# INTEGRATING CORONARY ANGIOGRAPHY INTO THE CARDIAC OPERATING ROOM

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## Contents

## 1. Acknowledgements

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This thesis studied the ability of different methods for graft evaluation such as coronary angiography, transit time flow measurements, epicardial ultrasonography and transesophageal echocardiography to predict surgical outcome. The work had not been possible without the close collaboration between The Interventional Centre and the Departments of Radiology, Cardiology and Cardiothoracic surgery. Many persons have contributed and I will thank them all. A special thank to the whole staff at the Interventional Centre for great support and a lot of fun.

Finally, I express gratitude to my wife Ellen and my children Kristiane and Amund, who patiently have given me time to complete the work.

## 2. List of papers

This thesis is based on the following papers, which will be referred to by their Roman numerals:

I. Hol PK, Fosse E, Lundblad R, Nitter-Hauge S, Due-Tønnessen P, Vatne K, Smith HJ. The importance of intraoperative angiographic findings for predicting long-term patency in coronary artery bypass operations. Ann Thorac Surg 2002 Mar;73(3):813-8.

II. Hol PK, Lingaas PS, Lundblad R, Rein KA, Vatne K, Smith HJ, Nitter-Hauge S, Fosse E. Intraoperative angiography leads to graft revision in coronary artery bypass surgery. Ann Thorac Surg 2004 Aug;78(2):502-5.

III. Hol PK, Fosse E, Mørk BE, Lundblad R, Rein KA, Lingaas PS, Geiran O, Svennevig JL, Tonnessen TI, Nitter-Hauge S, Due-Tonnessen P, Vatne K, Smith HJ. Graft control by transit time flow measurement and intraoperative angiography in coronary artery bypass surgery. Heart Surg Forum 2001;4(3):254-7.

IV. Hol PK, Andersen K, Skulstad H, Halvorsen PS, Lingaas PS, Andersen R, Bergsland J, Fosse E. Epicardial ultrasonography - a potential method for intraoperative quality assessment of coronary bypass anastomoses? Accepted for publication in Ann Thorac Surg 2007

V. Hol PK, Geiran O, Andersen K, Vatne K, Offstad J, Svennevig JL, Fosse E. Improvement of coronary artery fistula surgery by intraoperative imaging. Ann Thorac Surg 2004 Dec;78(6):2193-5.

## 3. Abbreviations

| | |
|---|---|
| CT | Computed tomography |
| IMA | Internal mammary artery |
| LAD | Left anterior descending coronary artery |
| LAO | Left anterior oblique |
| LIMA | Left internal mammary artery |
| MR | Magnetic resonance |
| PCI | Percutaneous coronary intervention |
| RAO | Right anterior oblique |

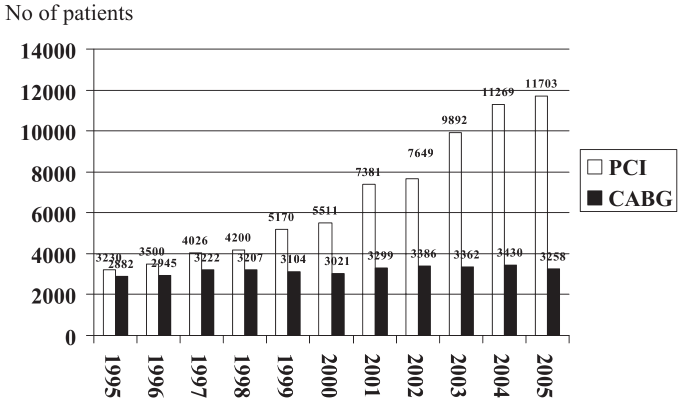
## 4. Introduction

The era of open heart surgery was initiated by the introduction of cardiopulmonary bypass and myocardial protection methods in the 1960s. Through modification of the heart-lung machine, like coating of the artificial surface of the bypass circuit with heparin[1] and improving membrane technology, cardiac surgery with cardiopulmonal bypass (on-pump) has gained widespread acceptance for all types of cardiac surgery, not only for procedures requiring opening of the heart but also for surgery on the epicardial coronary arteries. Cardiac surgery without cardiopulmonary bypass (off-pump) was performed as isolated coronary artery bypass procedures already in the beginning of the 1960s by Robert Goetz[2] and Vasilii I. Kolesov[3], and was reintroduced by Frederico Benetti[4] and Enio Bufollo[5] in the 1980s. Due to avoidance of cardiopulmonary bypass the risk of cerebral microembolization is reported to be reduced.[6] Valid concern, however, has been raised about the quality of the anastomoses.[7]

Full revascularization of multivessel disease is traditionally achieved by on-pump surgery through a median sternotomy with the anastomosis of the left internal mammary artery (LIMA) to the left anterior descending coronary artery (LAD) while vein or other arterial grafts are used elsewhere. After the introduction of off-pump or beating heart surgery, minimally invasive direct coronary artery bypass (MIDCAB) surgery with surgical access through a left thoracotomy was used for anastomosis of LIMA to the LAD in single vessel disease.[8] A hybrid approach was introduced to achieve full revascularization. In the latter approach, the LIMA is anastomosed to the LAD through a small thoracotomy combined with percutaneous coronary interventions (PCI) of the other vessels.[9] Through median sternotomy full revascularization may be performed with off-pump coronary artery bypass (OPCAB) technique.[7] In off-pump surgery traction devices are used to gain access to the posterior part of the heart, and mechanical stabilizers are applied to reduce the motion of the heart in the anastomotic area. The LAD could be occluded by snares on both sides of the vessel incision to achieve a bloodless field, while performing the distal LIMA-LAD-anastomosis. A temporary intracoronary shunt could be used to establish distal perfusion.

Although on-pump coronary artery bypass surgery is reported to give excellent clinical results,[10] cardiac surgery must verify its place in a medical environment under constant development. In all surgery there is a trend towards minimal access and less traumatic methods, and at the same time percutaneous techniques for cardiac interventions have improved with the result that an increasing numbers of patents can be successfully treated by these techniques. In Norway, as in most of the western world, PCI is performed almost three times more than surgery for coronary revascularization. The drive towards less invasive surgery and hybrid procedures was probably influenced by the development of image guided radiological techniques.

*Percutaneous coronary intervention (PCI) in Norway versus coronary artery bypass grafting (CABG)*



Source: The Norwegian Association of Cardiothoracic Surgery
The Norwegian Cardiologic Society

The implementation of off-pump coronary artery bypass surgery varies worldwide. In USA approximately 20% of coronary bypass surgery was performed off-pump in 2000,[11] in Canada about 16% in 2002,[12] in Japan 60% in 2004,[13] while only 8% of the surgery was performed off-pump in the Nordic countries in 2003.[14]

When a new surgical technique is introduced, quality testing is mandatory to ensure satisfactory patient outcome. In coronary artery bypass surgery, the simplest form of quality control is manually to “feel the pulse” by tactile sensation. But this method is subjective and non-quantitative.[15] Transit time flow measurements are easy to use, give direct volume flow-data and are the most used tool in quality assessment of bypass surgery.[16, 17] Flow velocity can also be measured by continuous Doppler and pulsed wave Doppler or combined with cross-sectional morphologic data in duplex color Doppler ultrasound.[18, 19] Recently, high-frequency mini-transducers for epicardial application have been introduced, giving high-quality data of both morphology and flow.[20-25] Some reports exist on the use of fluorescence and thermal imaging.[26-29] Invasive methods such as use of intra-arterial flow and pressure wires, angioscopy and intravascular ultrasonography imply passing of the devices through the recently sutured anastomosis and are not implemented in clinical practice.[30-33] Coronary angiography gives morphologic information on vessel lumen and is considered the “gold standard” of graft quality assessment, but the method has not had a defined role in intraoperative imaging.

In the cardiac operation theatre, surgery has been performed guided by preoperative angiographic examinations performed at radiologic or cardiologic laboratories, normally days before surgery. Integrated surgical suites, where high-quality angiographic equipment is installed, have for some years been a reality in peripheral vascular surgery, allowing procedures combining imaging and surgical intervention.[34] The first attempt on integrating angiography into the cardiac operating room was done with transportable C-arm equipment.[35-38] By the establishment of The Interventional Centre at Rikshospitalet University Hospital in Oslo in 1996, advanced angiographic equipment was installed in a specially designed operation room, allowing high quality angiographic imaging to be performed during the cardiac surgical procedure.[39, 40]

In the cardiac operation theatre coronary angiography can have multiple missions. Angiography is an integrated part of the hybrid concept of coronary revascularization combining PCI and cardiac surgery. Intraoperative angiography can otherwise be used as guidance for the surgical procedure (paper V) or as a quality control of the surgical result at the end of the procedure allowing a possibility for immediate on-table surgical revision (papers I-IV).

# 5. The aims of the study

The main aim of the study was to evaluate the role of coronary angiography in the cardiac operating room. Intraoperative angiography as quality assessment tool in coronary artery surgery was assessed and compared to transit time flow measurements and epicardial ultrasonography. The impact of image guidance on the results of coronary artery fistula closure was also investigated.

## 5.1 Specific aims

1) To describe the lesions found at on-table angiography and to evaluate the significance of these immediate angiographic findings for the long-term graft patency in coronary artery surgery (Paper I)

2) To quantify the on-table revision rate in coronary artery bypass surgery initiated by intraoperative angiography (Paper II)

3) To compare the relationship between intraoperative transit time flow measurements and angiographic evidence of graft patency in patients undergoing coronary artery bypass surgery (Paper III)

4) To evaluate graft quality assessment in coronary artery surgery by epicardial ultrasonography and to compare this technique with transit time flow measurement, intra- and postoperative coronary angiography (Paper IV)

5) To assess whether intraoperative imaging by angiography and transesophageal echocardiography would contribute to and improve the results of coronary artery fistula surgery (Paper V)

# 6. Material

All patients described in this thesis had coronary artery surgery performed in the combined surgical and angiographical suite at The Interventional Centre, Rikshospitalet University Hospital in Oslo, except three patients in paper V that were operated at The Department of Thoracic and Cardiovascular Surgery, Rikshospitalet University Hospital.

In paper I, 45 patients (41 male and 4 female) with median age of 63 years (range 38-79 years), who underwent off-pump coronary bypass surgery from August 1996 to April 1999 were included. Nineteen patients were operated through a small left thoracotomy, 18 through a median sternotomy and 8 patients with a hybrid approach combining a small left thoracotomy and PCI.

In paper II, 186 patients with a mean age of 65 ± 8.7 years having coronary artery bypass surgery were studied in the period from August 1996 to March 2003. Thirty-one of the patients were operated off-pump through a small left thoracotomy and 155 through a median sternotomy, 63 of these had on-pump and 92 off-pump surgery. Forty-four of the patients in this study were also included in paper I. One-hundred-and-twenty of the patients in paper II constituted a randomized study comparing off- and on-pump coronary bypass surgery, clinical results have been reported by Lingaas et al.[41, 42]

In paper III, a total of 72 patients operated in the period from December 1996 to March 2000 were studied. Twenty-one of these patients (mean age 68 ± 7.8 years) were operated on-pump and 51 patients (mean age 65 ± 8.7 years) were operated off-pump. Sixty-eight of these patients were also included in paper II.

In paper IV, a total of 39 patients operated off-pump through a median sternotomy from November 2002 to January 2005 were included. There were 33 males and 6 females with a median age of 66 years (range 40 to 85 years). Four of these patients were also included in paper II.

In paper V, seven patients surgically treated for coronary artery fistula between 1992 and 2002 were included. There were 4 men and 3 women with a median age of 54 years (range 43 to 67 years). The first three of these patients were operated at The Department of Thoracic and Cardiovascular Surgery.

In all studies the patients gave written informed consent, and all studies were approved by the regional ethics committee on human research.

## 7. Methods

### 7.1 Coronary angiography

Intraoperative coronary angiography was used in all studies. In the first period our combined suite was equipped with Advantix digital subtraction angiographic unit (General Electric (GE) Medical System, Milwaukee, WI, USA) and the equipment was used in paper I, III and partly in paper II. The angiographic unit was replaced by Angiostar OR (Siemens, Erlangen, Germany) in the year 2000, and Angiostar was used in the rest of the patients in paper II, and in paper IV and V. The follow-up angiographic studies were performed on the same angiographic equipments as the intraoperative studies.

Angiography is the study of blood vessels by roentgen contrast media. After Conrad W. Roentgen's discovery of the X-rays at the end of the year 1895,[43] the X-ray-technique rapidly spread in the medical community. Already in January 1896 angiograms of the blood vessels of an amputated hand were made,[44] but much investment had to be made in the development of X-ray-opaque contrast media well tolerated when administrated intravenously. In the 1940s and 1950s the development of film changers and image intensifiers were made. In 1953 Seldinger introduced his method of percutaneous catheterization.[45] The modern area of coronary angiography started when Sones developed a technique for selective catheterization of the coronary arteries in 1959 utilizing the brachial approach,[46] and with the development of techniques for selective coronary angiography by transfemoral approach with matching catheter design by Ricketts and Abrams,[47] Judkins[48] and Amplatz[49] in the 1960s. Due to heart motion, cine-film became the preferred archival method for coronary angiography. In the 1980s and 1990s the development of digital imaging systems established the modern coronary angiography. In Norway 15 122 coronary angiographic examinations were performed in 2000,[50] increasing to 26 063 in 2004.[51]

### *7.1.1 Technique of intraoperative coronary angiography*

For guidance of surgery, as closure of coronary fistulas, angiography has to be performed with maintained access to the chest cavity. For graft quality assessment, intraoperative angiography can be performed after closure of the chest allowing revision of graft failure while the patient is still under anesthesia.

Intraoperative angiography includes selective catheterization of all arterial and vein grafts and if required, the left and right coronary artery by specially designed catheters (IM curve style, LCB, RCB, LC, RC; Boston Scientific Scimed, Maple Grove, MN, USA). An arterial sheath inserted into the femoral artery has a rubber valve at the proximal end facilitating rapid changing of the catheters. All catheters are at the proximal end connected to a three-stopcock manifold that, in a closed system, allows easy manipulation of the catheter and at the same time rapid switching from pressure monitoring to contrast injection or flushing of the catheter with saline. By intermittently monitoring the arterial pressure at the catheter tip during the procedure, obstruction of the coronary lumen by the catheter can be avoided.

During catheterization of the different ostia, the curves of the catheter tips are preferably seen in profile. The patients are viewed in a left anterior oblique (LAO) projection when catheterizing the left and right coronary artery, most of the aortocoronar bypasses and when entering the subclavian artery for imaging the internal mammary artery (IMA) grafts. Catheterization of the ostium of the IMA is done under slight right anterior oblique (RAO) projection. For optimal visualization multiple projections are obtained during angiography of native vessels and grafts, including LAO, RAO, frontal, lateral and even cranial and caudal angulated LAO or RAO projections. For each distal anastomosis at least two projections angulated approximately 90 degrees at each other have to be obtained.

At our institution, non-ionic contrast material (Visipaque 320 mgI/ml; GE Bioscience Amersham, Oslo, Norway) is injected by hand, and image series are recorded with a 512 x 512 matrix at a rate of 12.5 images per second.

### *7.1.2 Quantification of angiographic findings*

Selective coronary angiography gives morphological information on the vessel lumen, but the exact quantification of the degree of stenosis is difficult, demonstrated both as discrepancies between coronary angiograms and necropsy findings[52-54] and significant inter- and intraobserver variability.[55] Several grading systems have been suggested to describe the relation between arterial stenosis and flow,[56-58] with the common basis that lesions with more than 50 percent narrowing of the luminal diameter (representing 75 percent reduction in cross-sectional area) are thought to be hemodynamically significant.

Quantitative coronary angiography is a computer-based technique for measurements of coronary arterial dimensions on digital images allowing calculation of the percentage stenosis, giving a more accurate estimation than visual grading.[59, 60] Absolute measurements are possible to obtain using the known diameter of the angiographic catheter as a scaling device. Quantitative coronary angiography is also operator-dependent and factors like variability in selection of the arterial segment to be analyzed, frame-to-frame variability due to degree of opacification and projection of the lesion in a rapidly moving artery, crossing vessels and eccentric lesions make quantitative coronary angiography inaccurate. Quantitative analysis used in repeated coronary angiography examinations requires images to be obtained at exact same angulations of the X-ray tube and at same distances between patient and image-intensifier and between patient and X-ray-tube. It is particularly difficult to obtain images with the same angulations of the X-ray-tube when comparing intraoperative angiography with post-operative follow-up as the anatomy shifts after closure of the chest.

### *7.1.3. Complications to coronary angiography*

Major complications to coronary angiography include death, myocardial infarction, arrhythmia, stroke, vascular access site complication and contrast media reaction. Local vascular complications at the catheter entry site like bleeding, occlusion, dissection, pseudoaneurysm and arteriovenous fistula may occur. The reported incidence of the different major complications vary between less than 0.1% and up to 3%, but carefully performed examinations with modern equipment are associated with low complication rates.[61-64] The complication rate at our institution is low.[65-68] It is higher in older patients, patients with worse New York Heart Association (NYHA) functional class and multivessel involvement.[61-63] Factors such as low patient load[61, 69] and prolongation of the procedure time[63, 70] are associated with higher complication rates.

### 7.2 Transit Time Flow Measurements

Graft flow measurements using a transit time ultrasonic flowmeter (Cardiomed, Medi-Stim, Oslo, Norway) were obtained in paper III and IV.

Flow measurements were performed with electromagnetic flowmeters in the 1970s.[71, 72] The technique of the transit time flow measurement (TTFM) has been known since the 1960s.[73, 74] It was introduced into clinical practice in the 1990s, and is now the most commonly used tool for quality control in vascular surgery.[16, 75-78] Two ultrasound crystals are placed at a distance on the same side of the vessel with a reflecting mirror midway between the crystals at the opposite side of the vessel. An ultrasound pulse is transmitted by the upstream crystal via the mirror to the downstream crystal and vice versa. Because ultrasound travels slightly faster in the flow direction, a small time difference for the two signals can be recorded, and this time difference, named the transit time, forms the basis for flow calculation. The transit time flowmeter gives direct volume flow, no calibration is necessary, and the measurements are independent of the thickness of the vessel wall and the hematocrit fraction. The angle between the crystals and the vessel is not critical, as any change of angle between the upstream crystal and the vessel will be compensated by a corresponding change of angle between the downstream crystal and the vessel. The flowmeter has to be placed around the vessel to be examined, and acoustic fluid must be present between the flowmeter and the blood vessel to ensure good acoustic coupling.

The two leading vendors (Medi-Stim AS, Oslo, Norway and Transonic Inc, NY, USA) deliver easy-to-use devices with real-time visualization of flow curves, flow values, pulsatility indexes and memory for storage and post-processing.

Transit time flow measurement has shown to be reliable and accurate in measuring flow in both in vitro and in vivo studies.[17, 79-82] The capability to detect anastomotic failures in coronary bypass surgery is dependent on many factors, such as the hemodynamic status of the patient, the distal run-off, the coronary vessel flow resistance, the degree of collateral filling, and the presence of a non-occluded proximal LAD lesion causing competitive flow. Correct interpretation of transit time flow measurement is therefore difficult.[16, 17] *The flow curve* should be coupled with ECG tracing to correctly differentiate systolic from diastolic flow. In the coronary artery circulation the blood flows mainly during diastole with minimal systolic peaks during the isovolumetric ventricular contraction, typically seen in LAD and left circumflex grafts. In graft failure the flow curves become spiky and mainly systolic. Grafts to the right coronary artery may normally have larger component of systolic flow as the blood flows into the right coronary system during both phases of the cardiac cycle. *The pulsatility index* (PI) is defined as the absolute value of the difference between the maximum flow and the minimum flow divided by the mean flow. A PI of more than 5 is considered indicative of technical error.[16] *The mean flow value* is expressed in mL/min, and is per se a poor indicator of the quality of the anastomosis.[16] It is more dependent on the quality of the revascularized coronary artery as the vessel diameter and vascular resistance are involved in determining the actual flow value together with the driving pressure. Flow values of less than 5 mL/min is thought to imply poor graft performance, although low flow value per se should not lead to graft revision.[16] The mean flow value should be interpreted together with the flow curve and the pulsatility index.[16]

To increase the reliability in interpretation of transit time flow measurement, examination both with and without proximal snares of the native coronary vessel are recommended.[16] Competitive flow from non-occluded native vessel and lesions at the level of the toe of the anastomosis can then be detected. Walpoth et al[83] suggested coronary flow reserve as a method to help in correctly diagnose anastomotic failures, but this has not gained widespread acceptance. To further increase the accuracy and reliability in classifying degree of stenosis even the use of spectral analysis of the graft flow[84] and a neural network pattern recognition analysis system[85] have been suggested.

### 7.3 Transesophageal echocardiography

With the availability of high-frequency transducers and color Doppler imaging transesophageal echocardiography became commonplace in the cardiac operation theatre in the 1980s, and has been widespread in use since the 1990s.[86] Transesophageal echocardiography (TEE) does not interfere with the surgical field and provides continuous anatomic and hemodynamic information of the heart, including global ventricular function, volume status, regional wall motion and valve function. It gives valuable data both for the surgeon and for the anesthesiologists, provides important information in various surgical procedures, and is useful in guiding therapy in haemodynamically unstable patients both in the operating room and the intensive care unit.[86, 87]

Transesophageal echocardiography has been used for quality assessment of left internal thoracic grafts,[88] but has not gained a place as a quality assessment tool of coronary anastomoses. In this thesis data available from transesophageal echocardiography examinations (GE Vingmed Ultrasound, Horten, Norway) were used in paper V to evaluate the anatomy and closure of coronary fistula.

### 7.4 Epicardial ultrasonography

A system FiVe, Vivid 5 or Vivid 7 digital ultrasound scanner (GE Vingmed Ultrasound, Horten, Norway) with a 10-MHz linear array GE Vingmed mini-transducer was used to obtain epicardial ultrasound information in paper IV.

In the 1980s, high-frequency epicardial transducers were shown to give information on target sites in the coronary tree.[89, 90] Recent technical developments have resulted in minitransducers that can be applied epicardially during coronary artery surgery,[20-25] providing improved information on both morphology and flow of the distal bypass anastomosis. *Gray-scale imaging* or B-mode (Brightness mode) ultrasound gives morphological information. The reflected intensity of the transmitted ultrasound waves creates two-dimensional gray-scale sectional images in real-time.

Ultrasound flow measurement is based on the Doppler theory first described by Christian Doppler in 1843.[91] When ultrasound is reflected from moving blood, the frequency is changed (the Doppler shift, $f_D$) according to the Doppler equation:

$$f_D = 2 \cdot f_0 \cdot v \cdot \cos\alpha \, / \, c$$

where $f_0$ is the emitted frequency, v is the velocity of the blood cells, α is the angle between the ultrasound Doppler beam and the direction of blood flow, and c is the velocity of the ultrasound in the medium. The Doppler shift is thus dependent on the angle between the ultrasound probe and the vessel, if this angle is 90º there will be no Doppler shift and no information obtained regarding blood flow. Separate measurement of the vessel diameter must be obtained to calculate volume flow from the measured flow velocity. In *color Doppler* the Doppler information from a selected region is superimposed on the B-mode image, where the different velocities are displayed using a color scale. The color in each pixel indicates the average flow velocity toward or away from the probe, and provides a quick visualization of the blood flow.[18, 19] In *pulsed wave Doppler* short bursts of ultrasound are transmitted at regular intervals, and the measured velocity are related to a specific depth in the tissue, determined by the investigator using the B-mode.[19] In *power Doppler* imaging the integrated power of the shifted echoes is color encoded, visualizing the presence of moving blood, without information about velocity or direction.[92, 93] Power Doppler has advantages over color Doppler imaging: is angle-independent, does not produce signal aliasing and is more sensitive to slow flow and visualization of small vessels.[92, 93] Power Doppler visualizes coronary arteries well and is reported to accurately depict graft anastomoses during coronary bypass surgery.[94]

Epicardial ultrasonography can be a potential tool for quality assessment in coronary bypass surgery. Grayscale imaging gives morphological information, color Doppler and pulsed wave Doppler can measure flow at any site of the anastomotic area, also in the proximal and distal part of LAD. In epicardial ultrasound scanning, however, particular emphasis must also be paid to the interaction between surgeon and ultrasonographer. In epicardial ultrasonography it is important to slowly move the probe over the vessel to be scanned, and to keep the probe in place without movement during the time required for flow measurements. Ideally the probe should be held by the same person operating the ultrasound scanner, thus the surgeons must be trained in the use of ultrasound equipment or the cardiologist or radiologist has to be present in the surgical field.

# 8. Summary of the papers

## Paper I. The importance of intraoperative angiographic findings for predicting long-term patency in coronary artery bypass operations. Ann Thorac Surg 2002 Mar;73(3):813-8

The aim of this study was to describe the lesions found at on-table angiography in off-pump coronary artery bypass surgery, and to evaluate the significance of these lesions for the long-term patency.

Forty-five patients with median age of 63 years and with a total of 42 internal mammary artery grafts and 15 saphenous vein grafts were studied.

The most frequent finding on-table was spasm. This was seen in about 50% of the grafts, and it was not present at follow-up. Twenty-three percentages of the grafts had pathological lesions on-table. Out of nine kinks, only one developed into a significant stenosis at follow-up. Of two grafts with dissection, one was found open and one occluded at follow-up. Out of 44 grafts that were normal on-table, 37 (84%) were normal at follow-up, and out of 11 grafts with significant lesions on-table, eight (73%) were normal at follow-up. The positive and negative predictive values of intraoperative angiography in predicting findings at follow-up were 0.38 and 0.84, respectively.

This study demonstrated that on-table angiograms occasionally can be difficult to interpret because not all findings are important for later patency.

## Paper II. Intraoperative angiography leads to graft revision in coronary artery bypass surgery. Ann Thorac Surg 2004 Aug;78(2):502-5

The aim of this study was to quantify the on-table revision-rate in coronary artery bypass surgery initiated by intraoperative angiography.

The study consisted of 186 patients with a total of 427 grafts. The mean age of the patents was 65 years, 82% were males. On-pump surgery was performed in 34%, off-pump through a median sternotomy in 49%, and off-pump surgery through a left thoracotomy in 17%.

Eighteen of 427 grafts (4.2%) were revised due to the findings at intraoperative angiography. Revision rate after on-pump surgery was 1.1%, after off-pump surgery through a sternotomy 6.4% and after off-pump surgery through a thoracotomy 6.5%. All but one were successfully revised.

It was concluded that intraoperative angiography saves a potential number of grafts that otherwise could have been occluded.

## Paper III. Graft control by transit time flow measurement and intraoperative angiography in coronary artery bypass surgery. Heart Surg Forum 2001;4(3):254-7

The aim of this study was to compare the relationship between transit time flow measurements and angiography in predicting long-term graft patency in coronary artery bypass surgery.

Seventy-two patients underwent coronary artery bypass surgery, 21 patients were operated with extra-corporeal circulation (on-pump) and 51 without extra-corporeal circulation (off-pump). Sixty-seven LIMA and 57 saphenous vein grafts were studied. After construction of the bypass grafts, flow was measured at the distal part of the graft using transit time flow measurements, with recording of mean flow, pulsatility index and waveform of each graft. After closure of the chest, coronary angiography of the grafts was performed while the patients were still under general anesthesia. Follow-up angiography was performed after three months. All angiograms were evaluated visually and the patency graded as described by FitzGibbon,[95] where grade A was defined as normal graft or graft with lesion of less than 50% reduction in diameter, grade B as graft with lesion of more than 50% reduction in diameter and grade O as occluded.

There were no significant differences in flow and pulsatility index between grafts constructed off- or on-pump or between type A and type B grafts. There were no significant differences in flow and pulsatility index between intraoperative type B grafts that remained pathologic or normalized at follow-up angiography.

This study showed that mean flow value and pulsatility index obtained with transit time flow measurements could not identify significant lesions in arterial or vein grafts, and could not predict graft patency.

## Paper IV. Epicardial ultrasonography - a potential method for intraoperative quality assessment of coronary bypass anastomoses? Accepted for publication in Ann Thorac Surg 2007

The aim of this study was to evaluate intraoperative graft quality assessment in coronary artery bypass surgery by epicardial ultrasonography and to compare this technique with transit time flow measurements and with intra- and postoperative coronary angiography.

Thirty-nine patients with median age 66 years who underwent off-pump surgery with IMA to LAD were studied. Epicardial ultrasonography, transit time flow measurements and coronary angiography were performed intraoperatively and coronary angiography at follow-up.

Diameter measurements obtained by epicardial ultrasonography correlated poorly with the same diameter measurements obtained by angiography. Epicardial ultrasonography revealed five abnormal distal anastomoses (13%), transit time flow measurement none and intraoperative angiography nine (23%). At follow-up angiography four distal anastomoses (11%) were pathological. Epicardial ultrasonography and transit time flow measurement indicated no need for graft revision, intraoperative angiography suggested need for revision in three cases. The positive and negative predictive values of epicardial ultrasonography for long-term patency were 0.2 and 0.9, respectively. The positive and negative predictive values of intraoperative angiography for long-term patency were 0.33 and 0.96, respectively. The negative predictive value of transit time flow measurements was 0.89.

This study indicated that intraoperative angiography is superior to epicardial ultrasonography and transit time flow measurements in detecting grafts in need of revision. Angiography must be considered the gold standard in intraoperative imaging. Epicardial ultrasonography could be a useful method in graft quality assessment, but needs to be further evaluated, preferable in comparative studies with intraoperative angiography.

### Paper V. Improvement of coronary artery fistula surgery by intraoperative imaging. Ann Thorac Surg 2004 Dec;78(6):2193-5

The aim of this study was to assess whether intraoperative fistula imaging could contribute to and improve the final surgical result.

During a 10-years period seven adult patients, with a median age of 54 years, were operated for symptomatic coronary arteriovenous fistula. In three patients the fistulas were closed without any image guidance, and in four patients they were closed controlled by intraoperative angiography. Intraoperative transesophageal echocardiography was additionally used in one case. Exercise electrocardiography, echocardiography and selective coronary angiography were performed both preoperatively and postoperatively.

Coronary artery fistulas may have complex anatomy and multiple sites of origin, and may therefore be difficult to close. All 4 patients who had image guidance achieved complete and persistent closure. In contrast, 2 of 3 patients who underwent operation without image guidance had residual left-to-right shunts at follow-up.

This study demonstrated that image guidance was helpful and increased the success rate of surgical closure of coronary artery fistulas.

# 9. Discussion

In this thesis it is confirmed that intraoperative angiography performed during coronary artery surgery, can give valuable information leading to immediate surgical revision. To avoid unnecessary diagnostic pitfalls, high image quality is imperative. Adequate image quality can be achieved when angiography is performed with advanced and fixed angiographic equipments.[40] Mobile C-arms give inferior image quality and are less suitable for obtaining multiple views of grafts and anastomoses. Essential is also good catheterization technique. Proper handling of the catheter coupled with short examination times will contribute in keeping the complication rate at a minimum. Adequate selective examination of the graft ostia should ensure that false diagnoses of occluded grafts are avoided. However, despite high image quality and proper angiographic technique, interpretation of the findings at intraoperative angiography may be difficult.

### *Lesions found at intraoperative angiography*

Intraoperative angiography will reveal lesions that are not significant for later patency as shown in paper I in this thesis, where 45 patients with a total of 57 grafts constructed off-pump were studied both with intraoperative and follow-up angiography. Seventy-seven percent of the grafts were normal at intraoperative angiography, and 9% of these grafts developed significant lesions at follow-up examination, probably due to thrombosis formation, graft remodeling or progression of the atherosclerotic disease. However, 73% of the grafts with significant lesions on-table, normalized at follow-up. These on-table findings can be due to localized spasm or temporary changes like thrombosis formation, edema or hematomas in the vessel wall. Spasm can be catheter-induced, spontaneous or due to surgical manipulation,[96-99] but the main cause of intraoperative spasm is probably the surgical manipulation of the arteries. Spasm was found in as many as 50% of the grafts, disappearing at follow-up. All these findings that normalize at follow-up angiography make the interpretation of intraoperative angiography difficult.

Particularly the high rate of spasm makes both interpretation of intraoperative angiography and also comparison of different quality assessment tools difficult. The grade of spasm may change during the surgical procedure, as indicated in paper IV, where there was a time delay between epicardial ultrasonography and intraoperative angiography. Significant lesions found at epicardial ultrasonography were resolved at on-table angiography and vice versa.

### *Graft occlusion and anastomotic failures*

Early graft occlusion could be due to pre-existing atherosclerosis in the graft, operative injury, slow blood flow, small luminal size of the grafted artery, inadequate distal run-off and mechanical failures at the anastomotic sites. Anastomotic failures may be caused by too tights sutures, edema or hematomas in the vessel wall, dissection of the graft or the grafted artery, suboptimal insertion site or distortions caused by too long or too short bypass grafts. Avoiding early thrombosis is essential. Intraoperative angiography can reveal occlusions, dissections, kinks, strangulations and “stenotic lesions” as demonstrated in paper I, II and IV. Further subgroup division of the collective term “stenotic lesions” was not possible with intraoperative angiography.

### *Graft patency*

In conventional on-pump coronary artery bypass surgery the intermediate patency rate varies between 94% and 99% for arterial grafts and between 80% and 90% for vein grafts.[100] The available data in off-pump surgery indicates that there is no statistical difference in patency rate compared to on-pump surgery. But there are reports of higher revision rate and tendency of higher percentage of stenosis in the off-pump group compared to on-pump.[41, 100, 101] Within one week after off-pump surgery (both thoracotomy and sternotomy incision) the overall patency rate is reported to vary between 95 and 99%,[102-104] and for IMA-grafts (mainly thoracotomy incisions) between 97 and 100%.[105, 106] Mack reported the intraoperative patency rate for IMA-grafts to be 99%.[107] The randomized study including 120 patients that was a part of paper II in this thesis, stated the intraoperative patency rate of IMA-grafts to be 100% and of vein grafts 97%.[41] The studies in this thesis found the on-table patency rates of IMA-grafts and vein grafts to be 95-100% and 96-100 %, respectively. At follow-up, the patency rates of IMA-grafts and vein grafts were found to be 93-97% and 81-87%, respectively (papers I-IV).

### *Graft revision*

The revision rate induced by intraoperative angiography in our study was 4.2% in paper III, 5% in paper II and 8% in paper IV; in all three studies all grafts except one were successfully corrected. In paper III, we found a difference in revision rate between on-pump (1.1%) and off-pump (6.4%) surgery, indicating that off-pump surgery could be technically more demanding at least in the learning phase. In paper IV three grafts were revised due to findings at angiography, not detected by epicardial ultrasonography or transit time flow measurement, and in all technical errors were revealed at surgical inspection. These findings indicate that intraoperative angiography can save a number of grafts, otherwise likely to be occluded.

Izzat et al. and Mack et al. both reported a revision rate indicated by angiography of 8%.[37, 107] It is, however, important to avoid unnecessary revision. As the intraoperative or immediate postoperative patency rate of IMA-grafts is reported to be between 95 and 100%, theoretically a revision rate grater then 5% should not be expected, presuming most grafts to be revised are occluded. But also dissections and strangulations, although graded as not-occluded following FitzGibbon classification, should probably be revised. The true wanted revision rate is therefore unknown.

Clear definitions for when to revise a graft need to be established. In our studies we have revised grafts that were judged to be occluded, or that most likely would have occluded due to dissections or severe torquing. Particular emphasis has to be paid to spasm of both the grafts and the grafted arteries. Spasm is difficult to identify with all quality assessment tools[35, 99, 104, 107] (paper II and paper III). We have therefore become cautious in performing revision based on one measurement only. If spasm is suspected, papaverine or nitroglycerine should be injected, but spasm will not always dissolve completely. Repeated examination after a time-delay is indicated before re-anastomosing the graft.

### *Transit time flow measurement*

The relationship between morphology and flow is complex. The driving force for myocardial perfusion is the diastolic aortic pressure, and vessel diameter is an important factor for volume flow. Distal run-off, coronary vessel resistance and hemodynamic status of the patient are other factors of importance for flow. The volume flow measured in the distal part of the graft by the transit time flow measurement device is therefore not necessarily related to the degree of stenosis at the distal anastomosis.

Barnea et al[108] and D'Ancona et al[16] suggested technical error to be present when transit time flow measurement showed graft flow less than 5 ml/minute and when the pulsatility index was above 5. Low flow values are reported to be present in fully patent anastomoses,[16] and the pulsatility index is thought to be a good indicator for the quality of the anastomoses. Correct interpretation of transit time flow measurements is, however, difficult.[16] In clinical practice the mean flow value and the pulsatility index are often used to make statements of the presence of significant graft stenoses or occlusions.[76] This is addressed in paper III in this thesis, where flow value and pulsatility index are compared with intraoperative and follow-up angiographic findings.

In paper III transit time flow measurement evaluated by mean flow value and pulsatility index could not identify significant lesions in arterial or vein grafts, and even failed to detect an occluded IMA-graft as shown by intraoperative angiography. But the results of this study must be interpreted with care, as a strict protocol for using transit time flow measurements was not implemented. The study demonstrated the weakness of the transit time flow measurement method when the measurements were performed as commonly used by many surgeons.

In paper IV simultaneously interpretation of mean flow values, pulsatility index and flow curves were evaluated, but transit time flow measurements could not detect any of the lesions described by epicardial ultrasonography or intraoperative angiography. The time delay between transit time flow measurements and intraoperative angiography could explain the conflicting findings between these methods. Transit time flow measurements and epicardial ultrasonography were performed close in time, but transit time flow measurements were unable to detect the lesions described by epicardial ultrasonography. These findings confirm that transit time flow measurements probably are not able to detect significant lesions, only occluded or nearly occluded grafts are identified.[16]

D'Ancona et al[16] reported that transit time flow measurement was able to detect technical errors leading to revision, including dissection. In our study transit time flow measurement was unable to detect three grafts in need of revision as demonstrated by intraoperative angiography in paper IV, two of these grafts had dissection. Technical errors at the anastomotic site not compromising flow are probably undetectable by transit time flow measurement. Exact criteria for when to revise a graft, with special emphases on avoiding unnecessary revision, still need to be defined.

### *Epicardial ultrasonography*

Similar to transit time flowmeters, epicardial ultrasound scanners are cheap and mobile. The epicardial probe is placed upon and not around the vessel as in transit time flow measurement. Graft, anastomotic areas and recipient coronary vessels can all be examined by epicardial ultrasonography. Information from both morphological images in B-mode scanning and flow information in color Doppler mode or pulsed wave Doppler mode can be achieved. Epicardial ultrasonography is already reported to be successfully used,[20-25] but paper IV in this thesis is the first study comparing epicardial ultrasonography with intraoperative angiography.

Paper IV demonstrated that epicardial ultrasonography had inferior intra- and inter-observer correlation between diameters at the IMA-LAD-anastomoses compared to intraoperative angiography. Both epicardial ultrasonography and transit time flow measurement failed in detecting three grafts in need of revision as demonstrated by intraoperative angiography.

Epicardial ultrasonography needs to be further evaluated in comparative studies with intraoperative angiography. The use of power Doppler mode[94] or intravenous injection of ultrasound contrast media could increase the accuracy of epicardial ultrasonography.

### *Closure of coronary fistula*

Intraoperative angiography can also be used as guidance during the surgical procedure, exemplified by closure of coronary artery fistula. Adult patients with coronary artery fistula in need of surgical treatment are rare. In the ten-years-period from 1992 to 2002 only seven patients were operated at our institution. The anatomy can be complex, and complete surgical closure can therefore be challenging.

In paper V, three patients were operated for coronary fistula without image guidance and four patients were operated with image guidance in the combined angiographical and surgical suite at The Interventional Centre. All seven patients had follow-up examination with coronary angiography, exercise electrocardiography and stress echocardiography. Two out of the first three patients who underwent operation without image guidance had residual shunts at follow-up. All four patients who were operated with image guidance had complete and persistent closure. The study demonstrated that intraoperative angiography was helpful. All cases with surgical closure of coronary fistula at our institution are now performed in the combined angiographical and surgical suite.

# 10. Conclusions and future aspects

## 10.1 Conclusions

Intraoperative angiography can have a role in the cardiac operating room. Intraoperative angiography can save a potential number of grafts that otherwise would have occluded, and may increase the success rate of surgical closure of coronary artery fistulas.

On-table angiography can be difficult to interpret as not all findings are of importance for later patency. Angiography is superior to transit time flow measurement and epicardial ultrasonography in detecting grafts in need of revision. Angiography must be considered the gold standard in intraoperative graft quality assessment, and should be used as reference method in comparative studies.

Spasm is a frequent finding intraoperatively, and should always be taken into account when on-table quality assessment is performed. Measurement of zero or low flow values should always be repeated before leading to re-surgery.

The mean flow value and pulsatility index of transit time flow measurement could not identify significant lesions and could not predict graft patency. Transit time flow measurement could still be the method of choice in clinical practice, as the majority of grafts with significant lesions are probably not in need of revision.

Epicardial ultrasonography could be a useful non-invasive method in graft quality assessment, but further comparative studies with intraoperative angiography are needed to evaluate the accuracy of the method.

Surgical closure of coronary fistula should be performed with image guidance, preferable in a combined angiographical and surgical suite.

## 10.2 Future aspects

Intraoperative coronary angiography is invasive, costly and time consuming and therefore expected not to be widespreadly used in cardiac surgery. As shown by this thesis, however, intraoperative angiography gives valuable information and should have a role for quality assessment when new surgical techniques are introduced, and in comparative studies evaluating new techniques for intraoperative quality control in coronary artery surgery.

With further technical improvements of the non-invasive digital imaging modalities, the role of intraoperative imaging will probably change. Recent developments of modern magnetic resonance (MR), computed tomography (CT) and ultrasonography hold promise for a change in the established approach of coronary artery imaging. Multislice CT scanning has a great potential in the non-invasive assessment of coronary artery morphology,[109] and CT angiography is expected to replace conventional angiography in coronary imaging. Minimal invasive surgery has so far not gained much ground in the cardiac operating room. In the future, surgery may be performed in an augmented reality where digitized ultrasound information obtained transesophageally or epicardially, and the digitized angiograms obtained from angiography, CT or MR could merge with the thoracoscopic images, leading to a more active use of the total imaging information during the surgical procedure. To evaluate the role of angiograms obtained intraoperatively is therefore an important step in the implementation of image guided cardiac surgery.

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