even if the quality of the anastomosis remains excellent as often happens when the coronary has a very poor run-off. Therefore, mean flow should not be considered, *per se*, as a good indicator of graft patency and its value should always be interpreted taking the other parameters into consideration (13).

The flow curve (Fig.6) is the graphic representation of the hemodynamic function of the graft. Within the flow curve itself, we can distinguish percentage of systolic flow, percentage of diastolic flow, and total areas under the curve for systolic and diastolic flow. The curves should always be coupled with the ECG tracing to correctly differentiate the systolic from the diastolic flow. Diastolic filling percentage (DF %) indicates the percentage of coronary filling in diastole. By using ECG synchronization, the DF is the blood volume filling in diastole divided by the total blood volume in one heart cycle. DF is especially important because it indicates the diastolic forward flow that, during diastole, goes within the coronary while the muscle is not contracting. Some authors have classified the flow curve pattern according to dominancy: systolic dominant when peak systolic flow exceeds peak diastolic flow by 10%; diastolic dominant or balanced when peak diastolic flow exceeds peak systolic flow by 10% (14). Different patterns may be related to the target vessel: grafts on the left coronary system will have a higher diastolic flow when compared to grafts on the right coronary (where the right ventricular muscle's squeezing effect is weaker).

Another parameter that can be detected from the flow curve is the percentage of backward flow (%BF), i.e., the percentage of flow that, through the anastomosis, is directed backward within the graft (area below zero) compared with the total forward flow (area above zero) of the same cardiac cycle. As we will discuss in the next paragraphs, the lower the rate of backward flow, the better the quality of the grafting.

The pulsatility index (PI) is summarized in the formula Qmax – Qmin/ Qmean where mean flow is calculated across five cardiac cycles (Qmean), maximum flow is recorded in one cardiac cycle (Qmax), and minimum flow is recorded through one cardiac cycle (Qmin). The Qmin is a negative number if there is backward flow (14). The PI is proportional to the vascular resistance and therefore a high PI is an indicator of poor graft or anastomosis quality.

Many authors have tried to define threshold values for the different TTFM findings and to distinguish patent from occluded grafts.

A mean flow of 15 mL/min or less, a PI of 5 or higher, and a BF of 4 or higher seem to be the optimal cut-off criteria to predict early graft failure (14-16).

For what concerns flow curves, a systolic dominant flow curve pattern is a risk factor only in grafts to the left coronary artery (16).

When comparing TTFM results with intraoperative fluorescence imaging, Balacumaraswami reported that TTFM alone may prompt unnecessary graft revision (17).

In a similar comparison between intraoperative fluorescence imaging and TTFM where the reference standard was coronary angiography, Desai et al. found that the sensitivity and specificity of transit-time ultrasonic flow measurement to detect greater than 50% stenosis or occlusion was 25% and 98.4% respectively (12).

In our opinion, correct interpretation of TTFM findings should take into account other variables such as confidence in the anastomosis performed, quality of target vessel and conduit, EKG, and hemodynamic findings. In addition, multiple measurements should be taken when doubts occur including snaring of the native coronary proximally to the anastomosis, and simulation of stress testing by increasing blood pressure with inotropic agents.

Although TTFM technology can clearly show differences between hemodynamically normal and abnormal grafts, correct interpretation is limited by our inability to analyze the flow curves in their different components.

This feature should be provided within an automated analysis of flow curves.

Further information may be derived from a more complex analysis of the flow curves with fast Fourier transformation (FFT). The FFT is a mathematical transformation of the flow waveform (18) that allows for a numerical representation of flow curves. The analysis is based upon the principal that all periodic waveforms (such as flow curves) can be broken down into a series of pure sine waves or harmonics.

The pulsatile waveform of graft flow in CABG can be considered to have a fundamental frequency (i.e., the patient's heart rate) and its power is defined as F0. The power of the following harmonics in which the original waveform is broken down, through the FFT analysis, can be represented with the letter H followed by a number (H1 for the first harmonic, H2 for the second and so on).

Patent grafts seem to have an FFT ratio (F0/H1) greater than 1.0 (18) and a significantly lower power of the remaining harmonics (19).

Although FFT analysis could be, in the future, a good base for automated flow curves interpretation, at the present there are no cut off values to guide graft revision.

Doppler Technology and Epicardial Ultrasound

Although ultrasound based Doppler technology was initially proposed to monitor anastomosis quality after surgical myocardial revascularization (20), its wide application has been limited by the introduction of TTFM technology on the market.

Recently, it has been demonstrated that the performance of a newly designed dual beam Doppler flowmeter compared favorably to TTFM (21).

Doppler technology is limited to the investigation of flow parameters, and epicardial ultrasound may add anatomical information and very suggestive iconographic reproductions of the coronary anastomosis.

In the future epicardial ultrasound may become the gold standard for intraoperative coronary graft patency verification due to its dual ability to provide both morphological and functional information.

In this regard, some authors have recently started to consistently dedicate their research on epicardial coronary Doppler performed with custom-made Doppler probes in both porcine models and in the ex-vivo human beating heart (22-25).

The possible applications of a custom-made 13 MHz epicardial coronary Doppler probe were investigated demonstrating its ability to successfully visualize and assess coronary arteries and anastomoses on all sides of the heart in both animal models and ex-vivo in humans (23, 24). (Fig.7)

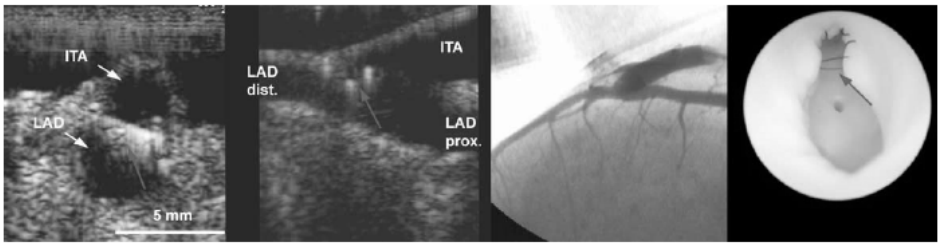

Figure 7: Suture crossover anastomosis: panels from left to right, transverse and longitudinal ultrasonographic images, angiogram, and angioscopic image taken from ITA toward outflow corner. Note in the longitudinal ultrasonographic image the suture traversing the anastomotic orifice twice (arrow). The transverse image was taken at the level of the overcrossing suture. The anastomosis appeared normal on the angiogram. Dist: Distal;
Prox: proximal. This picture was published in Budde RP, Meijer R, Dessing TC, et al. Detection of construction errors in ex vivo coronary artery anastomoses by 13-MHz epicardial ultrasonography.J Thorac Cardiovasc Surg129(5):1078-83, 2005

Moreover, micro-probe Doppler has allowed for safe graft vessel harvesting (left internal mammary artery) and for selection of optimal anastomotic target site (25).

Very recently, Hol et al. (26) have compared epicardial ultrasonography with TTFM and intraoperative angiography.

It seems clear that epicardial ultrasonography is a promising method in graft quality assessment, but needs further evaluation in comparative studies.

Outcome data of intraoperative graft patency verification

Although the intraoperative benefits of graft patency verification have been described theoretically, to our knowledge there are no prospective randomized studies where the impact of intraoperative graft verification tools has been tested in a case/control fashion. Although such trials could further validate a wider adoption of the described technologies, it is also true that for surgeons seeing the daily benefits of intraoperative graft patency verification tools is difficult to refrain from their use for research purposes in an eventual control group.

For this reason, results should be compared with historical cohorts of patients where no graft verification was adopted.

For what concerns prediction of long-term graft patency, it should be said that the process for the development of fibrous intimal hyperplasia or atherosclerosis could be simply due to patient characteristics, and it cannot be completely predicted by intraoperative measurements alone. However, in TTFM the combination of the 3 major parameters (mean flow, pulsatility index, and percentage of backward flow) results in the chance to predict a graft failure (either anatomic or functional) within the first postoperative year. Di Giammarco et al.and Tokuda et al. (15, 16) have shown that the intraoperative TTF parameters are predictive

of mid-term follow-up angiographic findings. Particularly, lower mean flow and higher pulsatility index and percentage of backward flow values are independent risks of midterm angiographic failure.

To our knowledge, there are no further studies that have evaluated the predictive value of the above mentioned intraoperative tools for long-term coronary graft status.

CONCLUSION

Every medical procedure requires a quality control method, and this is particularly true for complex procedures such as heart operations. Medical practice is urging us towards quality control for scientific, clinical, ethical, as well as legal purposes. For these reasons, all the available armamentaria should be applied to provide evidence of good clinical practice. When new technologies are introduced on the market, they do not enter into clinical practice most often for lack of economic resources, lack of a clear advantage with respect to traditional methods, and lack of evidence-based information to support their routine use. It should be our aim, as medical care providers, to evaluate and eventually document the clinical applicability of these technologies and justify, this way, the economic burden required for their acquisition.

The intraoperative tools that surgeons presently have to test coronary graft patency include imaging techniques and flow assessment devices. Most surgeons use none of these technologies possibly for lack of knowledge, lack of economic resources, lack of interpretation guidelines or simply for overconfidence in their operative skills.

Correct use of graft patency verification tools and interpretation of their intraoperative findings is not always immediate and has a learning curve. In this regard we believe that these techniques should be part of a routine examination that will help surgeons in familiarizing with the technology. A selected use only in the dubious and more complicated cases could actually lead to erroneous interpretations and further aggravate the clinical picture.

Most often imaging modalities do not clearly demonstrate the functional capacity and reserve of the anastomoses and, on the other side, flow assessment devices do not clearly address the degree of patency or stenosis of the anastomoses. As both methods have clear limitations, in the near future we should consider adopting the two different technologies simultaneously. Moreover, intraoperative trans-esophageal echocardiography (TEE) could be used as an added precious tool to early detect new wall motion abnormalities that can result from graft

malfunction. In this context, TEE may help in the interpretation of graft imaging and flow measurements and guide a correct graft revision process.

Furthermore, manufacturing companies should focus on the development of a device that could allow surgeons to simultaneously identify anatomical and functional parameters of the newly constructed coronary anastomoses.

In conclusion, the authors would like to emphasize that most of the existing intraoperative coronary graft patency verification tools have been tested using angiography as reference standard. In this regard, the biplane anatomical evaluation obtained with standard angiography is not always a good indicator of graft function. For this reason, MRI has been previously proposed to be an adequate postoperative control for the existing intraoperative graft patency verification tools (27).

We auspicate that in the future postoperative graft patency and graft flow verification (at rest and under stress) will be performed using MR angiography and MR flow measurements and this technology will be used as the most appropriate reference standard to test the different intraoperative graft quality control tools (28).

Furthermore, we auspicate that large controlled outcome studies will be undertaken to determine the long term outcome efficacy of adopting one or more of these technologies into routine practice.

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Chapter 13

Is Hybrid Coronary Revascularization Favored by Cardiologists or Cardiac Surgeons?

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ABSTRACT

We investigated the present use of integrated coronary revascularization (ICR) by interviewing a sample of United States invasive cardiologists and cardiac surgeons. Both groups still favor left internal mammary artery (LIMA) grafting to revascularize the left anterior descending (LAD) coronary artery. There remains a lack of exposure to and acceptance of ICR, especially for surgeons. We report the findings of this national survey of 180 cardiologists and 160 surgeons, as they may serve as an indicator of the current opinions about ICR and its future applicability as a standard method of coronary artery revascularization. We discuss the limited popularity of minimally invasive hybrid procedures and the importance of further exposing cardiologists and surgeons to ICR.

INTRODUCTION

Since its introduction in the early 1990s, minimally invasive direct coronary artery bypass grafting (MIDCAB) via a left anterior small thoracotomy (LAST) without cardiopulmonary bypass (CPB) has become increasingly accepted as a procedure [1]. The effectiveness of this operation in the treatment of coronary artery disease (CAD) limited to the left anterior descending (LAD) coronary artery has been proven at midterm clinical and angiographic followup [2,3]. Furthermore, MIDCAB, in combination with percutaneous transluminal coronary angioplasty (PTCA) or coronary artery stenting, has been advocated recently to achieve complete myocardial revascularization in patients with multivessel CAD [4, 5]. Although the conceptual framework of the "hybrid" approach to CAD is of interest, its large scale application remains limited. Therefore, we have investigated the present use of integrated coronary revascularization (ICR) by interviewing a sample of United States invasive cardiologists and cardiac surgeons. We report the findings of this national survey, as they may serve as an indicator of the current opinions about ICR and its future applicability as a standard method of coronary artery revascularization.

METHODS

Semistructured surveys were mailed to 250 interventional cardiologists and 250 cardiac surgeons working in academic and community hospitals in the United States.

The aim of the questionnaires was to determine attitudes and perceived benefits of hybrid procedures. Surgeons received one set of questions, and cardiologists another. Surgeons were asked about their experience with MIDCAB procedure, their strategy and conduits of choice to revascularize LAD or non-LAD coronary targets, and their opinion about percutaneous interventions (PCI). Cardiologists were asked their opinion regarding MIDACB procedure, their favored revascularization conduit for non-LAD targets, their favored therapeutic option for non-LAD targets (saphenous vein graft [SVG] versus PTCA versus stent), and their actual experience with ICR.

RESULTS

One hundred sixty surgeons (64%) completed the survey. For 152 (95%) of them, left internal mammary artery (LIMA) graft is the graft of choice to revascularize the LAD. Of the 160 respondents, 128 surgeons (80%) perform <5 MIDCAB/year. SV to non-LAD targets is the conduit of choice for 120 surgeons (75%). Opinions about PCI and ICR are more homogeneous. The majority of the surgeons (140, 87.5%) object to PCI, reporting that "stents have poor patency rates." Only 16 surgeons (10%) believe that longterm patency of non-LAD targets treated with PCI is better than patency of SV grafts to non-LAD targets. Only 16 surgeons (10%) are in favor of ICR. Cardiologists' participation was higher, with 180 (72%) of them returning the completed survey. Surprisingly, only 2 cardiologists have referred patients for MIDCAB or robotically assisted minimal access procedures with ICR. The large majority of the respondents (178, 99%) chose LIMA as the graft of choice to revascularize the LAD. One hundred forty cardiologists (78%) believe that non-LAD targets should be revascularized with arterial conduits during coronary artery bypass grafting (CABG). Half of the respondents (90, 50%) believe in ICR and 122 (68%) believe that current stents have better patency rates than SV grafts to non-LAD targets. Although only

Table 1. The Hybrid Revascularization Survey: Opinions of 160 Interviewed Surgeons

	No. Surgeons
LIMA graft of choice to LAD	152 (95%)
Perform <5MIDCAB/year	128 (80%)
SV graft of choice to non-LAD targets	120 (75%)
Stents have poor patency rates	140 (87.5%)
Patency of stents to non-LAD targets is better than SV's patency	16 (10%)
In favor of ICR	16 (10%)

Table 2. The Hybrid Revascularization Survey: Opinions of 180 Interviewed Cardiologists

	No. Cardiologists
LIMA graft of choice to LAD	178 (99%)
Arterial conduits for non-LAD targets	140 (78%)
In favor of ICR	90 (50%)
Patency of stents to non-LAD targets is better than SV's patency	122 (68%)
Have already performed ICR	2 (1%)

2% of the cardiologists have already used ICR, 90 (50%) of them are looking forward to ICR procedures using coated stents.

Results of the surgeons' and cardiologists' surveys are summarized in Tables 1 and 2.

DISCUSSION

The recent introduction and popularization of off-pump coronary surgery has galvanized interest in developing new strategies to achieve complete myocardial revascularization using alternative and less invasive surgical approaches. The concept of ICR, as first introduced by Angelini et al [4], seems to fully satisfy the issues of completeness of revascularization and minimal invasiveness. In this regard, PTCA and coronary stenting are effective treatments for multivessel CAD. In spite of a nonnegligible rate of restenosis observed especially in LAD interventions, PCI has become standard treatment for multivessel CAD, thanks to its relative effectiveness in decreasing symptoms, maintaining low morbidity rates, and maintaining costs when compared to traditional CABG [6]. No survival benefits of CABG over PCI exist at midterm follow-up [6].

The major benefit of surgical intervention lies in the longterm patency of the LIMA to the LAD coronary artery. Although the MIDCAB operation theoretically provides long-lasting revascularization of the LAD with the LIMA, its application cannot be extended to the majority of surgical candidates with multivessel CAD. MIDCAB and PTCA (or stenting) have major limitations if used alone but may acquire higher therapeutic potential when adopted simultaneously. Our survey finds that surgeons present the major obstacles to wider application and acceptance of ICR procedures. Two particular surgical issues are highlighted by our survey results. First, only a small number of surgeons are exposed to MIDCAB procedures and may not acquire enough surgical expertise to easily perform this operation. Second, the majority of surgeons (90%) remain skeptical toward PTCA or stenting patency rates and believe vein grafts are still the best treatment for non-LAD revascularization. Although results of pioneering groups using MIDCAB are encouraging [2, 3], this operation has a steep learning curve. In MIDCAB surgery, suturing may be hampered by limited space of the surgical field, and mobilization of the LIMA graft may be technically demanding. These difficulties may be aggravated in the presence of intramyocardial, tortuous, calcified, and diffusely atherosclerotic LADs. Good candidates for MIDCAB may be difficult to find, and in most instances, patients with good LAD targets are treated with PCI. It has been demonstrated that for

limited type-C lesions of the LAD, 1-year survival and major adverse clinical events are similar with MIDCAB and PTCA [7]. Those patients refused for invasive cardiac treatment may not be good candidates for MIDCAB because of an inadequacy of coronary targets. As shown in our survey, 80% of the interviewed surgeons perform fewer than 5 MIDCABs per year. This data reflects the lack of adequate referral for MIDCAB. How Can Surgeons Gain Broader Exposure to MIDCAB? How Can They Master This Challenging Technique? ICR may be the answer. The popularity of hybrid procedures is limited most strongly by the recent success of off-pump coronary artery bypass (OPCAB). Patients with multivessel CAD who are presently being treated with OPCAB could be treated, in the majority of cases, using a different approach—a hybrid procedure. By applying this alternative approach, surgeons would have the opportunity to master MIDCAB and broaden its application. But for those who do not believe in the long-term patency rate of PCI, OPCAB remains a strong competitor. How Can We Convince 90% of the Represented Surgeons That PCI May Lead to acceptable Long-term Patency Rates? The results of randomized trials have clearly shown the superiority of CABG versus PTCA in reducing recurrency of angina and reintervention rates [6, 8]. These comparisons were done before the introduction of stents, which have improved long-term results compared to routine PTCA [9]. The ERAC II randomized trial has shown that multivessel stenting has a significantly lower incidence of major procedural adverse cardiac events when compared with conventional CABG (1.8% in PTCA patients versus 11.4% in CABG patients). However, the 6-month incidence of target lesion revascularization was 13.7% in the stent group and 4.8% in the CABG group [10]. But the recent introduction of coated stents and vascular radiation therapy will further improve the long-term outcome of multivessel CAD patients undergoing percutaneous revascularization. In this regard, a 100% 1-year patency rate was reported using sirolimus-eluting stents in a small noncontrolled registry [11]. These results are also confirmed in a larger double-blinded randomized trial in Europe and Latin America (RAVEL), which found at 6 months that restenosis was reduced from 26% in patients receiving placebo to 0% in those receiving sirolimus-eluting stents [12]. Various medicated stents are currently in clinical trials, particularly new "intelligent" polymeric-coated stents that may release drug combinations at different rates and on different timelines. If the present data continue to be supported by ongoing placebo-controlled randomized trials, cardiologists will soon be able to offer to all patients a minimally invasive and durable revascularization technique. Some of the classic contraindications to PCI, such as multivessel CAD, left main stenosis, small diameter coronary arteries, and long atherosclerotic lesions will be easily approached and treated

with drug-eluting stents with minimal restenosis rates. The threshold for surgical intervention will be lowered further, and surgeons will find themselves able to treat the sickest patients who have been refused for PCI.

CONCLUSION

Present changes in the referral pattern for CABG are forcing us to reshape our therapeutic strategies. Although the long-term benefits of complete surgical myocardial revascularization are well known, an increasing number of patients of advanced age and multiple comorbidities are simply not good candidates for this operation. MIDCAB combined with catheter-based therapies could be used in the future to reduce therapeutic invasiveness, achieving at the same time a durable myocardial revascularization. Although ICR presently provides a less invasive approach for select patients with multivessel CAD, its future applicability could be extended to a majority of surgical candidates. The mid to long-term results of ICR should be evaluated with the new stent technology available (coated stents), and until then, MIDCAB procedures must be standardized for wider applicability. Innovations in the surgical field should be evaluated in order to facilitate MIDCAB and ICR procedures. In this regard, new technologies such as robotic endoscopic surgery and mechanical anastomotic devices could be used in the future to further ease the performance and reduce surgical trauma of MIDCAB. The amounts of chest wall retraction, rib and costal cartilage sacrifice, and incisional pain remain important issues in MIDCAB surgery. Recent advancements in robotic endoscopic surgery allow left internal thoracic artery (LITA) mobilization via 3-mm and 5-mm port access with minimal chest wall trauma. The final goal is the adoption of totally endoscopic robotic closed-chest coronary bypass that will be the least invasive surgical procedure to revascularize the LAD with the LITA [13].

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Chapter 14

Ischemic mitral valve regurgitation: the new challenge for magnetic resonance imaging

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SUMMARY

Ischemic mitral valve regurgitation (IMVR) refers to mitral regurgitation in patients with ischemic heart disease (IHD) in the presence of a structurally normal mitral valve.

IMVR contributes significantly to morbidity and mortality in patients with IHD.

The thresholds for clinical management, surgical intervention, and the choice of surgical procedure continue to evolve and independent determinants for surgical success in the pre and post-operative evaluation of IMVR are still controversial.

Although echocardiography has been valued as the gold standard in the evaluation of IMVR, new technologies such as magnetic resonance imaging (MRI) may reveal as applicable to the investigation of this complex pathology.

MRI may allow for detection of parameters that could help clinicians and surgeons to better assess IMVR and eventually guide appropriate treatment whenever necessary.

The present manuscript discusses the main parameters that should be routinely investigated while adopting MRI technology to assess patients with IMVR.

The review is the result of a multidisciplinary approach to this complex etiopathogenic entity and involves expertise spanning from radiology, cardiology, and cardiac surgery.

INTRODUCTION

Ischemic mitral valve regurgitation (IMVR) is a condition with a complex and controversial diagnostic-therapeutic pattern and, for this reason, is often associated with uncertain evolution and prognosis. The clinical definition of IMVR implies a situation where MV insufficiency occurs after myocardial infarction (MI) in the presence of structurally normal MV leaflets and subvalvular apparatus (1, 2). This state develops in up to 15% of patients after AMI and is associated with excess cardiac morbidity and mortality. Although attention has been very recently focused on the importance of regional (posterior) mitro-annular enlargement and posterior MV leaflet tethering, the etiology and pathogenesis of IMVR are more convoluted and involve interactions of several anatomic structures and their functional status. As the morphology and function of these structures is often difficult to determine simultaneously, choice of the therapeutic approach to IMVR remains controversial.

In this regard, the ability to predict whether a given patient's IMVR will improve after surgical correction is critical in guiding treatment and determining prognosis.

Because the surgical approach to IMVR may simultaneously address the diseased coronary targets (with bypass surgery) and the faulty MV (with MV repair), the preoperative diagnostic methodology adopted should routinely evaluate aspects concerning the ventricular muscle, its perfusion and contractility, as well as the MV morphology and function.

Ideally, a comprehensive imaging modality should address all information needed in a single imaging session. Although echocardiography is, at the present, the main armamentarium routinely accepted to guide therapeutic decision making in IMVR, its status could be challenged by more updated diagnostic tools such as cardiac magnetic resonance imaging (MRI).

Preoperative cardiac MRI Evaluation in IMVR

Although the standard approach to IMVR includes an undersized MV annuloplasty, recurrent IMVR has been reported in more than 20% of patients undergoing this procedure (2). These findings could suggest that a good proportion of patients with IMVR should be treated differently rather than with simple MV annuloplasty. In reality, only a limited number of preoperative variables have been proposed as focal to guide the decision making process for the surgical treatment of IMVR. Furthermore, the possible applications of MRI in defining the geometric and functional variables associated with IMVR and eventually in guiding surgical decision making, are poorly represented in the existing literature

Table 1: Relevant papers evaluating ischemic mitral valve regurgitation (IMVR) with MRI and Echocardiography.

	MRI	ECHO
Yu HY et al. J Thorac Cardiovasc Surg 2004;128:543-51	correlation between LVESV, PMs distance to MV annulus, MAD, and functional IMVR correlation between LVEF and LVESV	
Kaji S et al. *Circulation 2005;112; 409-414*	correlation between LVESV, PMs distance to MV annulus, MAD, and functional IMVR	
Kon MW et al. J Heart Valve Dis 2004; 13:600–7.	volumetric assessment of MVR with cardiac MRI	
Gelfand EV et al. J Cardiovasc Magn Reson. 2006;8(3):503-7.	volumetric assessment of MVR with cardiac MRI and correlation with qualitative echocardiography	
Schvartzman PRet al. Am Heart J. 2003 Sep;146(3):535-41.	grading of myocardial segmental scarring	
Srichai MB, Ann Thorac Surg. 2005 Jul; 80(1):170-8.	correlation between regional myocardial perfusion and regional scarring in patients with IMVR	
Grigioni F et al. Circulation. 2001 Apr3; 103(13):1759-64		Prognostic value of ERO
Jorapur V et al. Echocardiography. 2005 Jul;22(6):465-72		correlation between AMLL, PM distances, and IMVR
Calafiore AM et al. Ann Thorac Surg 2001;71:1146 –1153		correlation between CD and recurrent MVR after repair
Kongsaerepong V et al. Am J Cardiol. 2006 Aug 15;98(4):504-8		correlation between MAD, tenting area, and recurrent MVR after repair

LVESV: left ventricular end systolic volume; PMs: papillary muscles; MV: mitral valve; MAD: mitral annular diameter; ERO: effective regurgitant orifice; AMLL: anterior mitral leaflet length; CD: coaptation depth.

(Table 1). In spite of this, we believe that cardiac MRI, if available within the hospital premises, should be routinely performed in any case suspect for IMVR unless contraindicated for other reasons.

In our Institute, typical cardiac MRI sequences include:

a) Basal acquisitions:

- Steady state free-precession sequences (Fiesta sequences), on short axis and long axis view, 2-3 and 4 chambers views. These are useful to study heart kinesis and function, to visualize the degree of MVR (qualitative measurement), and to obtain data on the geometric parameters of the left atrio-ventricular plane (such as tenting area, interpapillary distance, coaptation depth, length of the anterior mitral valve leaflet, and annular dimensions).
- Black blood sequences (Double and Triple IR), used to define the morphology of the ventricular walls.

- Phase contrast sequences, obtained over the aortic valve plane and on the left atrio-ventricular plane, used to quantify, as an absolute value, the entity of MVR (quantitative measurement).

b) Acquisitions after administration of a paramagnetic contrast media:

- Resting perfusion sequences (Fast GRE; short axis two chambers views), to detect ischemic areas.
- Delayed enhancement sequences (GRE IR), 12 minutes after contrast agent administration, (short axis two chambers views, radial and 3D acquisitions), to assess the myocardial vitality and the presence of necrotic areas.

For specific surgical selection and planning in patients with IMVR, few key variables should be routinely recorded by cardiac MRI and categorized as: left ventricle and mitral valve morphology variables, left ventricle and mitral valve functional variables, and myocardial vitality/perfusion- scar assessment variables.

Left Ventricle and Mitral Valve Morphology

The importance of left ventricular end systolic volumes and diameters (LVESV and LVESD) in predicting outcome and mortality after AMI and CABG has been emphasized in previous studies (3, 4).

Cardiac MRI studies have shown a strong relationship between LVESV, ventricular geometric variables (interpapillary muscles distance and anterior mitral annulus to medial and lateral papillary muscles distance), and functional IMVR (5, 6). All these variables may play a crucial role in the development of IMVR. In patients with coronary artery disease (CAD), an increase in LVESV is associated with inadequate approximation of the MV leaflets during systole as a consequence of increased interpapillary muscles distance, and mainly an increase in the distance between the anterior MV annulus and the root of the medial and lateral papillary muscles (5). Moreover, left ventricular ejection fraction (LVEF) is inversely correlated to LVESV (5).

Although Echocardiography allows for measurements of LVESV and LVESD, calculations are derived on the assumption that the LV is an ellipsoid. This is not always the case, especially whenever the LV acquires a more spherical shape as consequence of AMI and muscular overstretching.

Recent advances of the balanced steady state free precession sequence for cine MRI have allowed for reproducible measurements of LVESV and LVESD. To avoid the assumption of the LV elliptical shape, measures should be derived from a series of contiguous short axis slices (fig.1) of gated cine-MRI.

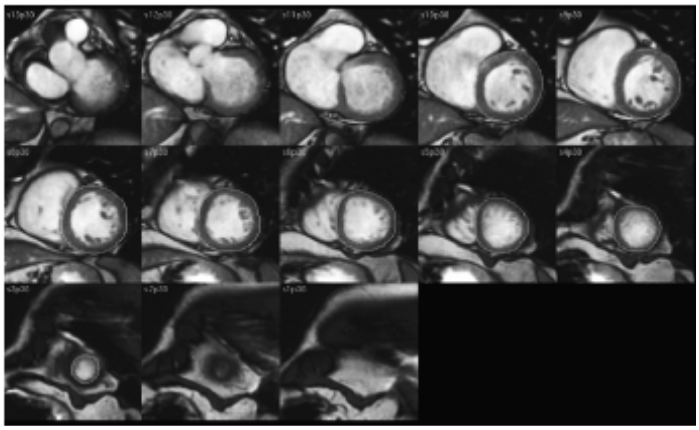

Fig. 1 Short axis image, Cine-MRI (Fiesta sequence), 2-chamber view from base to apex to measure systolic and diastolic volumes and diameters

Left atrial volumes and diameters (LAV/D) seem to play a less important role in the pathogenesis of IMVR and their changes are rather a consequence of IMVR than a primary cause of it and, for this reason, are omitted from the present analysis.

In a recent echocardiographic analysis, mitral annular diameter (MAD) was defined by multiple stepwise logistic regression as the strongest independent predictor for failure after mitral annuloplasty for IMVR (7). A value of pre-operative MAD more than 3.7 cm could predict a 50% failure of simple MV annuloplasty.

The MAD, or septo-lateral annular diameter, is defined as the distance between the hinge points of the anterior and posterior mitral leaflets. In MRI analysis, significantly higher MAD has been shown in patients with IMVR (5, 6). MRI measurements can be derived in 4 chambers views and should be performed during systole and diastole to document the sphincter function of the MV annulus. The slice obtained should represent a true diameter of the mitral annulus and should not be taken off center to prevent underestimation of the real value (fig.2).

It seems that the correlation between LVESV and MAD is only moderate and a clear threshold to distinguish patients with IMVR on the basis of MAD by MRI measurements has not been defined at the present.

Anterior mitral leaflet length (AMLL) is another purely anatomical MV variable that can be of practical use to evaluate patients with IMVR. AMLL is one of the very few MV anatomical parameters that remain unchanged in patients with IMVR compared to healthy controls and patients with CAD without IMVR (8). This finding emphasizes the importance of using AMLL as an indexing factor

to better define the impact of other variables such as MAD and interpapillary muscle distance (IPD) in patients with IMVR.

AMLL can be easily detected with cardiac MRI using long axis 4-chamber view (fig.3).

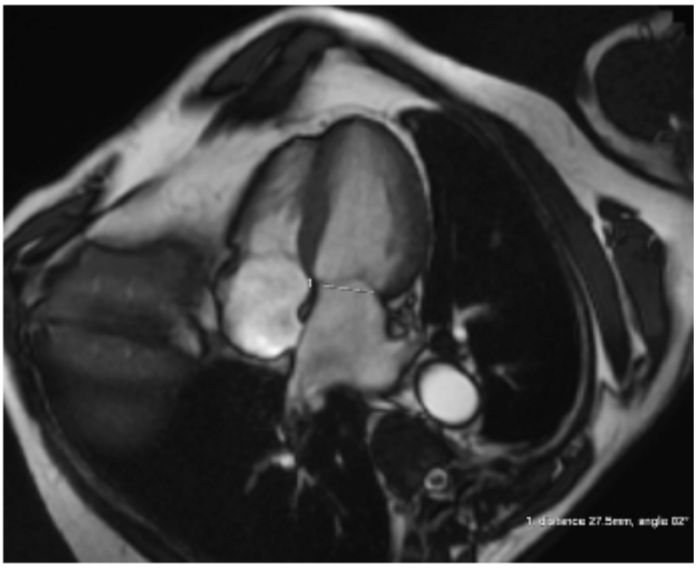

Fig. 2 Long axis image, Cine-MRI (Fiesta sequence), 4-chamber view. The white line defines the measure of the septo-lateral annular diameter

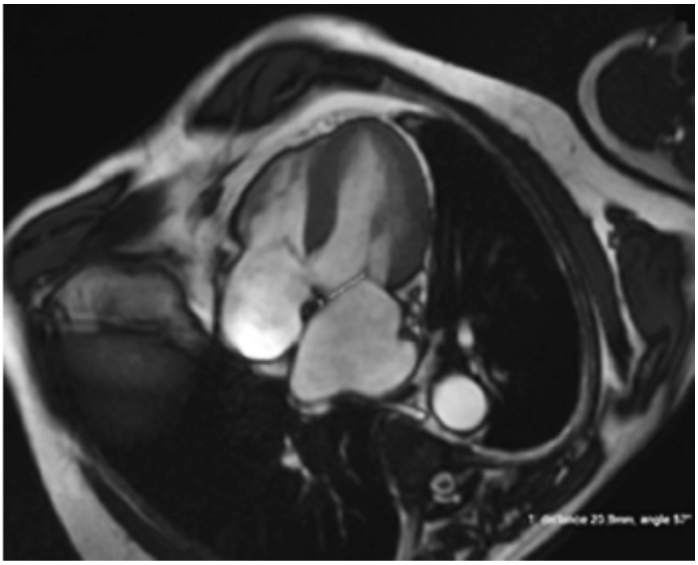

Fig. 3 Long axis image, Cine-MRI (Fiesta sequence), 4-chamber view. The white line defines the measure of the anterior mitral valve leaflet.

Left Ventricle and Mitral Valve Function

Although LVESV seems to have the strongest prognostic factor in patients with CAD, clinicians and surgeons often refer to left ventricular ejection fraction (LVEF) as a valuable parameter in patients with IMVR.

As previously said, LVEF was found to be inversely correlated to LVESV and a significantly lower LVEF has been shown when comparing MRI findings of patients with IMVR to those of patients with isolated CAD (5, 6). LVEF may be easily derived by MRI values of LVES and LVED volumes.

MRI determination of LVEF should be coupled with a wall motion scoring index as often is done during echocardiography testing. MRI readings could be summarized by a quantitative measurement as suggested by the guidelines of the American Society of Echocardiography to define the LV wall motion scoring index through an accurate and distinct analysis of the contractility of the different LV segments at cine-MRI (9). This concept acquires an even more stringent importance whenever the analysis is extended to patients with IMVR where the presence of segmental wall motion abnormality may generate asymmetry in the opening and closing of the MV leaflets with consequent MV regurgitation. Following the American Society of Echocardiography recommendations, the LV is divided in 16 segments, as follows:

- Short axisis **A** apical 4 segments: septal, anterior, lateral, inferior; **B** middle ventricular 6 segments: anetrior septal, posterior septal, inferior, lateral, anterior, posterior; **C** basal ventricular 6 segments: septal anterior, septal posterior, inferior, lateral, anterior, posterior.

Values are assigned to every segment on the basis of the segmental kinesis: score 1 for normokinesis, 2 for hypokinesis, 3 akinesis, 4 diastolic dyskenesis, 5 systolic dyskenesis.

Scores are added up to obtain a global score that is divided by the number of investigated segments to generate a wall motion score index (9).

Following these guidelines, a normally contracting ventricle with 16 well functioning segments should have a wall motion score indexing of 1.

MV function in IMVR is mainly summarized by the degree of volume regurgitation. Doppler echocardiography readily identifies MR and allows for the imaging basis for clinical follow-up. Quantitative assessment of regurgitation severity should be the gold standard to eventually define guidelines for therapeutic management of IMVR. Effective regurgitant orifice area (ERO) has been recently described as a useful prognostic parameter in chronic MR (10). This parameter is derived using the proximal isovelocity surface area (PISA) method. This modality can be difficult to apply in particular cases whenever the regurgi-

tation jet is eccentric or the image quality does not allow for flow convergence to be well seen (11, 12).

In this context, volumetric assessment of MVR with cardiac MRI has been shown to be accurate, reproducible (13), and easy to correlate with qualitative echocardiography (14). Mitral regurgitant volume can be calculated with MRI as the difference between the left ventricular stroke volume and the forward aortic flow volume.

Other functional indexes in IMVR are the coaptation depth and the MV tenting area. The mechanism of IMVR is possibly related to LV remodeling and PMs displacement producing apical tethering or tenting of the leaflets (restricted systolic leaflet motion). When global LV dilation occurs, both PMs are displaced posteriorly, laterally, and apically. As a consequence, the tethering forces on both leaflets increase, reducing leaflet mobility. Tethering height is defined as the shortest distance during systole from the coaptation point of the anterior and posterior mitral leaflets to the mitral annular plane. The tethering area is defined as the smallest area during systole bounded by the leaflets and the mitral annular plane.

In 1 of the few studies examining preoperative echocardiographic predictors of annuloplasty failure, Calafiore and colleagues found that a MV coaptation depth of more than 11 mm was associated with a return of substantial MR after annuloplasty (15). Other authors have emphasized the additional importance of the mitral annular diameter and tethering area demonstrating that when the mitral annular dimension is more than 3.7 cm in the intraoperative 4-chamber TEE view with a tenting area of more than 1.6 cm2 in the long-axis view, mitral annuloplasty will fail in 50% of patients during follow-up (7).

Although these findings are still too premature to be adopted as general rule, both coaptation depth (tethering height) and tenting area are easily measurable with cardiac MRI in systole in the 2 and 4 chambers views (fig. 4a-b-c).

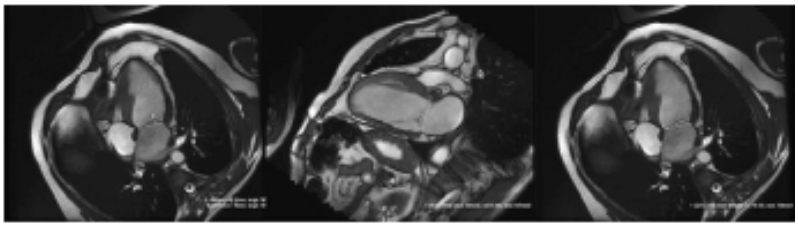

Fig. 4-a-b-c: a) Long axis image, Cine-MRI (Fiesta sequence), 4-chamber view. Tethering height (number 2) is defined as the shortest distance during systole from the coaptation point of the anterior and posterior mitral leaflets to the mitral annular plane (number 1). **b)** The tethering area (white triangle) is defined as the smallest area during systole bounded by the leaflets and the mitral annular plane. **c)** Long axis image, 2-chamber view. The tethering area (white triangle) is defined as the smallest area during systole bounded by the leaflets and the mitral annular plane.

Altered PM geometry (in particular increased distance between the anterolateral and posteromedial PMs) seems to be part of the pathogenesis of IMVR (5, 8). Using two-dimensional echocardiography, Jorapur et al. (8) showed a difference in PM separation between normal control patients, patients with dilated LV but without functional MR, and patients with dilated LV with functional MR. In 50 normal controls, the PM separation was 1.49 ± 0.24 cm in diastole. In 15 patients with dilated LV but without MR, this separation was 2.02 ± 0.36 cm , while in 15 patients with dilated LV and MR PM separation was 2.91 ± 0.30 cm ($p<0.0001$). PM separation was also associated with severity of MR (8).

In a smaller study including 9 healthy volunteers (control group), 12 patients with chronic CAD without functional mitral regurgitation (CAD group), and 8 patients with chronic CAD with functional mitral regurgitation (CAD+FMR group), Yu et al performed cine magnetic resonance imaging to acquire multiple short-axis cine images from base to apex and to demonstrate that PMs distance of greater than 3.2 cm and distance from the anterior mitral annulus to the medial PM root of greater than 6.4 cm readily distinguished the CAD+FMR group from the other groups (5).

As already emphasized, multiple co-related factors eventually leading to IMVR obviously exist including PM distance, MV MAD, regional wall motion, and LV size.

Although the weighted contribution of each of these variables is still unknown, cardiac MRI could allow for each of these variable to be exactly and simultaneously quantified achieving better guidelines for future treatment.

In this regard, PMs distance is an easy measurement to perform in systole and diastole from the cine MRI images through a short axis slice at the mid-ventricular level (Fig.5a-b). If a basal slice is used, careful inspection is required since there may be multiple PM chordal insertion heads and whenever a more apical slice is used, care should be taken to check for the presence of trabeculations involving the anchoring points of the PMs. In this situation, the dominant

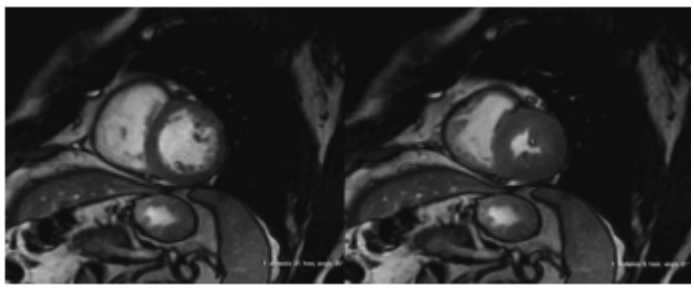

Fig. 5-a) Short axis, Cine-MRI (Fiesta sequence), 2-chamber view. Papillary muscle distance in diastole. **b)** Papillary muscle distance in systole.

body of the PM should be used to find the center of the PM. To avoid these pitfalls, measurements are more reliable when done at the midventricular level (16).

Myocardial Scar Assessment

MRI has advantages over the more commonly used methods of viability assessment and viability by MRI includes detection of both regional function and morphology.

The main clinical tool for MRI viability assessment is gadolinium contrast agent. Nonviable scar tends to have a significantly higher concentration of contrast 10–20 min following infusion than the concentration in normal, viable myocardium (delayed enhancement). With the inversion-recovery imaging techniques, easy visualization of nonviable, scarred regions, is possible as these territories will appear very bright and normal myocardium will be dark on the myocardium nulled inversion-recovery images (fig.6).

The extent of myocardial segmental scarring (MRI hyperenhancement) can be graded using a previously described method (17). After dividing the ventricle in 16 segments as above suggested to investigate the LV regional contractility (9), the amount of hyper-enhancement from scar (infracted myocardium) to nulled signal (viable myocardium) can be semi-quantitatively evaluated in each segment using a 6-grade system as follows: 0= 0%, 1=1% to 24%, 2= 25% to 49%,

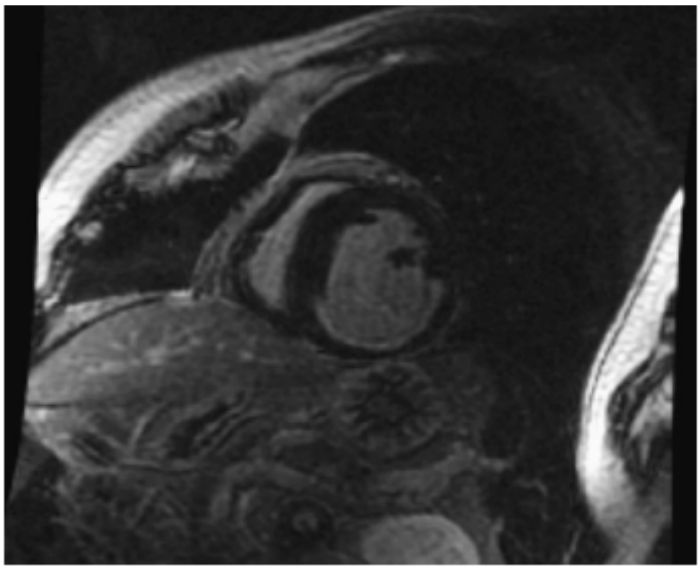

Fig. 6 Short axis, 2-chamber view. Delayed enhancement sequence shows large area of sub-endocardial necrosis (fibrosis) of the mid-ventricular inferior wall.

3= 50% to 74%, 4= 75% to 99%, and 5= 100% segmental scar (17). Total scarring can be calculated as the average of the scar grade over the entire LV.

The importance of regional myocardial perfusion and regional scarring in patients with IMVR has been poorly investigated. Srichai et al. evaluated MRI left ventricular geometric, functional, and scar measurements in addition to mitral valve geometric variables in a series of 60 patients with varying degrees of MR (none, mild, moderate, and severe) determined by echocardiography (18). At multivariate analysis, mitral systolic tenting area ($p < 0.0001$) in a statistical model with scarring of the anterior-lateral region ($p < 0.05$) proved to be the most powerful independent predictor of MR severity (18). These results differ somewhat from other studies that have shown higher incidences of IMVR in patients with inferior compared with anterior myocardial infarction (19, 20). However, diagnosis of regional scarring in these studies was not performed with MRI and was based on regional contractility dysfunction which may represent only myocardial hibernation as opposed to transmural scarring. Interestingly in Srichai et al. MRI evaluation, impairment of ventricular contractile function in the inferior-posterior, but not in the anterior-lateral region, was associated, at univariate analyses, with increasing severity of MR (18). However, as said, degree of regional scarring (particularly antero-lateral) as opposed to regional function proved a stronger determinant of IMVR severity in multivariate analysis.

Quantitative MRI with delayed-enhancement imaging for assessment of LV myocardial scarring could add to our understanding of the diverse mechanisms involved in the development of IMVR and eventually lead a more appropriate and tailored approach to its treatment. In this context, there is possibly a plethora of patients with more complex IMVR patterns including primary involvement of the anterolateral as opposed to the posteromedial PM and adjacent ventricular segments, and/or associated severe left ventricular geometrical distortion requiring a more complicated surgical approach rather than a simple annuloplasty to address the mitral regurgitation.

CONCLUSION

Although cardiac MRI offers certain intrinsic advantages over other diagnostic tools in the study of MV function, there is at the present lack of a standardized scheme for data collection and analysis that could eventually direct the decision making process for cardiac surgeons and cardiologists and lead future understanding for accurate diagnosis, operative planning, and follow-up of IMVR.

The present manuscript summarizes those that are, in our opinion, the main parameters that should be routinely investigated while adopting MRI technology to assess patients with IMVR. Our considerations are the result of a multidisciplinary approach to this complex ethiopathogenetic entity and involve expertise spanning from radiology, cardiology, and cardiac surgery all aiming at defining those that are the crucial parameters to guide adequate understanding in the complexity of IMVR pathogenesis and, as a result, to allow for correct therapeutic planning.

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Chapter 15

Ischemic mitral valve regurgitation in patients with depressed ventricular function: cardiac geometrical and myocardial perfusion evaluation with magnetic resonance imaging

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ABSTRACT

Objective

To investigate geometrical and functional changes involving the left ventricle (LV) and mitral valve (MV) apparatus in patients with depressed LV ejection fraction (LVEF) and ischemic MV regurgitation (IMVR).

Methods

A series of patients with 3 vessels CAD and depressed LVEF underwent cardiac MRI to investigate MV/LV geometry and function, and myocardial perfusion/vitality. Geometrical data were indexed by anterior MV leaflet length. Two groups were identified: CAD without IMVR (Group CAD), and with IMVR (Group IMV).

Results

Eleven patients were enrolled in the CAD group and 13 in the IMV group.

IMVR volume was significantly higher in the IMV group (24.0± 12.0 vs. 4.5±5.2; p<0.0001). LVEF% was comparable (IMV 34.6±13.0 vs. CAD 31.5±13.0; p=ns). Indexed MV/LV geometrical variables were comparable in the two groups. Perfusion/vitality study showed inferior myocardial necrosis occurred more often in the IMV group (p=0.01). At Pearson test, MV regurgitation occurrence correlated with inferior myocardial necrosis (r=0.5; p=0.006), non-indexed systolic/diastolic annular inter-commissural diameters (r=0.4; p=0.04) and MV annular areas (r=0.4; p=0.04). Papillary muscles distance (PMD) and LV volumes inversely correlated with LVEF% (r=-0.6; p<0.05 and r=-0.8; p<0.001). At multivariable analysis, no independent determinants for IMVR were identified and LV volumes were the sole determinants for LVEF% (p<0.05).

Conclusion

In patients with depressed LVEF%, IMV cannot be explained by LV geometrical modifications alone. Although PMD, LV volumes, and LVEF% are correlated, they have no direct impact in the development of IMVR. In contrast, inferior myocardial necrosis and increased inter-commissural MV diameters may lead to deformity of MV complex and subsequent IMV.

INTRODUCTION

Ischemic mitral valve regurgitation (IMVR) has a controversial patho-physiology that assumes an even more complex aspect in patients with depressed left ventricular ejection fraction (LVEF%). LV remodeling, dilatation, and dysfunction result in geometrical changes in the MV apparatus, including papillary muscles (PMs) displacement and MV annular dilatation that, consequently, can lead to IMVR.

Although a global change in the geometrical relationships among the various components of the unit ventricle-mitral valve apparatus may take place in patients with impaired LV function, these modifications may not always justify the development of IMVR.

In this regard, in our clinical practice we frequently observe a plethora of patients with severely compromised cardiac contractility and dilated ventricular chambers that present with absolutely preserved MV function.

To understand why patients with equally impaired LVEF behave differently in relation to their MV continence, we should extend our analyses beyond the simple geometrical evaluation of the heart and consider, simultaneously, the impact of regional myocardial vitality and perfusion. For this purpose, a comprehensive imaging modality such as cardiac magnetic resonance imaging (MRI) could allow us to depict a clearer image of IMVR in patients with depressed LVEF thus clarifying the purely geometrical and functional modifications that lead to this deleterious occurrence.

MATERIALS AND METHODS

In our Institution, patients with depressed LVEF% of ischemic origin are routinely submitted to cardiac MRI.

We have summarized our standardized protocol for cardiac MRI in patients with IMVR, and specified the variables of interest to specifically evaluate MV function/morphology, LV function/morphology, and myocardial function/vitality (global and segmental) (1).

In this manuscript, we report our cardiac MRI findings in a series of non-consecutive patients with 3 vessels coronary artery disease (CAD), depressed LVEF (<40%), and with or without IMVR.

After admission, patients underwent trans-thoracic echocardiography to confirm cardiac function and evaluate MV function/morphology.

Patients who presented MV or MV apparatus structural abnormalities were excluded from this analysis as well as those that had already undergone any sort

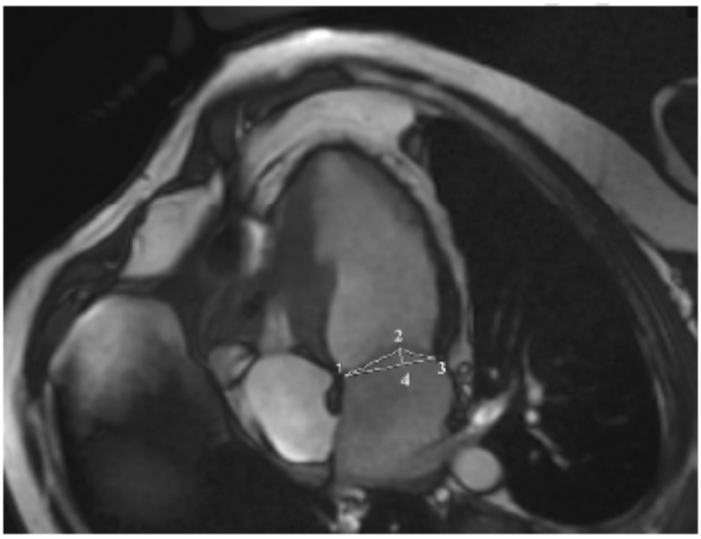

Figure 1. Cardiac MRI imaging and evaluation of mitral valve geometrical parameters: 1-3: septo-lateral diameter; 1-2 anterior leaflet length; 2-4: coaptation depth; the triangle 1-2-3 is the tenting area

of interventional procedure (either invasive cardiology or surgical approach), or had any contraindication to MRI (hemodynamic instability, claustrophobia, presence of in-body paramagnetic material).

After quantitative evaluation of MV regurgitation with echocardiography, two groups were identified: CAD without IMVR (Group CAD) and with IMVR (Group IMV). Cardiac MRIs recorded variables included: anterior MV leaflet length, MV annular septo-lateral diameter, MV annular inter-commissural diameter, MV annular degree of circularization (septo-lateral diameter / inter-commissural diameter), MV annular area, inter PM distance (PMD), coaptation depth (CD) in 2 and 4 chambers, tenting area (TA) in 2 and 4 chambers (Fig.1). Whenever appropriate, measurements were taken in systole and diastole. Furthermore, quantitative evaluation of MV regurgitation was performed when present, together with LV end systolic volume (ESV), LV end diastolic volume (EDV), LVEF% (EDV-ESV/EDV x100), and forward LVEF% (EDV-ESV-MV regurgitant volume/EDV x 100). Perfusion/vitality study was also performed with gadolinium and data recorded following the American Society of Echocardiography scheme of 17 ventricular segments (2).

Data were prospectively recorded and analyzed. Normality was tested by means of Wilk-Shapiro test. Differences between the two groups were tested using the unpaired Student t-test, Mann-Whitney test, and Fisher exact test whenever appropriate.

To investigate correlation between the different MRI geometrical variables, the presence of MVR, and LVEF%, Pearson correlation test was performed in the overall group.

As LVEF% did not have a normal distribution, logarithmic transformation of LVEF% was used.

Multivariable analysis was performed to identify independent determinants for occurrence of IMVR (logistic regression, stepwise forward procedure) and for Log LVEF% (linear regression, stepwise procedure).

The two multivariable analysis models were built including all those variables that at Pearson correlation test had a correlation with IMVR and LVEF% ($p<0.05$). All statistical analyses were performed using SPSS (SPSS Inc., Chicago, Ill, United States).

RESULTS

Eleven patients were enrolled in the CAD group and 13 in the IMV group.

Geometrical measurements were considered before and after indexing for anterior MV leaflet length, as previously indicated (3). Univariate analysis findings are summarized in table 1. As expected, MV regurgitation volume was significantly higher in the IMV group (24.0± 12.0 vs. 4.5±5.2; $p<0.001$) (Table 1). Conventional LVEF% was comparable in the two groups (IMV 34.6±13.0 vs. CAD 31.5±13.0; p=ns) as well as forward LVEF% (IMV 24.4±12.1 vs. CAD 33.6±12.4; p=ns) (table 1). Although annular MV area, and annular inter-commissural diameters in systole and diastole were significantly higher in the IMV group, after indexing for anterior MV leaflet length no statistically significant difference was noticed between the two groups (table 1).

Gadolinium perfusion/vitality study was performed to evaluate the presence of necrotic segments (myocardium that after contrast infusion presents with a pattern of delayed enhancement). The total number of necrotic segments was comparable in the two groups (IMV 6.3±4.1 vs. CAD 6.7±4.9; p=0.8) (Table 2). A specific analysis of the different segmental areas involved (inferior, lateral, anterior, septal, apical), showed a higher occurrence of inferior myocardial necrosis in the IMV group (IMV 61% vs. CAD 9%; p=0.01) and a trend towards a higher rate of septal necrosis in the CAD group (IMV 54% vs. CAD 91%; p=0.07) (Table 2).

At Pearson test, inferior myocardial necrosis had the strongest correlation with occurrence of IMVR (correlation ratio R=0.54; p=0.006) (Table 3). Other variables significantly correlated with occurrence of IMVR were: non-indexed

Table 1. Univariate comparison between patients with depressed LVEF%, 3 vessels CAD, and w/o IMVR. Data are expressed in systole (s) and diastole (d) and before and after indexing for anterior leaflet length when appropriate.

	CAD	IMV	p-value
Age (years)	61.4±10.8	61.9±5.7	0.80
Gender M/F	9_2	9_4	0.20
LVEF%	31.5±13	34.6±13	0.77
Forward LVEF%	33.6±12.4	24.4±12.1	0.12
MVR Volume cc	4.5±5.2	24.0± 12.0	< 0.001
Anterior MV leaflet length mm	25.5±4.0	28.6±2.2	0.07
LV End Systolic Volume cc	142.2±94.6	148.4±63.7	0.80
LV End Diastolic Volume cc	208.1±32.5	225.3±64.0	0.60
Papillary muscles distance (s) mm	18.6±9.8	18.8±5.0	0.90
Papillary muscles distance (d) mm	24.8±8.4	26.7±5.2	0.50
Indexed Papillary muscles distance (s)	0.6±0.1	0.7±0.2	0.60
Indexed Papillary muscles distance (d)	0.9±0.1	0.9±0.2	0.70
Septo-lateral diameter (s) mm	32.0±3.6	34.6±2.7	0.08
Septo-lateral diameter (d) mm	33.6±3.4	36.4±2.7	0.06
Indexed Septo-lateral diameter (s)	1.2±0.1	1.2± 0.1	0.30
Indexed Septo-lateral diameter (d)	1.3±0.07	1.3± 0.1	0.20
Inter-commissural diameter (s) mm	31.2±2.5	35.0±4.5	0.04
Inter-commissural diameter (d) mm	33.0±3.6	37.0±4.3	0.04
Indexed Inter-commissural distance (s)	1.2±0.1	1.2±0.1	0.80
Indexed Inter-commissural distance (d)	1.3±0.1	1.3±0.2	0.80
MV Area (s) mm^2	788.0±128.1	960.7±185.0	0.03
MV Area (d) mm^2	876.9±168.4	1068.7±204. 3	0.04
Indexed MV Area (s)	31.1±3.8	33.6±5.9	0.30
Indexed MV Area (d)	34.6±5.8	37.2±5.7	0.30
MV Circularization degree (s)	1.0±0.1	0.9±0.08	0.50
MV Circularization degree (d)	1.0±0.08	0.9±0.05	0.30
Coaptation Depth 2chambers mm	7.7± 1.6	8.2± 1.7	0.50
Coaptation Depth 4 chambers mm	7.7± 2.2	7.8± 3.0	0.80
Tenting Area 2 chambers cm^2	1.4±0.9	1.5± 0.4	0.70
Tenting Area 4 chambers cm^2	1.5±0.9	1.4± 0.3	0.70

Table 2. Cardiac MRI vitality study: Mean total number of necrotic segments (within a 17 segments schema) and rate of necrosis within the different segmental areas in the CAD and IMV groups.

	CAD	IMV	p-value
Delayed Enhancement Total Segments	6.7±4.9	6.3±4.1	0.80
Inferior	9%	61%	0.01
Lateral	18%	46%	0.21
Anterior	45%	54%	1.00
Septal	91%	54%	0.07
Apical	64%	70%	1.00

Table 3. Pearson Correlation between the presence of ischemic MV regurgitation and cardiac MRI geometrical and vitality parameters. R= correlation coefficient, (s): systole, (d): diastole

	R	p-value
Inter-commissural diameter (s)	0.46	0.04
Inter-commissural diameter (d)	0.46	0.04
MV Annular Area (s)	0.48	0.03
MV Annular Area (d)	0.46	0.04
Inferior Necrosis	0.54	0.006
Septal Necrosis	-0.46	0.04

Table 4. Pearson Correlation between Log LVEF% and cardiac MRI findings. R= correlation coefficient, LV: Left Ventricular, (s): systole, (d): diastole

	R	p-value
Papillary Muscles Distance (s)	-0.67	0.004
Papillary Muscles Distance (d)	-0.56	0.02
LV End-systolic Volume	-0.83	<0.001
LV End-diastolic Volume	-0.73	0.001

Table 5. Logistic regression (stepwise forward procedure) analysis. Dependent Variable: occurrence of ischemic MV regurgitation, (s): systole

	p-value
Inferior Myocardial Necrosis	0.16
MV Annular Area(s)	0.99

Table 6. Linear regression (stepwise procedure) analysis.

	p-value
LV End Systolic Volume	0.022*
LV End Diastolic Volume	0.036*

Dependent Variable: Log_{10} LVEF %.
LV: Left Ventricular

inter-commissural diameter and MV annular area (both in systole and diastole), and septal myocardial necrosis (Table 3).

Left ventricular volumes (end-systolic and diastolic), and inter-papillary muscles distance (in systole and diastole) had the strongest negative correlation with the logarithmic transformed of LVEF% (Table 4).

Those variables that had a significant correlation with occurrence of IMVR and the logarithmic transformed of LVEF% were tested with multivariable analysis.

No independent determinant for occurrence of IMVR was identified (table 5). Left ventricular volumes (end-systolic and diastolic) were the sole independent determinants for Log_{10} LVEF% (table 6).

DISCUSSION

MV insufficiency occurs in 15% of patients after myocardial infarction (MI) and in the presence of structurally normal MV leaflets and subvalvular apparatus (4). IMVR is associated with a controversial diagnostic-therapeutic pattern as its patho-physiologic bases have yet to be fully elucidated.

As this condition is associated with excess cardiac morbidity and mortality even in the presence of mild to moderate regurgitation (5), many authors have focused their research on identifying the mechanisms that would lead to the development of IMVR in an attempt to better stratify patients at risk and guide treatment.

Correct understanding of mechanisms leading to IMVR is even more crucial in patients with depressed LVEF%.

We have evaluated with cardiac MRI the impact of LV global and segmental myocardial scarring, LVEF%, as well as various geometric and functional variables of the MV apparatus, on the development of IMVR in patients with LV dysfunction.

Use of cardiac MRI in a similar context has been previously suggested by Sirchai et al (6).

Our main finding is a higher rate of necrotic areas in the inferior myocardial segments in patients with IMVR. Furthermore, myocardial segmental delayed enhancement had the strongest univariate correlation with occurrence of MV regurgitation.

In our experience, LV dimensions and LVEF% seem to have no direct impact on the development of IMVR and, consequently, equally enlarged ventricles may develop unequal degrees of MV regurgitation.

We believe that, *per se*, an enlarged ventricle will not automatically lead to an ischemic MV and that the location of the myocardial necrosis will play the main role in the ethio-pathogenesis of MV regurgitation. Similar results were reported by Kumanohoso et al. (7) in an evaluation involving patients with prior myocardial infarction (MI) (anterior and inferior) and normal control subjects. The authors evaluated the grade of IMVR by means of quantitative echocardiography and reported that, although global LV dilatation and dysfunction were significantly less pronounced in patients with inferior MI, the percentage of mitral regurgitation jet area and the incidence of significant regurgitation were greater in these patients (7).

This would confirm that IMVR may occur in normally sized ventricles and, in the event of extreme LV dilatation, will occur mainly if the inferior myocardium is necrotic.

We should also emphasize the fact that, in our present analysis, most of the patients had only mild MV. In fact, in patients with more advanced mitral regurgitation, the effect of blood volume loading on the left ventricle would become more substantial and, at this advanced stage, it would become more difficult to recognize cause from effect.

The role of MV annular dilatation in the pathogenesis of ischemic MV regurgitation remains controversial. In this regard, many authors have reported that isolated annular dilation does not usually cause important functional mitral regurgitation as leaflet tissue redundancy protects against leaflet abnormal coaptation in isolated annular dilatation (8,9).

However, many others have reported, in different cohorts of patients with IMVR and in animal experimentation, significant increases in either MV septolateral or inter-commissural diameters (10-14).

Differently from the majority of the available literature, and as suggested by Jorapur et al (3), we have used anterior mitral leaflet length to index geometric measurements of the MV apparatus. Anterior leaflet and intertrigonal distance (the distance between the trigones, which corresponds to the fibrous portion of the mitral annulus) are not significantly affected by left ventricular remodelling and have been used as reference measurements for sizing mitral annuloplasty rings.

The importance of using an indexing parameter is reflected in our univariate analysis where MV inter-commissural distance and MV annular area are significantly correlated to occurrence of MV regurgitation only before being indexed by anterior MV leaflet length.

The current leading surgical technique for the treatment of ischemic MV regurgitation is based on the assumption that MV annulus is firmly anchored along the circumference of the anterior leaflet by the tough fibrous skeleton of the heart and, therefore, dilatation of the MV annulus primarily affects the posterior leaflet. As a consequence, all current operative mitral repair strategies contemplate reduction of the MV inlet area by posterior leaflet annuloplasty.

We believe that ischemic MV regurgitation occurs within a more complex scenario that is actually reflected by the high rate of MV regurgitation recurrence after simple posterior annuloplasty (15). In this context, Gelsomino et al. have recently shown that independent predictors of recurrent MV regurgitation after restrictive annuloplasty include mainly ventricular variables such as end systolic volume, systolic sphericity index, myocardial performance index, and wall motion score index (16).

Altered PMs geometry has been hypothesized as part of the pathogenesis of ischemic MV regurgitation (3,7).

In several MRI studies, Kaji et al. confirmed the importance of the posterior PM displacement (with consequent increase in posterior papillary muscle-septal annulus distance) (11). Yu et al. reported similar findings concluding that the inter- PMs distance of more than 32 mm and the distance from the anterior mitral annulus to the posterior PM root of more than 64 mm readily distinguished ischemic MV patients from healthy controls and isolated CAD patients (14).

Finally, inter- PMs distance was proposed as an independent predictor for mid-term failure after MV repair for IMVR (15).

In our analysis, inter-PMs distance (absolute and indexed) was homogeneously distributed in patients with and without IMVR and, furthermore, there was not significant correlation between inter-PMs distance and occurrence of MV regurgitation in the overall group. Our findings may be biased by the fact we did not calculate the distance between PMs and MV annulus although we did focus on inter- papillary muscles distance. On the other hand, we found no correlation between the amount of IMVR and the coaptation depth (which would be a surrogate of the distance between PMs and MV annular plane).

In our univariate analysis, non-indexed inter- PMs distance correlated with LVEF%. At multivariable analysis, LV volumes were the sole independent determinants for LVEF%.

This confirms the fact that PMs distance may be a good indicator of LV function and dilatation albeit not necessarily correlated to the degree of IMVR.

LIMITATIONS

We should emphasize that our multivariable analysis showed none of the investigated parameters have an independent impact towards occurrence of IMVR. This could be explained by the small size of the investigated sample. Also, in our analysis we considered 10 cc as cut-off to divide patients with and without IMVR and, within the patients with different degrees of IMVR, we made no distinction between moderate and severe MV regurgitation. Although this decision was dictated by sample size limitations, findings could have been different especially when comparing the severe IMVR patients with the sole CAD ones.

Finally, as already underlined in the discussion, evaluation of inter-PMs distance was limited to the inter-PMs measurements without taking into consideration the distance from the PMs to the MV annulus. We deliberately decided

to concentrate on this parameter as we accepted MV coaptation depth and MV tenting area as good indirect indicators of the distance between PMs and MV.

CONCLUSION

Although various factors play a role in the ethio-pathogenesis of IMVR, we believe that a comprehensive imaging modality such as MRI could allow us to depict a clearer image of this elusive condition.

We are aware that the relatively small number of patients studied in the present analysis may not be sufficient to clearly differentiate the causes in the genesis of IMVR.

At the same time we can suggest that in patients with depressed LVEF%, ischemic MV cannot be explained by global LV and MV geometrical modifications alone. Although PM distance, LV volumes, and LVEF% are correlated, they have no direct independent impact in the development of IMVR. In contrast, inferior myocardial necrosis and increased inter-commissural MV diameters may lead to deformity of MV complex and subsequent IMVR.

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Chapter 16

Discussion

Giuseppe D'Ancona, MD

Every medical procedure requires a quality control method, and this is particularly true for complex procedures such as heart operations.

Medical practice is urging us towards quality control for scientific, clinical, ethical, as well as legal purposes. For these reasons, all the available armamentaria should be applied to provide evidence of good clinical practice.

Intraoperative graft patency verification after coronary surgery should be routine part of the operation.

Aim of coronary artery bypass grafting is to increase blood flow to ischemic myocardium and it is important to document objectively the procedure success. This statement acquires further impact if we realize that 5-20% of performed grafts fail before discharge from the hospital and up to 30% before 1 year.

Many of these early failures are probably secondary to technical issues that could be promptly solved if adequately diagnosed intraoperative.

As reported in chapter 11, cardiac surgeons are overtly sceptic towards intraoperative graft patency verification and most of them still trust their fingertips' tactile feedback as evidence of coronary graft patency.

In being complementary with PCI, cardiac surgery has lost its supremacy in the treatment of coronary artery disease, and cardiac surgeons should concentrate on how to optimize the quality of care they are providing.

In perspective, and as summarized in the various chapters of this thesis, there is enough scientific evidence justifying the use of intraoperative coronary graft patency verification tools.

The intraoperative tools that surgeons presently have to test coronary graft patency include imaging techniques and flow assessment devices.

Although most surgeons use neither of these technologies, in the future we should consider to adopt simultaneously the two different technologies.

In this context, future research should be supported by manufacturing companies and focus on two main goals:

1) the development of a device that will allow surgeons to identify simultaneously and intraoperative the anatomical and functional parameters of the coronary targets and newly constructed coronary anastomoses;
2) the realization of a system of automated interpretation of coronary graft flow curves and anastomosis status.

Imaging modalities most often do not clearly demonstrate the functional capacity and reserve of the anastomoses and, on the other side, flow assessment devices do not clearly address the degree of patency of the anastomoses.

A unique diagnostic tool could achieve a simultaneous iconographic and functional evaluation by integrating different technologies (fluorescence imaging and ultrasound?).

Alternatively, ultrasound technology may become the gold standard for intraoperative coronary graft patency verification due to its dual ability to provide both morphological and functional information.

Although perivascular transit time flow measurement (an ultrasound based technology) has been widely demonstrated as a sensitive tool for intraoperative quality assessment of newly constructed coronary grafts, its application cannot be extended to the evaluation of coronary targets due to limitations intrinsic to transit time technology.

Differently from transit time flow measurement probes, Doppler epi-coronary probes are formed by a single crystal and do not require dissecting and encircling the target artery under study and, therefore, are more easily applicable to test the status of the native coronaries and their blood flow before and after the revascularization has been performed.

In this regard, Doppler technology has recently resurged as a valuable intraoperative armamentarium to help cardiac surgeons select adequate coronary targets for revascularization and depicting both anatomical and functional features of newly constructed anastomosis.

As documented in our animal experiments (chapter 8), epicardial coronary artery Doppler represents a valuable tool to detect coronary arterial flow velocity in basal condition, after coronary occlusion, and during reperfusion. Moreover, potential applications of a custom-made epicardial ultrasound probe were previously investigated demonstrating its ability to successfully visualize and assess coronary arteries and anastomoses on all sides of the heart.

We auspicate that, in the very next future, multimodal ultrasound probes will be designed and will include, in the same product, the possibility to visualize coronary targets and coronary anastomoses, to evaluate coronary flows and flow velocities (with Doppler) before and after surgical revascularization, and to record grafts flow values and flow patterns (with transit time) at the end of the operation.

Correct interpretation of intraoperative findings is not always immediate and routine use and further technological amelioration of the existing devices will enhance the coronary graft quality control process.

Although transit time technology can clearly show differences between hemodynamically normal and abnormal grafts, correct interpretation is limited by our inability to analyze flow curves in their different components. In this

context, a system of automated interpretation of intraoperative findings should be designed keeping into consideration the flow curve patterns.

Chapter 17

Summary English

Summary Dutch

Curriculum vitae

List of publications

Acknowledgement

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Summary English

CHAPTER 1 & CHAPTER 2

Introductory Chapters: Intraoperative Graft Patency Verification in Coronary Surgery
These two introductory chapters (Chapter 1 and 2) summarize the basis of vascular flow measurement focusing on coronary rheology and discussing the technological aspects of flowmetry.

A comprehensive insight into ultrasound based transit time flow measurement is given.

Guidelines for correct interpretation of coronary grafts flow patterns are given.

Comment Phase Chapters: Clinical Experience with Transit Time Flow Measurement and Validation of Epicoronary Doppler in the animal model
This session discusses clinical use of transit time flow measurement to intraoperatively test graft patency during coronary surgery.

CHAPTER 3

Chapter 3 is a short communication commenting upon a previous publication and emphasizing how strict protocols for flow measurement have to be followed in order to achieve the maximal clinical benefit of this technology.

CHAPTER 4

Chapter 4 summarizes the clinical experience with transit time flow measurement in beating heart coronary surgery. The findings in over 1000 tested grafts are reported and indications for correct interpretation of flow patterns are given on the basis of the findings on revised grafts.

CHAPTER 5

Chapter 5 and 6 suggest some clinical applications for transit time flow measurement. Chapter 5 shows how flowmetry provides an extra tool to direct supportive measures such as cardiac pacing after CABG.

CHAPTER 6

Chapter 6 shows that in reoperative coronary artery surgery the physiologic significance of suspect lesions by angiography can be confirmed by direct intraoperative measurement of blood flow in the old grafts; such interpretation can prevent unnecessary graft revisions.

CHAPTER 7

In this chapter the influence of heparin dosing in patients undergoing off-pump coronary revascularization is evaluated in terms of coronary graft patency as detected by intraoperative transit time flow measurement.

CHAPTER 8

Chapter 8 validates, in an animal model, a newly-designed epicardial coronary artery Doppler probe. The experiments have been conducted in the laboratories of the Erasmus University hospital and have shown that epicardial coronary arterial Doppler represents a valuable tool to detect coronary arterial flow velocity in basal condition. Although changes in flow velocity are easily recorded after coronary occlusion and reperfusion, modifications after partial coronary stenosis are not clearly defined.

CHAPTER 9

Chapter 9 reports the use of intraoperative transit time technology as gold-standard to directly measure right ventricular output (intraoperative probe placement around the main pulmonary artery) and validate a new system for invasive cardiac output monitoring (True-Continuous Cardiac Output).

CHAPTER 10

In this chapter transit time flow measurement is used to test different techniques of coronary anastomoses construction.

CHAPTER 11

This chapter summarizes the finding of a survey about the clinical use of intraoperative graft patency verification by cardiac surgeons. It interestingly shows that the majority of surgeons use their finger tips to detect coronary grafts quality.

CHAPTER 12

Chapter 12 reviews the modern means available to intraoperative test and document the status of newly constructed coronary anastomosis. A distinction should be made between imaging techniques and flow assessment devices. Both methods have clear limitations, and we should consider, as a future perspective, using the two different technologies simultaneously.

CHAPTER 13

This chapter discusses the very controversial topic of coronary revascularization: should cardiologists and cardiac surgeons approach this pathology together and aim at hybrid coronary revascularization?

CHAPTER 14-15

The last two chapters report a very recent experience on a very elusive issue: i.e., ischemic mitral valve regurgitation.

In these chapters the author attempts to give an explanation of the pathophysiologic bases of ischemic mitral valve regurgitation by using a modern and complete diagnostic and investigational tool such as cardiac MRI.

Summary Dutch

Nederlandse samenvatting

HOOFDSTUK 1

In dit hoofdstuk worden de fysiologische aspecten van de bloedstroom in de coronairvaten besproken. Met name de rheologie in coronair vaten en de diverse aspecten van bloedstroom metingen worden belicht. Inzicht wordt gegeven in de op ultrageluid gebaseerde stroommetingen. Tevens worden richtlijnen besproken die dienen voor de juiste interpretatie van bloedstroom patronen in coronaire bypasses. De klinische toepasbaarheid ervan wordt toegelicht.

HOOFDSTUK 2

De toepassing van bloedstroom metingen tijdens coronair chirurgie wordt beschreven. Bij 161 patiënten die off-pump coronair chirurgie ondergingen werden in totaal 323 anastomosen gemaakt. Alle bypasses werden met behulp van TTFM (Transit Time Flow Measurement) gecontroleerd. In totaal warden 32 omleidingen gereviseerd (9.9%) op basis van afwijkende stroom patronen. Bij alle gereviseerde bypasses werd een technische onvolkomenheid gevonden.

HOOFDSTUK 3

Hoofdstuk 3 is een commentaar op een wetenschappelijke publicatie van Hirotani et al. (Hirotani T, Kameda T, Shirota S, Nakao Y. An evaluation of the intraoperative transit time measurements of coronary bypass flow. Eur J Cardiothorac Surg 2001;19:848–852). Benadrukt wordt hoe strikt protocollen voor bloedstroom metingen moeten worden gevolgd om tot de juiste beslissingen te komen of een bypass doorgankelijk is of niet.

HOOFDSTUK 4

Dit hoofdstuk vormt een beschrijving van de klinische ervaring van bloedstroommeting tijdens 'kloppend hart' coronair chirurgie. De bevindingen van

meer dan 1000 coronair bypass grafts worden gerapporteerd en aanwijzingen worden gegeven om tot een juiste interpretatie van de stromingspatronen te komen. Belangrijk hier is de discussie welke bypasses moeten worden herzien op basis van deze stroommetingen.

HOOFDSTUK 5

Hoofdstuk 5 beschrijft de toepassing van perioperatieve bloedstroom meting om myocardperfusie te optimaliseren door het elektrisch stimuleren('pacen') van het hart.

HOOFDSTUK 6

De afwijkingen in bypass grafts die met bloedstroom metingen kunnen worden vastgesteld, kunnen gerelateerd worden aan preoperatieve angiografische bevindingen. Tijdens een coronaire reoperatie kan zo vastgesteld worden welke afwijkingen daadwerkelijk fysiologische consequenties hebben en welke bypass grafts gereviseerd dienen te worden. Dergelijke metingen kunnen onnodige graft herzieningen voorkomen.

HOOFDSTUK 7

In dit onderzoek is onderzocht welke invloed de heparine dosering heeft op de doorgankelijkheid van coronair bypass grafts bij patiënten die een off-pump coronair revascularisatie ondergaan. Geconcludeerd wordt dat onvoldoende antistolling tijdens de operatie leidt tot trombose in de bypass graft.

HOOFDSTUK 8

Hoofdstuk 8 valideert, in een diermodel, een nieuw ontworpen epicardiale coronaire Doppler sonde. De experimenten tonen aan dat een epicardiale coronair arteriële Doppler meting een waardevol instrument is voor het bepalen van coronaire bloedstroom snelheid onder basale omstandigheden. Hoewel de veranderingen in de stroomsnelheid eenvoudig kunnen worden vastgesteld

na coronaire occlusie en reperfusie, zijn de veranderingen die optreden tijdens gedeeltelijke coronaire occlusie minder duidelijk.

HOOFDSTUK 9

In hoofdstuk 9 wordt het gebruik van 'intraoperative transittime' metingen vergeleken met een nieuwe continue cardiac output meting die berust op een thermisch principe.

HOOFDSTUK 10

In dit hoofdstuk worden stroom karakteristieken besproken voor de verschillende anastomose technieken tussen de linker arterie thoracica interna en de linker coronair arterie (LAD).

HOOFDSTUK 11

Dit hoofdstuk geeft de bevindingen weer van een enquête die gehouden is betreffende de vraag hoe chirurgen intraoperatief de doorgankelijkheid van grafts vaststellen. Het blijkt dat de meerderheid van de chirurgen hun vingertoppen gebruiken om de bloedstroom in een bypass te verifiëren.

HOOFDSTUK 12

Hoofdstuk 12 geeft een overzicht van de nieuwe methoden die beschikbaar zijn om intraoperatief de doorgankelijkheid van bypasses vast te stellen. Er wordt onderscheid gemaakt tussen beeldvormende technieken en technieken die de bloedstroom beoordelen. Beide methoden hebben duidelijke beperkingen, en overwogen moet worden of in de toekomst de twee verschillende technologieën beiden moeten worden gebruikt.

HOOFDSTUK 13

Dit hoofdstuk behandelt het controversiële onderwerp van coronaire revascularisatie: moet cardiologen en chirurgen deze coronair pathologie samen aanpakken en zich richten op behandeling door zowel CABG als PCI?

HOOFDSTUK 14-15

De laatste twee hoofdstukken beschrijven de pathosfysiologische aspecten van ischemische mitralisklep insufficiëntie. Deze insufficiëntie kan onderzocht worden met behulp van een cardiale MRI. De meerwaarde van deze methode zou ook liggen bij patiënten die een ischemisch mitralisklep lijden hebben in combinatie met een slechte linker ventrikelfunctie.

Curriculum vitae

Giuseppe D'Ancona is a Cardiac Surgeon working at the Mediterranean Institute for Advanced Therapies and Transplantation in Palermo Italy.

He graduated in Medicine at the University of Milan where he specialized in Cardiac Surgery after completing fellowships at the State University of New York (Buffalo) and Quebec Heart Institute (Laval University). During his training and afterwards he has developed a strong Academic approach to medicine and surgery contributing in over 100 publications in peer reviewed journals, editing 3 technical textbooks in cardiac surgery related topics, and presenting his clinical research findings at national and international meetings.

Dr. D'Ancona has developed many research interests including intraoperative graft patency verification in coronary surgery, quality control in cardiac surgery, ischemic mitral valve regurgitation physio-pathology, use of magnetic resonance imaging in cardiology, cell therapy for advanced heart failure, and percutaneous treatment of cardiovascular disease.

Dr. D'Ancona has enrolled in the COEUR PhD program at the Rotterdam University in 2004 and has focused his doctoral activity in the field of intraoperative coronary graft patency verification.

List of Publications

PAPERS

Santise G, **D'Ancona G**, Falletta C, Pirone F, Sciacca S, Turrisi M, Biondo D, Pilato M.
Donor pharmacological hemodynamic support is associated with primary graft failure in human heart transplantation.
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Apart from the friends and colleagues that have helped me in the last phases of this trip, my academic path spans back to my time at the State University of new York in Buffalo, where I started my clinical research career. In this moment, I want to remark my gratitude towards Drs. Salerno and Bergsland that, since 1998, have triggered my scientific curiosity and allowed me to develop my academic interests. Thank you always for your trust and support and long lasting friendship. I would also like to thank Dr. Karamanoukian for his constant "push to produce papers". You were a great motivator. Also, I want to thank all the Authors and friends that have contributed in 2001 to the printing of my first book on Intraoperative Graft Patency Verification.

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And finally, allow me to acknowledge my happy gratitude towards my life companion, “light” wizard, team-mate, and best friend Monica, that always supports me inspite of my restless entropic soul.

PhD Portfolio

Research School: COEUR
PhD period: 2004-2009

PhD Training	**year**	**Workload (ECTS)**
General Academic Skills		
Laboratory animal science (small animals) Institutional Animal Care and Use Committee (IACUC) Licence, University of Pittsburgh Medical Center, Pittsburgh, PA, USA	2007	1.5
Laboratory animal science (large animals) Institutional Animal Care and Use Committee (IACUC) Licence, University of Pittsburgh Medical Center, Pittsburgh, PA, USA	2007	1.5
In Depth Courses		
Endovascular Treatment of Thoracic Aorta pathology, Arizona Heart Center, Phoenix, AZ, USA	2009	1.8
Italian Society of Cardiac Surgery: Post-graduate courses	2008	0.6
Mitral Valve Repair for Degenaritive Mitral Valve Disease. Palma De Mallorca, Spain	2005	0.6
Presentations		
D'Ancona G et al: Myocardial revascularization on the beating heart after recent onset of AMI. Presented at the 80th AATS meeting, Toronto, Canada,	5/2000	0.6
D'Ancona G et al: OPCAB in high risk patients. Invited Speaker to the "Japan off-pump" meeting, Tokyo, Japan,	7/2000	0.6

D'Ancona G et al: Intraoperative graft patency verification. Invited speaker to the satellite symposium "TTFM in Coronary Surgery" EACTS meeting, Frankfurt, Germany,	9/2000	0.6
D'Ancona G et al: The Buffalo Experience with Transit Time Flow Measurement. Invited speaker to the IInd "Bosnia and Herzegovina" cardiac surgery meeting, Mostar, Bosnia and Herzegovina,	10/ 2000	0.6
D'Ancona G et al: OPCAB in Patients with Depressed LVEF%. Invited Speaker to the meeting "Innovative Surgical Therapies of CHF", Buffalo, NY, USA,	3/2001	0.6
D'Ancona G et al: GI complications in cardiac surgery. Presented at the EACTS meeting, Monte Carlo, Monaco,	9/2002	0.6
D'Ancona G et al: Off-pump vs. on-pump CABG: A surgeon matched study. Presented at the CCS meeting, Edmonton, Alberta, Canada,	10/2002	0.6
D'Ancona G et al: Use of MRI in Ischemic Mitral Valve Regurgitation. Presented at the Italian Association of Medical Cardiology, Florence, Italy,	6/2007	0.6
D'Ancona G et al: Surgery for Ischemic Mitral Valve Regurgitation: Single Center Experience. Presented at the Italian Association of Medical Cardiology, Florence, Italy,	6/2007	0.6
D'Ancona G et al: Aortic Valve Repair: Single Center Experience. Presented at the Italian Association of Medical Cardiology, Florence, Italy,	6/2007	0.6
Sciacca S, **D'Ancona G**, Santise G, et al. Entirely heparin coated extracorporeal membrane oxygenator: initial single center experience. Presented at European Society Organ Transplantation, Prague, Czech Republic,	10/2007	0.6
Santise G, **D'Ancona G**, Sciacca S , et al. Perioperative routine use of nitric oxide for heart transplantation: a single center initial experience. Presented at European Society Organ Transplantation, Prague, Czech Republic,	10/2007	0.6
D'Ancona G et al. Use of MRI in ischemic mitral valve regurgitation. Presented at the Denton Cooley Society, Houston, TX, USA,	10/2007	0.6

D'Ancona G et al: Ischemic mitral valve regurgitation: Morphofunctional and Myocardial Vitality Evaluation With Cardiac MRI. Presented at the 18th World Congress of the World Society of Cardio-Thoracic Surgeons, to be held at Kos Island, Greece.	4/2008	0.6
D'Ancona G et al: Extracorporeal Life Support : Time Related Performance of a Fully Heparinized Circuit and Polymethilpentene Oxygenator. Presented at the International Society for Heart and Lung Transplantation, Paris, France	4/2009	0.6
Ischemic Mitral Valve Regurgitation And Cardiac Magnetic Resonance Imaging: Independent Impact Of Segmental Myocardial Vitality. Presented at the Society for Heart Valve Disease, 5th Biennial Meeting, Berlin, Germany	6/2009	0.6

Conferences and Seminars

Italian Association of Medical Cardiology, Florence, Italy,	2007	0.9
European Society Organ Transplantation, Prague, Czech Republic	2007	1.2
Denton Cooley Society, Houston, TX, USA,	2008	0.9
18th World Congress of the World Society of Cardio-Thoracic Surgeons, to be held at Kos Island, Greece, from April 30th to May 3rd 2008.	2008	0.9
International Society for Heart and Lung Transplantation, Paris, France	2009	1.2
XXII Endovascular Symposium, Phoenix, AZ, USA	2009	1.8

Didactic Skills

Flow measurement in coronary surgery	2000-2009	0.9
Intraoperative graft patency verification	2000-2009	0.9

Teaching Activities

Teaching and assisting trainees in intraoperative and periopeartive management of cardiac surgery patients	2002-2009	9
Supervising trainees in research protocols designing, data collection, analysis and academic publications	2002-2009	9

Mentoring residents in cardiac surgery specialization thesis development	2007-2009	9
Responsible for Academic Research at the Department of Cardiac Surgery @ ISMETT	2006-2009	9
Abstract Reviewer for the EACTS Meeting	2009	1.5
Invited Discussant on Intraoperative Graft Patency Verification, EACTS Meeting	2009	1.5

Others

Reviewer Annals of Thoracic Surgery	2004- present	1.5
Member of the ISMETT ethical Committe	2008- present	1.5
Chief of the ISMETT Skin Care Committe	2008- present	1.5