No touch vein harvesting technique in coronary by-pass surgery
BENNY JOHANSSON

No touch vein harvesting technique in coronary by-pass surgery
Impact on patency rate, development of atherosclerosis, left ventricular function and clinical outcome during 16 years follow-up
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Abstract


This thesis was based on a prospective randomized trial which was started in 1993 to compare the no touch (NT) with the conventional (C) technique of saphenous vein harvesting for CABG.

In paper I, was demonstrated superior patency for the NT grafts at short-term (1.5 years; 95.6% vs 89%; p < 0.05) and long-term follow-up (8.5 years; 90% vs 76%; p = 0.01).

In paper II, at long-term follow-up there were significantly more patients free from recurrent angina and in NYHA-class I in the NT group (67.3% vs 43.2%; p = 0.02). In addition there was no cardiac death and a trend towards improvement of hard clinical endpoints in the NT group.

In paper III, we tested the hypothesis that the NT harvesting technique could provide a reduced progression of the atherosclerotic disease in the vein graft wall by using cineangiography and an intravascular ultrasound (IVUS) assessment. At short-term follow-up, the cineangiogram showed more normal grafts in the NT group (89% vs 75%; p = 0.006). The IVUS assessment showed less mean intimal thickness (0.43 (0.07) mm vs 0.52 (0.08) mm; p = 0.03), less grafts with considerable intimal hyperplasia (≥0.9 mm; 20% vs 78.6%; p = 0.011) and fewer patients with grafts containing considerable hyperplasia (≥0.9 mm; 25% vs 100%; p = 0.007) for the NT vein grafts. At long-term follow-up the cineangiogram showed more normal grafts, 91.2% in the NT group compared with 83.1% in the C group; there were fewer grafts with significant stenosis, with 7.7% in the NT group compared with 15.6% in the C group. The IVUS assessment showed fewer grafts containing multiple plaques (14.8% vs 50%; p = 0.008), less advanced plaque with lipid (11.8% vs 63.9%; p = 0.0004) and less maximal plaque thickness (1.04 (0.23) mm vs 1.32 (0.25) mm; p = 0.02) in the NT vein grafts.

In paper IV, was demonstrated a preserved left ventricular ejection fraction in the NT group compared with the C group (57.9 ± 9.5% vs 49.4 ± 13.3%; p = 0.004) at 16 years follow-up. Also, a smaller left atrium size, a lower BNP value and fewer patients with atrial fibrillation in the NT group indicated a better left ventricular diastolic function.

In conclusion: This thesis showed that the no-touch vein harvesting technique provided a superior long-term patency compared with the conventional technique due to a delayed atherosclerotic process in vein grafts. This was associated with a preserved left ventricular systolic function at 16 years follow-up and also with more asymptomatic patients during this follow-up period.

Keywords: atherosclerosis, coronary artery disease, coronary artery bypass grafting, vein grafts, no touch vein harvesting technique, intravascular ultrasound, echocardiography, clinical outcome, revascularization, outcome analysis, angina pectoris, myocardial infarction, mortality, randomized trial.
Original papers

This thesis is based on the following original publications which will be referred to in the text by their Roman numerals:


IV Johansson B.L, Samano N, Souza, DS, Bodin L, Filbey D, Bojö L. The No touch Pedicle Vein Graft for Coronary Artery Bypass Preserves the Left Ventricular Ejection Fraction 16 Years after Surgery: Long-term Data from a Longitudinal Randomized Trial. (manuscript submitted).
### Abbreviations

<table>
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<th>Description</th>
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<tr>
<td>CABG</td>
<td>Coronary artery bypass grafting</td>
</tr>
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<td>SV</td>
<td>Saphenous vein</td>
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<tr>
<td>NT</td>
<td>No touch</td>
</tr>
<tr>
<td>C</td>
<td>Conventional</td>
</tr>
<tr>
<td>I</td>
<td>Intermediate</td>
</tr>
<tr>
<td>LAD</td>
<td>Left anterior descending artery</td>
</tr>
<tr>
<td>Cx</td>
<td>Circumflex coronary artery</td>
</tr>
<tr>
<td>RCA</td>
<td>Right coronary artery</td>
</tr>
<tr>
<td>PDA</td>
<td>Posterior descending artery</td>
</tr>
<tr>
<td>OMA</td>
<td>Obtuse marginal branch artery</td>
</tr>
<tr>
<td>LITA</td>
<td>Left internal thoracic artery</td>
</tr>
<tr>
<td>EF</td>
<td>Ejection fraction</td>
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<tr>
<td>IVUS</td>
<td>Intravascular ultrasound</td>
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<tr>
<td>ECHO</td>
<td>Ecocardiography</td>
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<tr>
<td>NYHA</td>
<td>New York Heart Association</td>
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<tr>
<td>CCS</td>
<td>Canadian Cardiovascular Society</td>
</tr>
<tr>
<td>OR</td>
<td>Odds ratio</td>
</tr>
<tr>
<td>PCI</td>
<td>Percutaneous coronary interventions</td>
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<td>CAD</td>
<td>Coronary artery disease</td>
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Introduction

Coronary arteries

Two main coronary arteries supply the heart muscle with blood: The left and the right coronary artery (figure 1).

Left coronary artery: The left main coronary artery arises from the aortic root above the aortic valve and then divides into two branches, the left anterior descending (LAD) and the circumflex (Cx) coronary arteries. In some patients, a third branch arises in between the LAD and the Cx. This is known as the ramus intermedius. The LAD travels in the interventricular groove that runs in the anterior part of the heart between the left and the right chamber down the the apex region and sometimes extends beyond the apex and moves up on posterior part of the left ventricle posterior wall (dominant LAD). The LAD gives rise to the following two sets of branches (the diagonals and the septal perforator). The diagonal branches (usually two or three) runs diagonally away from the LAD over the anterior wall of the left ventricle and provides the blood supply to the myocardium in this part of the heart. The septal perforators (SP) runs into the anterior septum and provides its blood supply. After the departure of LAD the left coronary moves on as the circumflex (Cx) coronary artery. It travels in the left atrioventricular groove that separates the left atrium from the left ventricle and goes to the back of the heart. The major branches that it gives off are known as obtuse marginals (OM) branches (usually three). OM1 travels down the lateral part of the left ventricle and provides its blood supply. The OM2 and OM3 branches sometimes called posterolateral (PL) branches make their way to the back or posterior portion of the heart and supplies blood to this part of the left ventricle. In 85% of cases, the Cx terminates at this point (non-dominant). In the other 15% of cases, a dominant Cx terminates with a branch in the posterior septum (posterior descending artery), PDA which is usually coming from the right coronary artery.

The right coronary artery (RCA) originates above the right side of the aortic root and follows the groove that separates the right atrium from the right ventricle to the back of the right ventricle where it usually terminates as the PDA which goes down to the apex in the posterior septum and give that part of the heart its blood supply as well as the inferior wall. In its proximal – middle –distal part the right coronary artery gives away acute marginal branches which give the blood supply to the entire right ventricle. In the 85% of cases when the RCA is coming from the right coronary artery...
(dominant system) the terminal part of RCA also gives off one or two postero-lateral branches to the lower posterior wall in the left ventricle.

**Figure 1**

**Left coronary artery**

1. Left anterior descendens (LAD)
2. Intermediate branch
3. Diagonal branches
4. Circumflex artery
5. Left main artery
6. Obtuse branches
7. Postero-lateral branches

**Right coronary artery**

1. Conus branch
2. Sinus node artery
3. Acute marginal branches
4. Posterior descendens artery (PDA)
5. AV-node artery
6. Postero-lateral branches

LAO = Left Anterior oblique
RAO = Right Anterior Oblique
**Coronary artery disease (CAD)**

Coronary artery disease starts with the accumulation of blood lipids within the wall of the coronary artery which causes inflammation involving the macrophages consuming the lipid LDL (low density lipoproteins) forming foam cells which then rupture with increasing inflammation, a plaque formation has started. The components of this plaque will be a mixture of cholesterol, smooth muscle cells, fibrosis and calcification. As the plaque increases in size during the years a progressive narrowing of the lumen of the artery will occur thereby causing a limiting of the blood flow to the myocardium causing ischemia which in turn gives symptoms of angina pectoris (chest pain) especially at exercise. Figure 2a shows the plaque progression seen by IVUS (intravascular ultrasound). When the myocardium becomes ischemic, it does not function optimally and when large areas of the myocardium becomes ischemic, there can be impairment in the relaxation and contraction of the myocardium. If the blood flow to the tissue is improved by PCI or CABG the myocardial ischemia can be reversed and the angina pectoris disappears. However in many patients the symptoms start with a complete or partial plaque rupture due to high lipid contents or an erosion of the endothelium which along with the activation of the blood clotting system causes a non-occlusion or occlusion of the coronary artery i.e acute coronary syndrome (figure 2b). The clinical status appears as unstable angina pectoris (symptoms at rest) or a myocardial infarction and sometimes as a sudden death. An individual may develop a rupture of an atheromatous plaque at any stage of the spectrum of coronary artery disease. The CAD is the most common cause of sudden death and is also the most common reason for death of men and women over 20 years of age.
Figure 2a
IVUS images of the coronary artery

Normal coronary artery                  Plaque between 06-12                    Advanced plaque

Figure 2b
Histological picture of an acute coronary syndrome

Lipid plaque (white to the left) with rupture (at “noon”) and thrombosis in the lumen.

Treatment of coronary artery disease

Medical treatment
The first treatment of angina pectoris was medical treatment. During the 1970-80s, beta blockers, calcium-inhibitor, long and short term nitrates and aspirin had a substantial effect on the symptoms and some of them also had a possibility to improve the clinical outcome. However coronary stenosis themselves were not targeted by medical treatment until the 1990s when lipid lowering therapy could directly stabilize—but not remove or decrease it.
Coronary artery bypass grafting (CABG)

CABG is a surgical procedure performed to eliminate or relieve the symptom angina pectoris and in some circumstances reduce the risk of death from coronary artery disease. Arteries from the chest and veins from the legs are grafted to the coronary arteries to bypass atherosclerotic stenosis and improve the blood supply to the coronary circulation supplying the myocardium. This surgery is usually performed with the heart stopped, necessitating the usage of cardiopulmonary bypass; techniques are available to perform CABG on a beating heart, so-called "off-pump" surgery. The first coronary artery bypass surgery was performed in 1960 in the US. During the 1960s the technique rapidly advanced and for many years the CABG grafting procedure has been a combination using the LITA (left internal thoracic artery) to bypass the LAD and endoscopically harvested veins (U.S) from the legs to bypass the other stenosed coronary arteries 29 (Figure 3). During the conventional harvesting technique the veins is routinely stripped and then goes into a pronounced spasm. Therefore high pressure distension of the vein is necessary to overcome spasm and this is the main cause of vein wall damage especially to the endothelial layer, consequently jeopardizing the patency rate of the vein grafts.

Figure 3

LITA to LAD (13→06) and vein graft to other coronary arteries

CT-angiogram  Schematic illustration
Percutaneous coronary intervention (PCI)

During the late 1970s a new intervention percutaneous coronary intervention (PCI) became an alternative option to CABG in treatment of CAD. PCI is a non-surgical procedure used to treat the stenotic coronary arteries. A catheter from the inguinal femoral artery or radial artery is placed at the orifice of the coronary artery. Thereafter a deflated balloon on a catheter is placed distal to the lesion under the guidance of X-ray. Then the balloon is inflated to open up the stenosed artery, allowing blood to flow. A stent is often placed at the site of blockage to permanently keep the artery open. The great advantage with this approach is that the patient can leave the hospital very soon, often the same day and that the procedure can be easily repeated. PCI with drug eluting stents has proven to be as effective and less costly than CABG in patients with 1 or 2 coronary artery disease but for more complex disease the choice of revascularisation method has been unclear despite many randomized comparing studies. The SYNergy between percutaneous coronary intervention with TAXus and cardiac surgery (SYNTAX) randomized trial including 1800 patients compared PCI using drug eluting stents with CABG in patients with three-vessel disease and/or left main coronary disease. The 5 years follow-up data in this study has been published in Lancet this year. There were significantly fewer patients with myocardial infarction and significantly fewer repeat revascularisation in the CABG-group but no difference was seen in all-cause mortality or stroke. The recommendation was that in complex three-vessel disease lesions CABG should be preferred but otherwise PCI could be an acceptable alternative.
Vein graft evaluation

Graft cineangiogram
For many years a graft cineangiogram was the only tool to evaluate the status of the vein grafts in patients with reangina/myocardial infarction after bypass surgery. The degree of patency of the vein graft has been classified according to four levels. Normal – non-significant stenosis – significant stenosis (≥ 50% diameter stenosis) and occluded grafts. As the graft angiogram uses contrast injected into the lumen of the vein grafts, only the lumen is visible but not the vein wall itself where the atheromatosis and the atherosclerotic process is located. Therefore it is impossible with this method to see neither the early stages of atherosclerosis in the vein wall nor the different plaque components in more advanced plaque as well as the total plaque burden which can be of great clinical importance.

Intravascular ultrasound (IVUS)
Intravascular ultrasound (IVUS) is a medical imaging methodology developed in the 1980s where a specially designed catheter with a miniaturized ultrasound probe (30-40 MHz) is attached to the distal end of the catheter. The proximal end of the catheter is attached to computerized ultrasound equipment. Under guidance of the cineangiogram the probe is placed distally in the native coronary artery or a vein graft and then an automated pullback device draws the probe back to the aortic root at a constant velocity allowing for an exact evaluation of the vessel off-line. The ultrasound images visualizes both the lumen and the entire vessel wall with a resolution of 0.2-0.5 mm allowing for the diagnosis of early stages of atherosclerosis, the progressive accumulation of plaque within the vessel wall over decades, evaluation of the severity of advanced lesions as well as to identify the components of the plaque (soft, fibrotic, calcified, lipid and mixed plaque). The more the plaque narrows the lumen the bigger the risk is for symptoms of angina pectoris and the more lipid a plaque contains (vulnerable plaques) the bigger the risk is for plaque rupture and subsequent myocardial infarction or sudden death. IVUS is of use to determine plaque volume within the wall of the artery. It can be especially useful in situations in which angiographic imaging is considered unreliable; such as for the lumen of ostial lesions or where angiographic images do not visualize lumen segments adequately, such as regions with multiple overlapping arterial segments. It is also used to guide PCI procedures as well as to assess the result of the stent expansion. It can also be used to evaluate the results of medical lipid-lowering therapy over time (plaque stabilisation).
Long-term outcome in CABG using the conventional vein harvesting technique

The long-term success of coronary artery bypass surgery (CABG) depends on continued patency of the bypass conduits. Over the years the autologous saphenous vein has been the most commonly used coronary graft material in CABG. The major problems using vein grafts are acute thrombosis and intimal hyperplasia which are the main causes of a graft occlusion rate of 15-20% during the first year. This is followed by a progressive atherosclerosis that usually starts at 3-5 years postoperatively leading to a graft occlusion rate exceeding 50% after 10-15 years and a freedom from angina of less than 40% after 10 years. A number of factors contribute to the variability of the coronary artery bypass graft patency and clinical outcome. Patient-related factors which increase the risk of graft failure include diabetes, dyslipidaemia, hypertension, smoking and impaired renal function.

However, the damage to the entire vein wall, especially endothelial injury caused by high pressure distension, that is performed during the conventional harvesting technique to overcome spasm in the vein which has been considered a major cause for early and late graft occlusion.

No-touch harvesting technique

A new no touch (NT) vein harvesting technique where the saphenous vein is harvested together with a pedicle of surrounding tissue was developed by Domingos Souza in early 1990s. The entire vein wall will be preserved including the endothelium, intima-media and adventitia as well as the network of vasa vasorum and the amount of the endothelial nitric oxide synthase (eNOS), not only originated from the luminal endothelium, but also from the media and adventitia. This is illustrated in Figure 4a-c. This results in an increased thromboresistance, superior vaso-relaxation and abolition of venospasm. Therefore there is no need for high pressure distension of the vein. In addition the surrounding tissue acts like a mechanical support to prevent kinking of the vein after insertion as a graft. This NT harvesting technique looked very promising with a potential to “minimize” the problems related to the conventional harvesting technique i.e the acute thrombosis and subacute intimal hyperplasia in short-term as well as slowing down the process of atherosclerosis in long-term.
Figure 4a
The C vein and the NT vein

Figure 4b
The vein wall after harvesting (scanning electron micrograph)

Conventional technique (stretched and damaged) No touch technique (entire vein wall intact)
Figure 4c
Endothelium after harvesting (scanning electron micrograph)

No touch technique (endothelium intact)    Conventional technique (endothelium partially lost)

Figure 4d
eNOS in the endothelium

Conventional technique (eNOS almost lost)    No touch technique (eNOS intact)

Left panels are autoradiographs where NOS is shown as white grains on a black background (under dark-field illumination). Right panels are hematoxylin and eosin stained tissue underlying the autoradiographs.
Background to the thesis

In 1993 a prospective randomized CABG study was initiated to compare the NT vein harvesting technique with the conventional (C) harvesting technique and an intermediate harvesting technique (I) in patients with stable angina pectoris. There were 52 patients in each group. A cineangiographic short-term follow-up at 1,5 years after the operation showed a significantly higher patency rate for vein grafts in the NT group (95.4%) compared to both the C and I – harvesting groups (89 resp 86%) \(^4\). The I group was excluded from further follow-up studies due to the lowest graft patency at 1,5 year, and also due to limited economical resources.

Aim of the studies

Paper I
We tested the hypothesis that the NT vein grafts would maintain a higher patency rate compared to the conventional vein grafts at long-term follow-up (8,5 years).

Paper II
We tested the hypothesis that the superior long-term patency rate in the no-touch group after 8.5 years would be transferred into a better clinical outcome compared to the conventional group.

Paper III
We tested the hypothesis that the superior long-term patency rate using no-touch vein harvesting technique was due to a reduced progression of atherosclerotic disease and this was evaluated by performing both a cineangiogram and an intravascular ultrasound assessment both at 1,5 years and 8.5 years.

Paper IV
We tested the hypothesis that the delayed atherosclerotic process found in the no touch vein grafts at 8.5 years follow-up would be transferred into a better left ventricle function as well as an improved clinical outcome after 16 years compared to the conventional group.
## Study groups

A summary of study populations and criteria for exclusion for all four studies is shown in Table 1.

### Table 1

Study population and exclusion criteria in paper I – IV

<table>
<thead>
<tr>
<th>Paper</th>
<th>Study population</th>
<th>Exclusion criteria</th>
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<tr>
<td>I</td>
<td>In a randomized longitudinal single center study performed between 1993 to 1996, 156 patients were allocated randomly to 3 groups of 52 patients each according to 3 vein graft harvesting techniques. All patients alive in this study who were randomized to either the conventional or no touch vein graft harvesting group was offered a cineangiographic long-term follow-up at 8.5 years.</td>
<td>Age &gt; 70 years, unstable angina, combined procedure, redo CABG, severe peripheral vascular disease, insulin-dependent diabetes mellitus, serum creatinine &gt; 120 micromol/L, preventive use of anticoagulants, coagulopathy</td>
</tr>
<tr>
<td>II</td>
<td>All patients alive in the C-group and the NT-group after 8.5 years underwent a clinical follow-up. The cause of death of all deceased patients was established</td>
<td>None</td>
</tr>
<tr>
<td>III</td>
<td>All patients in the C-group and the NT-group who underwent the short and long-term cineangiographic follow-up and gave their written consent was evaluated by IVUS in the vein grafts considered normal by the cineangiogram</td>
<td>If the patient declined to participate in this substudy</td>
</tr>
<tr>
<td>IV</td>
<td>All patients alive in the C-group and the NT-group after 16 years underwent a complete clinical follow-up and all patients participating in the long-term CT-angiogram of the vein grafts underwent a complete ecocardiographic follow-up. The cause of death of all deceased patients was established</td>
<td>None</td>
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Methods

Vein harvesting procedure.
In all groups, the veins were harvested and implanted by the same surgeon. While the assistant surgeon took down the left internal thoracic artery (LITA) the head surgeon harvested the vein; thereafter they switched positions.

Vein harvesting technique
In paper I three different types of vein harvesting technique were tested.

Group C. The SV was exposed by a longitudinal leg incision, the adventitia stripped off, and side branches ligated. The vein was removed from the leg immediately after dissection, manually distended with saline at 300 mm Hg for 1 minute using a syringe connected to a manometer and stored in saline at room temperature.

Group NT. The SV was exposed by a longitudinal incision and all visible side branches ligated. The vein was then isolated together with a pedicle of surrounding tissue and left in situ until extracorporeal circulation was started to allow continuous heparinized blood perfusion. After removal, the vein was stored in blood obtained from the aortic cannula before cooling. To check for leakage from the distal anastomosis, the proximal end of the graft was briefly connected to the arterial cannula. Accordingly, the graft was neither flushed nor distended manually.

Group I. The SV was dissected as in group C. Instead of manual distension, the vein was left in situ and covered with a sponge moistened in saline-papavarine solution (1 mg/mL) until extracorporeal circulation was started. The vein was then removed and stored in blood obtained from the patient’s aortic cannula.

Cineangiography

Study group
In the long-term study (8.5 years), 74 patients (202 grafts) underwent a cineangiographic follow-up, including 37 patients (101 grafts) in the NT-group and 37 patients (101 grafts) in the C-group. Ninety-one out of 101 grafts in the NT-group and 77 out of 101 grafts in the C-group were open and evaluated according to the degree of patency as established by cineangiogram.
Cineangiography and analysis

In paper I and in paper III the graft cineangiograms were performed according to Judkins technique. Low osmolarity Visipaque contrast medium, 320 mg iodine/mL (Nycomed Amersham AB Stockholm) was used. All contrast injections were performed manually. All vein grafts were visualized in at least two projections. The cineangiographic assessment was performed by one radiologist with over 10 years experience of coronary angiography and who was blinded to which group the patient belonged. A graft was judged as occluded when the graft was not opaque. Usually, however, a slight bulge could be seen at the aortic anastomosis of the occluded graft. In patent vein grafts a stenosis was judged as significant when the narrowing of the lumen diameter was ≥ 50% and non-significant if < 50% compared with the normal lumen size of the vessel.

IVUS

Study group

In paper III an IVUS examination was performed in 17 grafts in the NT-group and 16 grafts in the C-group at short-term (1.5 years) and in 29 grafts in NT-group and 28 grafts in the C-group in the long-term (8.5 years) in vein grafts considered to be normal by the cineangiogram. The remaining patients refrained from participating in the IVUS substudy. The study was approved by the ethics committee at our hospital; patients were included after providing written informed consent.

IVUS-system and procedure

In paper 3 an IVUS system (Cardiovascular Imaging System, Inc., Boston Scientific/Scimed, Inc.) was used with a 30 MHz transducer mounted on the end of a flexible shaft that rotated at 1,800 rpm (2.9 Fr or 3.2 Fr imaging sheath). The IVUS examination of the vein grafts was performed following administration of 0.1–0.2 mg of intragraft nitroglycerin and 12500 IU of heparin iv to maintain the activated clotting time > 300 seconds. Under the guidance of the cineangiogram the IVUS transducer was advanced in the vein grafts as close as possible to the junction of the graft and the native coronary artery. The imaging procedure was performed using a motorized transducer pullback device that drew the IVUS transducer in a constant velocity (0.5 mm/s) from the distal position back to the aorto-ostial junction. The IVUS recording was stored on a S-VHS for further off-line analysis.
**IVUS analysis**

All IVUS analysis and calculations were performed manually by using the calculation program incorporated in the IVUS system.

**Graft lumen volumes**

For each vein graft, the lumen area was calculated every millimetre throughout the entire graft. The graft lumen volume was calculated as follows. The lumen area was considered circular with an area of $\pi r^2$. The lumen volume between two lumen areas separated by 1 millimetre was considered a cylinder. The average area of two lumen areas was calculated and multiplied with 1 millimetre (height of the cylinder) which gave the volume of a lumen cylinder. The cylinder volumes were then summed through the entire vein graft to obtain the graft lumen volume.

**Intimal thickness**

The (lumen + intimal) area was calculated every second millimetre as well as the lumen area (in the same way as with the lumen volumes above) and from these measurements you could calculate an average intimal thickness every second millimetre and finally an average intimal thickness of the entire vein graft was calculated.

**Plaque**

The (lumen + intima-media) area and lumen area were calculated every second millimetre. The plaque area was calculated by subtracting the lumen area from the (lumen + intima-media) area. An ecoluscent area within the intima-media was considered a lipid pool according to the ACC clinical expert concensus document from JACC 2001 of IVUS studies. The lipid, fibrosis and calcification content was evaluated and considered significant if detected in an arc $\geq 30$ degrees in two consecutive images two millimetres apart.
IVUS variables
The evaluated IVUS variables included graft lumen volume, mean and maximal intimal thickness, intimal hyperplasia, % intimal hyperplasia of total graft length, occurrence of plaque, plaque grading (soft, lipid, fibrotic, calcified, mixed), maximal plaque thickness and % plaque burden of total graft length.

Echocardiography (ECHO)

Study group
At 16 years follow-up, 34 patient out of 37 patients in the NT-group and 31 out of 37 patients in the C-group underwent an echocardiography examination. The remaining patients were unable to participate due to comorbidities.

Echocardiography system
A commercially available echocardiography system GE Vivid E 9 ultrasound system from GE Healthcare, General Electric Company, USA was used and a 3.5 MHz transducer.

Echocardiography analysis
The left ventricular ejection fraction (EF) was estimated using the Simpsons modified biplane method as (end diastolic volume – end systolic volume/end diastolic volume) x 100. The end diastolic and end systolic volumes were calculated in both apical 4-chamber view and 2-chamber view by outlining the inner endocardium at end diastole and end systole in both projections and a calculation program in the cardiac ultrasound machine automatically calculated the ejection fraction (Figure 5a). The size of the left and right atrium in cm² was calculated in the 4-chamber view by tracing the areas manually at end systole using a caliper incorporated in the echo system (Figure 5b). The size of the atriums was also corrected for the body surface. The left ventricular diastolic function was assessed by multiple Doppler measurements. The E-wave (early phase) and the A-wave (atrium contraction) Doppler signal of the blood flow over the mitral valve during diastole in the 4-chamber view was measured (m/s). The E/A ratio was then calculated. The tissue Doppler signal amplitude (e’) was assessed from the myocardium just below the AV-plane in the left ventricle in the 4-chamber view in both septal and lateral positions (cm/s). The E/e’-ratio was also calculated; E is the
maximal flow velocity of the early mitral inflow in the left ventricle and $e'$ is the average of the septal and lateral tissue Doppler signal amplitude in the position above.
Figure 5a
Principle for measurement of ejection fraction using the Simpsons modified biplane

2. Zoom on the LV
3. Trace the LV diastolic endocardial border

4. Roll the trackball to systole in the same cardiac cycle
5. Trace the LV systolic endocardial border

Figure 5b
Measurement of the left atrium size
Clinical follow-up at 8,5 and 15 years

Study groups
In paper II a clinical follow-up was performed at 8.5 years of all patients alive (49 patients in group NT and 44 patients in group C) and in paper IV a clinical follow-up was performed at 16 years in all patients alive (37 patients in both groups) by one cardiologist blinded to which study group the patient belonged.

Clinical analysis
The patients were assessed with respect to reangina using the Canadian Cardiovascular Society (CCS) classification I–IV as well as the occurrence of myocardial infarction and new revascularization during follow-up. In patients free from angina the New York Heart Association (NYHA) classification I-IV was used. Cardiovascular risk factors, complete lipid status, B-glucose, BNP (brain natriuretic peptide) and blood pressure were established. Hypertension was defined as blood pressure >140/90 mm Hg, LDL> 2.5 mmol/L was considered as hyperlipidemia. A BNP value ≥ 150 was considered pathological. The cause of death in all deceased patients was established by death certificate or medical records. In all patients who underwent a cineangiogram at 8,5 years, either as part of the long-term follow-up or due to acute coronary syndrome or recurrent angina, the status of the grafts and the coronary arteries was correlated with the patients’ clinical status.

Statistical Analysis

Paper I
Patency of graft: An outcome with two states (ie, patency or occlusion) was analyzed with logistic regression models and with Fisher’s exact test for 2-by-2 tables. The main predictor variable was the 2 different harvesting techniques: conventional and no-touch. Additional predictor variables for the logistic regression were examined individually, and those expected to have a significant relation to the outcome and also having an uneven distribution across the 2 harvesting techniques were selected and used in the final model. The logistic regression model was analyzed with graft as the unit of analysis with a total of 202 grafts. However, all patients but 1 had more than 1 graft, with a maximum number of 3 grafts per patient. Multiple grafts per patient might introduce dependencies between the observations, a violation of one of the
basic assumptions for the ordinary logistic regression model. A special form of the model was therefore used to allow for clustered observations, with each patient forming a separate cluster. The \( P \) values and confidence intervals were in this way corrected for the problem with correlated observations. This correction was not possible for Fisher exact test; therefore the primary results are those from the logistic regression. The outcome parameter of interest in the logistic regression model is the odds ratio (OR) and in this analysis all OR above 1.0 indicates increased chance for patency, and an OR below 1.0, less chance. Before reaching the final model we examined the possibility that the additional predictor variables had significant interactions with the main predictor variable, the harvesting technique. Computations were performed with SAS, version 8.2 (SAS Institute Inc, Cary, NC) and the procedure for the logistic model was GENMOD, with the ALR algorithm 9.

**Paper II**

Differences between the two randomized groups were tested with Student’s t-test for independent samples as concerns quantitative variables assumed to follow a normal distribution. For qualitative variables as well as dichotomous variables a chi-square test for group differences was applied. We performed this analysis with algorithms especially adopted for small samples. P-values <0.05 are considered statistically significant. The statistical program StatXact (Cytel Inc, Mi, US) was used for the computations since it contains the suitable small sample algorithms.

**Paper III**

Data are presented as absolute and relative frequencies, \( n \) (%), or mean values and standard deviation (SD) depending on metric properties. Group differences in nominal and ordinal data were analyzed by the chi-square test adapted for small samples. Data with metric properties corresponding to continuous data were analyzed with a mixed model similar to a linear regression analysis extended with correlations between repeated measures in the case of more than one graft from the same patient. The model estimated the difference in averages between the NT- and C-groups; the difference was supplemented with 95% confidence interval (CI) and the p-value for no difference between the groups. In all analyses, a p value <0.05 was considered statistically significant. The computations were performed with the program packages StatXact (Cytel Inc.) and SAS (SAS Inc.).
**Paper IV**

Differences between the two randomized groups at the pre-specified time-points (pre-study, 8.5 years or 15 years) were tested with Student’s t-test for independent samples as concerns quantitative variables assumed to follow a normal distribution. An analysis for all three time-points simultaneously was done with a GLM (General Linear Model) for repeated measures. This analysis was supplemented with Student’s t-test for each one of the evaluation time-points and in this case the Bonferroni correction for multiple testing was applied. For qualitative variables as well as dichotomous variables Fisher’s exact test and extensions of the Fisher test was applied. We performed this analysis with algorithms especially adopted for small samples. P-values < 0.05 are considered statistically significant. The statistical programs StatXact, version 8 (www.cytel.com/software/statxact) and SPSS, version 20 (www.ibm.com/software/se/analytics/spss/) were used for the computations.

**Ethics**

All studies were approved by the ethics committee either as a part of the main study (study I, II and IV) or separately in study III. The patients were included after providing a written informed consent.
Specific methods

Conventional vein harvesting technique (Paper I-IV)
The Saphenous vein was exposed by a longitudinal leg incision, the adventitia stripped off, and side branches ligated. The vein was removed from the leg immediately after dissection, manually distended with saline at 300 mmHg for 1 minute using a syringe connected to a manometer and stored in saline at room temperature. (Figure 6a)

No touch vein harvesting technique (Paper I-IV)
Group NT. The SV was exposed by a longitudinal incision and all visible side branches ligated. The vein was then isolated together with a pedicle of surrounding tissue and left in situ until extracorporeal circulation was started to allow continuous heparinized blood perfusion. After removal, the vein was stored in blood obtained from the aortic cannula before cooling. To check for leakage from the distal anastomosis, the proximal end of the graft was briefly connected to the arterial cannula. Accordingly, the graft was neither flushed nor distended manually (Figure 6b)

Figure 6a                                                          Figure 6b
Conventional vein harvesting                                        No touch vein harvesting
Figure 7 shows examples of the cineangiographic image in normal excessively long NT vein grafts and figure 8 a-c shows examples of IVUS images in vein grafts considered to be normal by the cineangiogram.

**Figure 7**
Cineangiographic images

Excessively long NT vein grafts without kinking

**Figure 8 a-c**
IVUS images in vein grafts considered normal by the cineangiogram

<table>
<thead>
<tr>
<th>C-vein graft</th>
<th>NT vein graft</th>
<th>C-vein graft</th>
</tr>
</thead>
<tbody>
<tr>
<td>Soft plaque (14→24)</td>
<td>Calcified plaque (12→22)</td>
<td>Lipid containing plaque (12-14)</td>
</tr>
</tbody>
</table>
Results

Paper I
A long-term (8.5 years) cineangiographic follow-up was performed in a total of 74 patients, 37 patients (101 vein grafts) in both the NT and the C group. There were 87 single grafts, 11 double sequential grafts, and 3 triple sequential grafts in group C and in the group NT there were 87 single grafts and 14 double sequential grafts. The patency rate was 90% (91/101) for group NT and 76% (77/101) for group C (p = .01). A total of 27% of the veins in the NT group were considered of poor quality perioperatively compared to 11% in the C group and the patency rate in these veins was 85.5% versus 36.4% (p = .002) in favour of the NT group. In the vein grafts with a low flow rate perioperatively (< 40 mL/min) the patency rate was 95.7% in the NT-group versus 72% in the C group (p = .002). Patent grafts that had flow rates ≥ 40 mL/min were 80.4% in group C versus 85.5% in the NT group (ns). Four sequential vein grafts in the C group were occluded versus none in the NT group. The multivariate analysis showed that the most important factors for graft patency were the technique of vein harvesting (OR =3.7, p = .007) for the no-touch versus the conventional technique and the vein quality at harvesting (OR = 3.2, p = .007) for veins that were of good quality. By comparison the patency rate of the left internal thoracic artery (LITA) was 90% (63/70). Most of the occluded LITAs were anastomosed to the LAD with 50% to 70% stenosis.

Paper II
The clinical outcome of all randomized patients (52 patients in each group) during the 8.5 years follow-up period could be established. There were no cardiac deaths in group NT versus three in group C. Seven PCI-revascularisations had been performed in the NT group versus three in the C group. Progressive atherosclerosis in native coronary arteries was found to be the underlying cause in four patients in group NT and in one patient in group C and vein graft failure in the remaining three respective one patient in the groups. There were a trend towards fewer patients with graft occlusion (24.3 vs. 43.2%; p=0.14) and patients with cardiac death or myocardial infarction (3.8 vs. 13.4%; p = 0.16) in group NT compared with group C. There were more patients free from angina (75.5 vs. 63.6%; p = 0.26) and significantly more patients free from angina and in NYHA class I (67.3 vs. 43.2%; p = 0.02) in group NT compared with group C. Nine patients in group NT had occluded grafts compared with 16 patients in group C. In group NT eight patients had one occluded graft and one patient had two.
occluded grafts. Three patients were free from angina, five patients had reangina and one patient suffered from a myocardial infarction. In group C 16 patients had graft occlusions, eleven patients had one graft occluded, four patients had two grafts occluded and one patient had all three grafts occluded. Six patients were free from angina, six patients had reangina and four patients suffered from a myocardial infarction. The only patient with all his grafts occluded at follow-up (including LIMA) was completely asymptomatic.

**Paper III**

The cineangiographic evaluation could be performed in all patent vein grafts, 118 grafts (45 patients) in the NT group and 112 grafts (46 patients) in the C group at short-term and in 91 grafts (37 patients) in the NT group and 77 grafts (37 patients) in the C group at long-term follow-up. The IVUS examination was performed and analysed in 15 vein grafts (eight patients) in the NT group and 14 vein grafts (eight patients) in the C group in short-term and in 27 vein grafts (14 patients) in the NT group and 26 vein grafts (15 patients) in the C group in long-term. No serious complications occurred during the procedures. In short-term follow-up there were significantly more angiographically normal vein grafts in the NT group compared with the C group (89% vs 75%; p = 0.006). IVUS showed in the NT group less mean intimal thickness (0.43 (0.07) mm vs 0.52 (0.08) mm; p = 0.03), less vein grafts with considerable intimal hyperplasia (≥ 0.9 mm; 20% vs 78.6%; p = 0.011) and fewer patients having vein grafts containing considerable hyperplasia (≥0.9 mm; 25% vs 100%; p = 0.007). No lipid deposits, fibrosis or calcifications were detected in any graft in the two groups. In the long-term follow-up the cineangiogram showed more normal vein grafts, 91.2% in the NT group compared with 83.1% in the C group and there were fewer vein grafts with significant stenosis (7.7% in the NT group vs 15.6% in the C group). IVUS showed fewer vein grafts containing multiple plaques (14.8% vs 50%; p = 0.008), less advanced plaque with lipid (11.8% vs 63.9%; p = 0.0004) and less maximal plaque thickness (1.04 (0.23) mm vs 1.32 (0.25) mm; p = 0.02) in the NT group compared with the C group.
Paper IV

Clinical: Fifteen patients in each group had died during the 16 years of follow-up. Six patients in the NT group and seven patients in the C group suffered from cardiac deaths (myocardial infarction, heart failure or arrhythmia). However for five patients in the NT-group and two patients in the C-group data are still missing from the Swedish death registry. The remaining 37 patients alive in both groups were followed clinically. Recurrent angina occurred in 14 patients in the NT-group and in 17 patients in the C group. Five patients in the NT-group suffered from an acute myocardial infarction compared to 10 patients in the C group (p = 0.25). Ten patients in the NT-group and 13 patients in the C group underwent an ischemia-driven cineangiogram. Eight patients in both groups had a PCI-revascularisation either in a vein graft, native coronary artery or both. In the remaining patients no PCI procedure was possible and they were treated medically. Twenty three patients in the NT-group were free from angina compared to 20 patients in the C group. In the NT group, 18 patients out of 23 were classified as NYHA-class I versus 10 patients out of 19 in the C-group. However this difference disappeared when we adjusted for other comorbidities that lowered the NYHA classification in these patients.

Echocardiography: In the NT-group 34 patient out of 37 patients and in the C-group 31 out of 37 patients underwent an echocardiography examination. The remaining patients were unable to participate due to comorbidities. The left ventricle ejection fraction was preserved in the NT group compared with the C group (57.9 ± 9.5 vs 49.4 ± 13.3%; p = 0.004). All 34 patients in the NT group had sinus rhythm compared to 26 out of 31 (83.9 %) in the C-group (p = 0.021). In the patients with sinus rhythm and no mitral valve disease the left atrium was significantly larger in the C-group compared with the NT group (23.9 ± 3.4 cm² vs 21.7 ± 4.3 cm²; p = 0.034) also when the size of the left atrium was corrected for the body surface (12.0 ± 1.8 cm² versus 10.9 ± 2.1 cm² ; p = 0.039). The BNP (brain natriutric peptide), a marker of incipient or overt heart failure (if ≥ 150) was elevated in 30.3% in the NT-group compared to 37.9% in the C-group. The smaller left atrium size in the patients with sinus rhythm, a lower BNP value and fewer patients with atrial fibrillation in the no touch group indicated a better left ventricle diastolic function.
Discussion

The long-term success of coronary artery bypass surgery (CABG) depends on continued patency of the bypass conduits. Over the years the conventional harvesting technique of the saphenous vein has been the procedure of choice for preparing the vein. The major problems using vein grafts prepared this way are acute thrombosis and intimal hyperplasia with an occlusion rate of 15-20% during the first year. This is followed by a progressive atherosclerosis that usually starts at 3-5 years postoperatively leading to a graft occlusion rate exceeding 50% after 10-15 years and a freedom from angina of less than 40% after 10 years. By using the NT-vein harvesting technique at CABG the entire vein wall will be preserved including the preservation of the endothelial nitric oxide synthase (eNOS), not only of the luminal endothelium, but also of the media and adventitia, resulting in increased thromboresistance, superior vaso-relaxation and abolition of venospasm.

The hypothesis that is tested in this thesis is that the NT-technique in CABG has the potential to “minimize” all the problems related to the conventional harvesting technique i.e. the acute thrombosis and subacute intimal hyperplasia in short-term as well as slowing down the process of atherosclerosis in long-term.

In short-term, the cineangiographic and IVUS follow-up at 1.5 years showed an early advantage for the NT group with a significantly lower graft occlusion rate reflecting a lowered thrombosis rate in this group and, in addition, IVUS revealed a significant decrease in intimal hyperplasia. Furthermore, in the conventional group, IVUS revealed a 4 fold increase in the number of grafts containing considerable hyperplasia and the cineangiogram showed a doubling of vein grafts containing stenosis. This data indicated a more advanced stage of the early atherosclerotic process in the conventional vein group which in turn would lead to a more advanced plaque disease in this group as well as an increasing difference in graft occlusion rate in advantages of the NT-technique at 8.5 years.

The IVUS substudy at this time provided overwhelming evidence that the process of atherosclerosis had been slowed down dramatically using the NT-technique which could be seen in many levels from a 50% reduction in the total number of plaques, a 70% reduction in the number of grafts containing multiple plaques, a more than 80% reduction of advanced plaque containing lipid (prone to rupture), a 25% reduction in plaque thickness, a 30% reduction in plaque length, a 40% reduction in the overall plaque burden and finally a 25% reduction in the number of patients having vein grafts containing plaques. The cineangiogram showed a 50% reduction in the number of significantly stenosed vein grafts as well as a 40% reduction in graft occlusion.
rate compared to the conventional harvesting technique. These dramatic differences occurred despite two facts that counteracted the NT-group. At first the multivariate analysis showed that the second most important surgical factors for graft patency after the technique of harvesting was the vein quality before implantation (odds ratio = 3.2, \( P = .007 \)) which was of poor quality in 27% of the grafts in the NT-group compared to only 11% in the C group at harvesting. Secondly the patency rate after 8,5 years in the conventional group (76%) was higher than ever reported before and still there was a highly significant difference in advantage of the NT harvesting technique which in addition had a patency rate similar to LITA (both 90%) despite the fact that NT-grafts were grafted to smaller arteries with smaller run-off territories than LAD. We could also show a significant clinical benefit of the slowing of the atherosclerotic process.

Around 67% of the patients in the NT-group were totally asymptomatic at this time point compared to only 43% in the conventional group and this patient group has earlier been shown to have a quality of life equal to healthy people and this is the main purpose of all CABG surgery since the survival benefit is limited. This study was not powered from the beginning to show significant differences in hard cardiac clinical endpoints. There was a trend towards fewer patients with recurrent angina, myocardial infarction and cardiac deaths (infarction, heart failure and sudden death) although this was not significant. However the number of revascularization procedures was low in both groups and there was no difference in PCI-revascularisation between the two groups. It was almost impossible in the ischemia-driven revascularizations to recognize from the medical records with accuracy if the culprit lesion was diseased in a vein graft or a new significant stenosis in the native coronary artery, since no myocardial scintigrams were performed to identify the culprit lesion. A PCI-procedure was performed if the stenosis was eligible.

At 8,5 years, the left ventricular systolic function as assessed by ejection fraction (EF) was still found to be preserved in both groups (58 v 57%).

With the support of the IVUS and the cineangiographic data at 8.5 years showing a much more advanced atherosclerosis in the conventional group at all levels we hypothesized that in real long-term at 16 years with a mean age of the patients around 73 years there would still be an increasing difference in graft patency rate between the two groups in advantage of the NT technique. We also believed that the supposed increased number of graft occlusions in the C group could have a significant impact on the left ventricular systolic and diastolic function. In addition we thought that maybe there would be a detectable significant difference in hard cardiac endpoint between the groups in this time-span despite the size of the study.
At 16 years we found that the graft patency rate was still excellent in the NT group but also that the patency rate in the conventional group was higher than ever earlier reported for vein grafts (in manuscript). We also found that the left ventricular systolic function was still preserved at 16 years and unchanged compared to the 8.5 years follow-up in the NT-group (58%) but had fallen from 57% down to 49.4% in the conventional group and this difference in EF at 16 years was highly significant. The smaller size of the left atrium in patients with sinus rhythm, a lower BNP (brain natriuretic peptide) and the absence of atrial fibrillation indicated a better diastolic left ventricular function in the NT group.

Clinically there were still more totally asymptomatic patients in the NT group but the co-morbidities at an average age of 73 years obscured the significance. Despite a doubling of the number of patients suffering from a myocardial infarction during the 16 years of follow-up in the C group neither at 8.5 years nor at 16 years there was any significant difference in hard clinical endpoints; recurrent angina, myocardial infarction, cardiac revascularization or in cardiac deaths. The reason could be explained by the fact that this study was powered for detecting differences in graft patency rate and but not powered for hard clinical endpoints which would have demanded many more patients. This issue will be addressed in an ongoing multicenter study including 40 centres around the world with a planned inclusion of 1400 patients.

During the 16 years of follow-up period in this study there has been an increasing interest in a new concept using complete arterial vascularization instead of vein grafts due to its poor long-term patency and clinical outcome using the conventional harvesting technique. The superior patency rate and the excellent long-term results associated with the left internal thoracic artery (LITA) has stimulated the use of arterial grafts in order to overcome the limitations of saphenous vein grafts. Currently there is increasing use of bilateral internal thoracic arteries and the radial artery (RA) to achieve a complete arterial revascularization although there are problems associated with the use of arterial conduits. The sites from which they are removed may become ischemic and sternal complications may be more common when 2 internal thoracic arteries are used, particularly in insulin-dependent diabetic patients. The potential for graft spasm is another serious concern that occurs with radial grafts as well as other free arterial grafts. In addition the severity of the stenosis in the native coronary artery must be > 70% otherwise there is a substantial risk for competitive flow and graft occlusion. Nevertheless a lot of papers have been published on this issue with very promising results. The patency rate of the radial artery is reported to be 80-90% at 5 (-10) years follow-up and almost 82% after 13.1 years in the longest follow-up
In comparison the patency rate in our study is 90% in the NT group at 8.5 years and the preliminary patency rate after 16 years is excellent (in manuscript).

There are reports of improved long-term survival, a low incidence of cardiac death and a low frequency of reoperations after 9.2 years using arterial graft \(^2,39\). If we wish to compare the clinical long-term results for the patients in the NT group with total arterial revascularization reported by others, we must make the comparison after approximately 8 years, the longest present follow-up for most all-arterial studies \(^1,34,41\). The arterial revascularization studies have shown a seven year survival rate of 88-91% compared to 94% in group NT, freedom from cardiac death was 92–96% versus 100% in group NT, freedom from myocardial infarction 92-97% versus 98% in group NT, freedom from recurrent angina 85-92% versus 75% in group NT, freedom from any cardiac event 78-85% versus 74% in group NT. In a recent study Puskas et al showed that the use of bilateral internal thoracic artery had a significantly increased survival rate at 8 years compared to the use of a single internal thoracic artery (89.3% v 68.3%) irrespective the diabetic status of the patients \(^36\). Achouh et al reported a total survival rate of 80% and a cardiac-related mortality of 7% after 9.2 years \(^2\). However there is some comparative information from real long-term all-arterial follow-up. Locker et al (in matched groups) showed a significantly better 15 year survival in the arterial revascularization group compared to the LIMA + saphenous vein group (70% v 60%) \(^25\). The cardiac related mortality was not commented in this study. In our study the 16 year survival was 71% with a cardiac-related mortality of 12% in the NT-group.

There is not so much published about the long-term ejection fraction after by-pass surgery. Achouh et al reported no change in ventricular function for patients with arterial revascularization after 9.2 years (55% compared to 56.7% preoperative) \(^2\). However in that publication all ejection fraction values within normal range were assigned a value of 65% which does not permit a direct comparison with our own 8.5 years follow-up where the ejection fraction was preserved in both groups (58 v 57%). So far there is no study published that shows the 16 years ejection fraction results using arterial revascularization.

It is well known that the treatment of the traditional risk factors after CABG is extremely important to slow down the atherosclerotic process in both the vein grafts and the native coronary arteries. In this study we found at 16 years a low number of smokers (10-15%). However the number of patients with hypertension (> 140/90 mmHg), although treated, was as high as 20-30% and the amount of patients with elevated b-
glucose $> 6.1$ mmol/L, which by definition is considered to be overt diabetes, was found in almost 60 percent in the no-touch group and more than 40% in the C-group, which was about doubled compared to the known number of diabetic patients in the two groups.

Probably the most important risk factor is the lipid levels. Despite a high number of patients treated with statins (around 90%) the S-LDL levels were still elevated in both groups, (2.5 – 2.7 mmol/l). However this was a significant improvement compared to the results from 8.5 years follow-up in the same study where the LDL level was 3.2 - 3.4 mmol/l. The percentage of patients reaching LDL $\leq 2.5$ mmol/l was about 58% at 16 years follow-up, compared to only about 25% after 8.5 years. This improvement in lipid control is important since a previous post CABG trial showed that aggressive reduction of LDL-cholesterol below 2.5 mmol/l, compared to moderate lowering to about 3.5 mmol/l, significantly reduced the progression of atherosclerosis in grafts. However the accepted goals for optimal LDL-treatment according to European guidelines from 2010 in this category of patients is $\leq 1.8$ mmol/l. This is obtained in only 20-25% of the patients in both groups at 16 years follow-up.

**Conclusion**

The no touch vein harvesting technique for CABG preserves the entire vein wall and slows down the progression of the atherosclerotic process and consequently provides an excellent patency rate and a preserved left ventricular ejection fraction up to 16 years follow-up and infers an improved left ventricular diastolic function. This thesis revives the position of the saphenous vein as an important conduit in CABG surgery with long-term results at least comparable with all-arterial revascularization.

**Future aspects**

Despite the fact that the no touch vein graft harvesting technique has a superior patency rate compared to the conventional vein harvesting technique, a significantly better patency rate than the radial artery in the only randomized study performed so far (Dreifeldt et al to be published in Ann Thorac Surg) and a patency rate after both 8.5 years and 16 years similar to LITA there has been a very modest interest in the NT approach to improve the CABG outcome worldwide especially among the thoracic centers in the United States. American centers showed no interest in participating in
the present ongoing multicenter randomized study including 40 centres around the world with a planned inclusion of 1400 patients to test the NT technique versus the conventional technique. This could partly be explained by economical aspects, a more complicated operation technique where endoscopic vein harvesting is not available so far and maybe cosmetic reasons with larger local scars on the leg. There is also a great resistance towards the no touch technique from those centra where the concept all-arterial revascularisation is the “gold standard”. However we will continue to publish long-term results with the no touch technique. The first paper in pipeline will be the CT angiographic results after 16 years in our study which are very interesting. Furthermore we will publish the angiographic patency rate after 10-15 years using the no touch vein grafting to LAD. The results are amazing. Finally we will evaluate the results of PCI using stent deployment in treating restenosis in vein grafts prepared either the no touch or the conventional way.

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