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New diagnostic and interventional methods in invasive cardiology

Ph.D. Thesis

by

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PUBLICATIONS

Full papers

I. Pálinkás A, Varga A, Forster T, Sepp R, Ruzsa Z, Ungi I, Csanády M. Detection of coronary artery stenosis with transthoracal echocardiography. Cardiologia Hungarica 32(2), 95-96, 2002.

II. Ruzsa Z, Nagy E, Ungi I, Forster T, Pálinkás A, Nemes A. Additional help to diagnose significant left main coronary artery stenosis: Doppler echocardiography. Hellenic Journal of Cardiology. 2010; 51: 540-543

IF:1.172

III. Ruzsa Z., Havasi K, Forster T, Tóth K, Tóth G, Ungi I, Varga A. Borderine coronary artery lesions: Detection of functional severity using different methods. Cardiologia Hungarica 2008; 38: 1-6

IV. Ruzsa Z, Palinkas A, ForsterT, Ungi I, Varga A Angiographically borderline left main coronary artery lesions: correlation of transthoracic Doppler echocardiography and intravascular ultrasound: a pilot study. Cardiovascular Ultrasound 2011 Jun 14;9(1):19.

IF:1.561

V. Ruzsa Z, Ungi I, Horváth T, Sepp R, Zimmermann Z, Thury A, Jambrik Z, Sasi V, Tóth G, Forster T, Nemes A. Five-year experience with transradial coronary angioplasty in ST-segment-elevation myocardial infarction. Cardiovasc Revasc Med. 2009 Apr-Jun;10(2):73-9.

VI. Pintér L, Cagiannos C, Ruzsa Z, Bakoyiannis C, Kolvenbach R. Report on initial experience with transradial access for carotid artery stenting. J Vasc Surg. 2007 Jun;45(6):1136-41.

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VII. Ruzsa Z, Tóth K, Koncz I, Gurzó M, Szelei B. Transradial renal stenting. Cardiologia Hungarica, 2009; 39; 40-42.

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INTRODUCTION

Ischemic heart disease is still one of the most serious problems facing modern cardiology and remains one of the leading causes of death in the developed countries. Coronary angiography is the standard procedure for assessing the severity of coronary artery stenosis; however, important limitations of coronary angiography has been clearly described (1-3) opening the door for invasive complimentary technologies such as intravascular ultrasound (IVUS) and fractional flow reserve (FFR) to improve accuracy in the assessment of coronary lesions. Intravascular ultrasound (IVUS) is a widely-used invasive method that provides accurate data about the dimensions of the lumen and wall of the vessels, and adequately visualizes the pathological changes of the endothelium (4). IVUS and pressure wire derived FFR measurements are the most common procedures used to assess the severity of borderline coronary stenosis (5,6). Although IVUS provides detailed anatomical information on the vessel lumen, it is an expensive and invasive procedure. In many cases, the planar 2-D silhouette of the arterial lumen may be unable to accurately define the severity of coronary stenosis, regardless of whether visual or quantitative methods are used (7). Myocardial blood flow is regulated at the level of the coronary arterioles. If myocardial oxygen consumption increases, coronary flow resistance decreases due to vasodilatation, thus increasing myocardial blood flow. Absolute flow reserve is defined as the ratio of hyperaemic to resting flow. When a flow-limiting stenosis is present, the dilatation of the distal microvasculature ensures proper and sufficient resting blood flow, but the maximum hyperaemic flow might be insufficient during exercise; in this case, the ratio of hyperaemic to resting flow is less than two. Several methods are used to measure coronary flow reserve (CFR). Invasive methods include intracoronary Doppler guidewire and intracoronary thermodilution (8-10); non-invasive methods include transesophageal echocardiography (11,12) and transthoracic echocardiography (13-15). Other procedures, such as positron emission tomography, are not widely available and/or are expensive (16).

The transradial approach to coronary, peripheral angiograpraphy and angioplasty has become a popular technique, however the place of the technique was questioned in the literature for the treatment of myocardial infarction and for carotid artery stenting.

THE PATHOPHYSIOLOGY OF MYOCARDIAL ISCHAEMIA

1. Coronary circulation

Although the heart chambers are filled with blood, it provides very little nourishment and oxygen to the tissues of the heart. The walls of the heart are too thick to be supplied by

diffusion alone. Instead, the tissues of the heart are supplied by a separate vascular supply committed only to the heart. The arterial supply to the heart arises from the base of the aorta as the right and left coronary arteries (running in the coronary sulcus). The venous drainage is via cardiac veins that return deoxygenated blood to the right atrium. The coronary arteries arise from the Ostia in the left and right sinuses of the aortic semilunar valve, course within the epicardium, and encircle the heart in the atrioventricular (coronary) and interventricular sulci**.** The coronary circulation supplies the heart with oxygen and nutrients to maintain cardiac function and thus supply the remainder of the body with blood. The systemic metabolic needs may change rapidly and widely, thus requiring adaptation of cardiac function and coronary blood flow. Imbalance in myocardial oxygen demand and supply can produce myocardial ischemia with contractile cardiac dysfunction, arrhythmias, infarction, and possible death. The flow throw the coronary artery is pulsatile, with characteristic phasic systolic and diastolic flow components. Systolic compression of the intramural coronary vessels causes mean systolic arterial flow to be reduced relative to diastolic flow, despite having a higher systolic driving pressure. The systolic flow wave has rapid, brief retrograde responses corresponding to phasic myocardial compliance over the cardiac cycle. Diastolic flow occurs during the relaxation phase after myocardial contraction with an abrupt increase above systolic levels and a gradual decline parallel with that of aortic diastolic pressure. Coronary venous flow is out of phase with coronary arterial flow, occurring predominantly in systole and nearly absent during diastole. The arterial and venous pulsatile flow characteristics describing the heart as a pump dependent on intramyocardial resistance. The intramyocardial capillary resistance influences both arterial and venous responses but predominantly acts in concert with outlet resistance. The coronary blood flow not only is phasic but also varies with the type of vessel and location in the myocardium. The nonlinear and time-dependent behaviour of the coronary flow may not be the neglible under specific experimental or clinical conditions.

Myocardial oxygen supply and demand relationship: The basic concept of the myocardial supply and demand relationship is that for any given oxygen need, the heart will supplied with a sufficient quantity to prevent underperfusion leading to ischemia or infarction. Myocardial oxygen demand (MVO2) has been indexed by the product of systolic aortic pressure and systolic duration. Myocardial oxygen supply (flow) can be indexed by the product of diastolic time and mean diastolic pressure. The heart, an aerobic organ, relies almost exclusively on the oxidation of substrates for energy generation. It can develop only a small oxygen debt. In a steady state, MVO2 provides an accurate measure of its total metabolism. MVO2 correlates

with the fraction of energy derived from the metabolism of fatty acids, which varies directly with the arterial concentration of fatty acids and inversely with that of glucose and insulin. The total metabolism of the arrested, quiescent heart is only a small fraction of that of the working organ.

Determinants of myocardial oxygen demand: The three major determinants of the MVO_2 are heart rate, myocardial contractility, and myocardial wall tension or stress (17).

Determinants of myocardial oxygen supply: *Oxygen transport and delivery*: Satisfactory oxygen transport and delivery require an adequate inspired quantity of oxygen and red blood cells with normally functioning haemoglobins. Hypoxia from pneumonia or carbon monoxide overdose, anaemia, or hemoglobinopathies can produce myocardial ischemia despite adequate coronary blood flow. *Regulation of coronary blood flow and resistance:* Approximately 75 percent of total coronary resistance occurs in the arterial system, which comprises conductance (R1), prearteriolar (R2), and arteriolar and myocardial capillary vessels (R3) (18).

Myocardial ischemia: Coronary artery disease is almost always due to athermatous narrowing and subsequent occlusion of the vessel. Early atheroma (from the Greek athera (porridge) and oma (lump)) is present from young adulthood onwards. A mature plaque is composed of two constituents, each associated with a particular cell population. The lipid core is mainly released from necrotic “foam cells”—monocyte derived macrophages, which migrate into the intima and ingest lipids. The connective tissue matrix is derived from smooth muscle cells, which migrate from the media into the intima, where they proliferate and change their phenotype to form a fibrous capsule around the lipid core. When a plaque produces a > 50% diameter stenosis (or > 75% reduction in cross sectional area), reduced blood flow through the coronary artery during exertion may lead to angina. The basic definition of myocardial ischemia is a greater myocardial tissue oxygen demand than oxygen supply. Anatomically, the most vulnerable layer of the heart is the subendocardium; because of the higher systolic wall stress in this layer compared to the mid- and epicardial layers, there exists a relatively greater metabolic demand. Coronary flow reserve (CFR), the capacity to increase coronary flow over basal levels, is normally about threefold in sedentary adults but can be six fold in world-class endurance athletes. Normally coronary blood flow can increase approximately four-to-six fold to meet increasing myocardial oxygen demands. This effect is mediated by vasodilation at the arteriolar bed, which reduces vascular resistance, thereby augmenting flow. The coronary reserve (CFR) represents the capacity of the coronary circulation to dilate following an increase in myocardial metabolic demands and can be

expressed by the difference between the hyperemic flow and the resting flow curve. In 1974, Lance K Gould (19) proposed the relationship between the anatomic condition and behaviour of coronary hyperaemic flow, whereby an inverse curvilinear relationship exists between the narrowing of lumen of coronary artery and hyperaemic capability, up to a completely abolished coronary reserve for stenosis >90%. This experimental paradigm can be accurately reproduced clinically in highly selected series of patients with single vessel disease, no myocardial infarction, no coronary collateral circulation, normal baseline function, no left ventricular hypertrophy, without evidence of coronary vasospasm, and off therapy at the time of testing. The perfect, predictable relationship found in the experimental animal or in a very selected patient population (20) is not so perfect in clinical practice (21,22), where many variables can modulate the imperfect match between epicardial coronary artery. stenosis and coronary flow reserve, such as the geometric characteristics of the stenosis, the presence of coronary collateral circulation, the microvascular component of coronary resistance, the presence of left ventricular hypertrophy modulating the myocardial extravascular component of coronary resistance, the viable or necrotic state of the myocardium distal to the stenosis, the presence of coronary macrovascular or microvascular spasm, and, last but not least, the presence of concomitant antiischemic therapy. CFR is a useful way to assess the physiological impact of coronary stenosis and the outcome of revascularization by coronary angioplasty or coronary artery bypass surgery. With either a pressure-monitoring or Doppler flow velocity wire one can measure the maximum pressure or coronary flow in comparison with the aortic response to the systemic administration of a vasodilator such as adenosine. Obstructions reducing coronary luminal diameter by less than 40% do not affect CFR, but reductions of >80% exhaust vasodilator reserve (23) (Coronary lesions less than 80% may show a poor vasodilator reserve response and therefore are candidates for angioplasty). Although the pressure and flow methods appear to have equivalent clinical value, the pressure measurements give additional information. Coronary artery “wedge” pressure distal to an inflated angioplasty balloon is normally less than 25% of aortic pressure; higher pressures reflect coronary collateral development (24).

VISUALISATION OF THE CORONARY ARTERIES WITH ULTRASOUND

1. Transthoracic echocardiography

Transthoracic Doppler echocardiography (TTDE) has been introduced as a new diagnostic approach to visualize coronary blood flow and measure CFR non-invasively for the LMCA, LAD (11-15, 25-28) and of the distal right coronary artery (29). TTDE for non-invasive

assessment of CFR provides useful quantitative information regarding the functional status of coronary arteries. In combination with coronary morphologic findings obtained from cardiac catheterization, CFR has relevant clinical implications for patients scheduled for invasive evaluation and treatment of coronary artery disease. TDE CFR assessment in the LAD and RDP of the right coronary artery closely agrees with invasive measurements (11-15, 25-29).

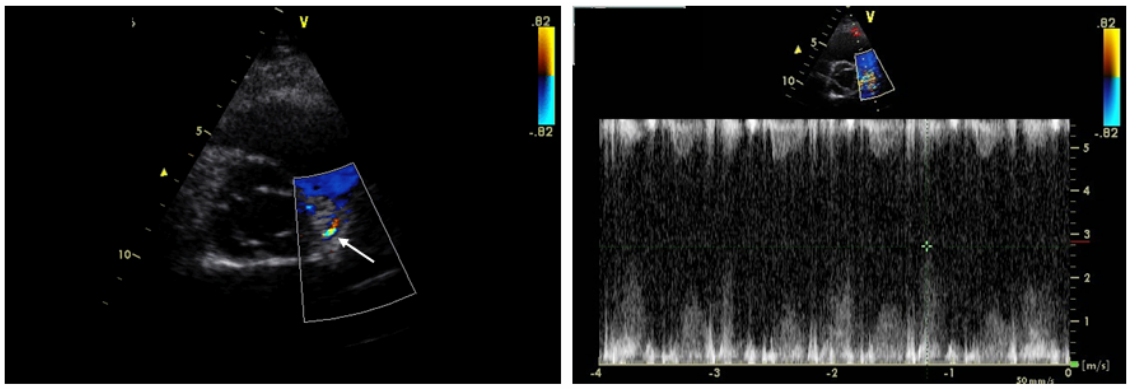


Figure 1. During TTE with pulsed-Doppler measurements (Toshiba Powervision 8000, Tokyo, Japan), significant increase in coronary flow velocities in distal LM after appropriate angle correction could be demonstrated.

2. Transoesophageal echocardiography and CFR measurement

Up to now, coronary flow reserve has been evaluated invasively in the cath. lab and in nuclear medicine through perfusion imaging. Only recently has coronary flow reserve entered the echo lab, with the combination of coronary flow assessment by Doppler and vasodilator stress. With either TEE (sampling proximal tract) or TTE (exploring mid-distal tract) the coronary blood flow velocity profile recorded with pulsed wave Doppler is consistent with the pathophysiological premises. Accordingly, coronary flow velocity by Doppler assessment appears to be biphasic, with a lower peak during systole and a higher peak during diastole (Figure 1). Myocardial extravascular resistance is higher in systole and lower in diastole due to the effect of myocardial contraction. The flow velocity variations are proportional to the total blood flow if the vessel lumen is kept constant, a reasonable assumption with the administration of drugs such as dipyridamole or adenosine. The coronary flow velocity variation between the baseline and peak effect of a coronary vasodilator allows a coronary flow reserve index in the left anterior descending artery territory to be derived. Peak diastolic flow is the simplest parameter to be measured and the most easily obtained, in addition to being the most reproducible and the one with the closest correlation with coronary perfusion

reserve measured by positron emission tomography. The coronary flow signal on LAD was first made possible by TEE with excellent diagnostic results but only more recently has there been an increase in clinical interest due to the development of the transthoracic method. There were technological factors which allowed the totally noninvasive transthoracic imaging of mid-distal LAD of the vessel. The estimated flow reserve can be accurate if the coronary functions only as a conduit, without changing in diameter during drug infusion. This assumption is reasonable with dipyridamole and less valid with dobutamine: this is an additional reason to stress coronary flow reserve with vasodilators.

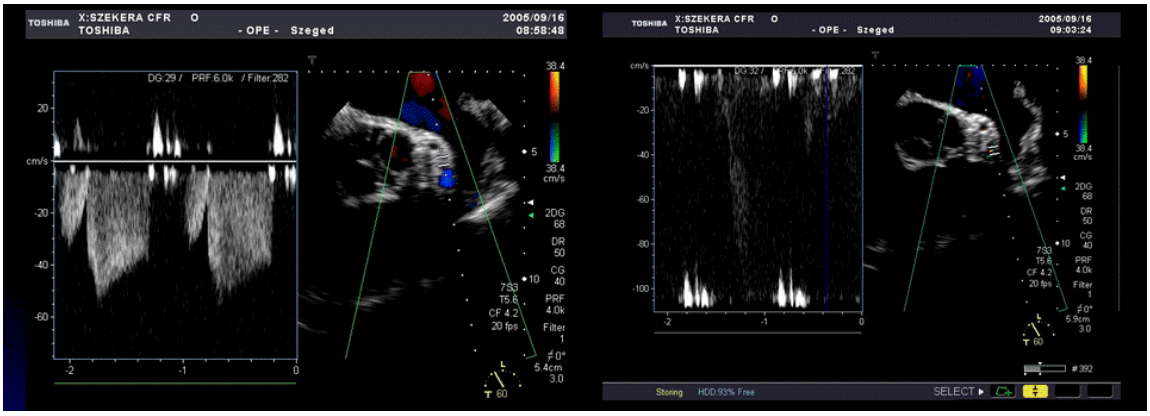


Figure 1. shows increase in PDV in the proximal LAD during iv. dypiridamole (Rest velocity: 53 mm/s, Peak velocity 120 mm/s, calculated CFR 2.26)

Coronary flow reserve: a new diagnostic tool The use of CFR as a "stand-alone" diagnostic criterion suffers from so many structural limitations as to make it little more than an academic somersault: firstly, only LAD is sampled; secondly, the coronary flow reserve cannot distinguish between microvascular and macrovascular coronary disease. Therefore, it is much more interesting (and clinically realistic) to evaluate the additive value over conventional wall motion for LAD detection. The assessment of CFR adds sensitivity for LAD disease – with a modest loss in specificity. In reality, the inherently quantitative information of LAD flow reserve allows a stratification of the response, integrating many different tests into one: greatly reduced CFR (<1.5) yields extraordinary specificity whilst mildly reduced CFR (<2.0) offers outstanding sensitivity. In addition, the flow information is relatively unaffected by concomitant antianginal therapy, which markedly reduces the sensitivity of ischemia-dependent regional wall motion abnormality and does not influence coronary flow reserve, or does so only to a limited extent. As a result, CFR can already help in the difficult task of

identifying patients with coronary artery disease in accordance with the classic ischemic cascade.

VISUALISATION OF THE CORONARY ARTERIES WITH INVASIVE TECHNIQUES

1. Coronary angiography

Coronary angiography is the reference standard for coronary artery imaging and provides the most reliable information for making treatment decisions about medical therapy, angioplasty, or bypass surgery.

Coronary artery anatomy: The heart is supplied by the left and right coronary arteries, which usually originate from the left and right sinuses of Valsalva, respectively. **Angiographic Lesion Quantification:** Under stress conditions, normal coronary artery flow can increase three- to fourfold (coronary flow reserve of 3 to 4). With luminal diameter reductions of greater than 50% (75% cross-sectional area reduction), the ability to normally increase coronary flow reserve may be impaired (i.e., less than 50% diameter narrowing is usually hemodynamically insignificant). Greater than 70% diameter stenosis (90% cross-sectional area) severely limits the ability to increase flow above resting level. A 90% diameter stenosis may reduce antegrade blood flow at rest (30). Also important is lesion length, whereby a 50% narrowed 10-mm lesion will be less hemodynamically significant than a 50% narrowed 30-mm lesion. The capability of coronary angiography to quantify the degree of stenosis is limited by the fact that the image is a “lumenogram.” Stenoses can be evaluated only by comparison to adjacent reference segments, which are presumed to be disease-free. The majority of arteries will have disease in the reference segment, leading to underestimation of stenosis severity. In addition, vessel segments adjacent to areas of denser contrast (e.g., an overlying branch artery) are prone to perceptual artefact due to the Mach effect (31), a consequence of the physiologic process of lateral inhibition. These neuroinhibitory interactions in the retina and central nervous system of the observer cause artery segments adjacent to the denser overlying artery to appear less dense and simulate stenosis. To enhance quantification of vessel size, the absolute diameter of the coronary artery can be compared to the size of the diagnostic catheter. This approach to lesion quantification is limited by its dependence on visual estimation and suffers from significant operator variability To overcome these limitations, digital callipers and quantitative coronary angiography (QCA) have been developed (Figure 1.), as have several computer-assisted approaches to quantitative angiography (32).

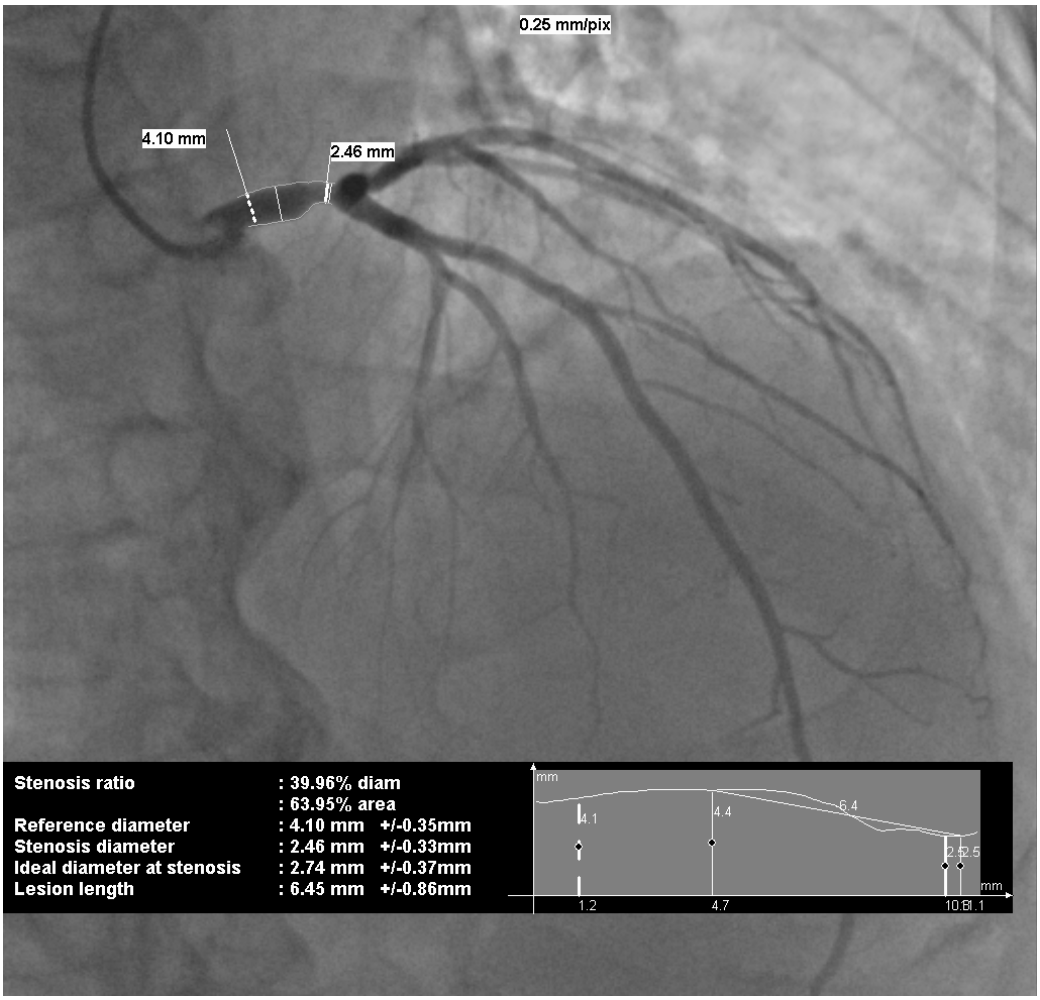


Figure 1. QCA measurement of borderline distal LM stenosis.

2. Intravascular ultrasound

The incremental value of IVUS compared to contrast angiography is due to its tomographic perspective and its ability to directly image atheroma and vessel wall (4). Angiography depicts cross-sectional anatomy as a planar silhouette of the lumen, whereas direct imaging by IVUS allows measurement of atheroma size, distribution, and composition. Although angiography remains the principal method to assess the extent of coronary atherosclerosis and to guide percutaneous coronary intervention, intravascular ultrasound has become a vital adjunctive imaging modality.

Advantage of intravascular ultrasound: IVUS has several important advantages over traditional angiography. First, IVUS allows precise quantitation of disease severity. (33). Second, the tomographic orientation enables visualization of the entire circumference of the

vessel wall, rather than a two-dimensional silhouette of the lumen (4). Third, IVUS allows characterisation of plaque composition, distribution, and length, which has important implications for device selection and assessment of results. Finally ultrasound allows the cardiologist to assess disease in vessels that are typically difficult to image by conventional angiography, including diffusely diseased segments, lesions at bifurcation sites, ostial stenosis, and highly eccentric plaques. Although vessel foreshortening and overlapping structures often preclude accurate quantitative angiography, IVUS by these factors. Advantages of IVUS are the precise quantitative measurements (lumen diameter, reference vessel diameter, cross-sectional area, lesion length) and the characterisation of plaque (arterial remodelling, plaque stability, plaque distribution, plaque composition, dissection)

Image interpretation:

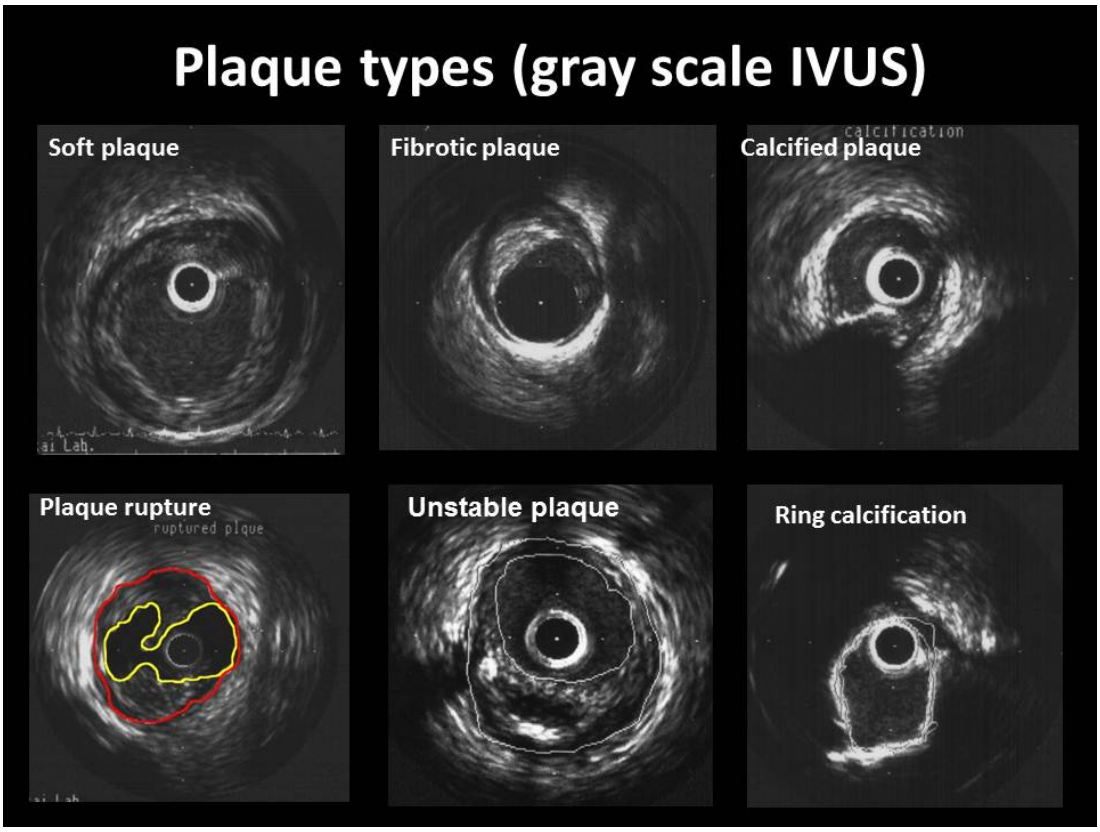
Normal coronary arterial morphology: IVUS often depicts the normal coronary artery as a trilaminar structure (34) The innermost layer (at the lumen/wall interface) represents the intima. When present, it appears as a delicate, echoreflective (white) band due to acoustic reflections from the internal elastic lamina. The media visualised as a distinct echolucent (black or dark gray) middle layer, which is bordered by a third, outer echodense media-adventitia interface. The characteristic trilaminar pattern is not observed in 30-50 % of normal coronary arteries; the thin intimal layer reflects ultrasound poorly and often leads to signal dropout and a monolayer appearence. (35) Wheather the artery is trilaminar or monolayered, the deepest layers of adventitia and peri-adventitial tissue exhibit a characteristic „onionskin" pattern. The outer border of the vessel is usually indistinct, primarily because there are no acoustic differences between the adventitia and surrounding tissues. Accordingly, total wall thickness cannot be measured reliably using ultrasound, except in vessels with a distinct outer border (such as saphenous vein bypass grafts).

Plaque composition: In practice, IVUS defines three broad classes of coronary lesions: soft lesions, where echogenicity of the atheroma is less than the adventitia, fibrous lesions, where the atheroma is of equal to the adventitia,and calcific or fibrocalcific lesions, where the atheroma is mor echodense than the adventitia. Overt calcification is highly likely when dense, bright echoes are accompanied by shadowing of the deeper structures.

Atheroma distribution: Plaque may be described as concentric or eccentric, with or without ulceration. Arterial remodelling: Remodelling is defined as a change in vessel area due to atherosclerosis. Remodelling can be positive (in which vessel area increases with atheroma development) or negative (in which the vessel area decreases). Glagov described an increase in arterial size that appeared to accommodate the deposition of atherosclerotic plaque. In

lesions with area stenosis <30-50%, the increase in arterial size “overcompensates” for plaque deposition, leading to an increase in lumen area. With more advanced lesions (area stenosis >40%), the degree of arteria enlargement is less, and luminal diameter becomes progressively smaller with disease progression (Glagov).

Unstable Lesions and Ruptured Plaque: No definitive IVUS features define a plaque as vulnerable (36). However, necropsy studies demonstrated that unstable coronary lesions are usually lipid-rich with a thin fibrous cap. Accordingly, hypoechoic plaques without a well-formed fibrous cap are presumed to represent potentially vulnerable atherosclerotic lesions. Ruptured plaques have a highly variable appearance by IVUS. In patients studied after an acute coronary syndrome, ultrasound imaging may reveal an ulceration, often with remnants of the ruptured fibrous cap evident at the edges of the ulcer. A variety of other appearances are common, including fissuring or erosion of the plaque surface.



Ambiguous Lesions: Angiographically ambiguous lesions may include: 1) intermediate lesions of uncertain stenotic severity; 2) aneurysmal lesions; 3) ostial stenoses; 4) disease at branching sites; 5) tortuous vessels; 6) left main stem lesions; 7) sites with focal spasm; 8) sites with plaque rupture; 9) dissection after coronary angioplasty; 10) intraluminal filling defects; 11) angiographically hazy lesions; and 12) lesions with local flow disturbances.

Intravascular ultrasound is frequently employed to examine lesions with the above characteristics, in some cases providing additional evidence useful in determining whether the stenosis is clinically significant (i.e., difficult to assess left main or borderline stenosis with continued symptoms). However, it must be emphasized that IVUS does not provide physiologic information per stenosis severity.

Dimensional measurements: All measurements during IVUS are taken "leading edge to edge". Intimal thikness is defined as the distance form the intima to the external elastic membrane (adventitial leading edge). Some investigators prefer to call this the "intima-media" or "plaque plus media" thickness, because this measurement includes both media and atheroma. The rationale for this conversation is that the normal media is frequently indistinct because its thickness is only slightly greater than the axial resolution of the imaging system. The most common IVUS measurements include the lumen cross-sectional area (Lcsa), external elastic membrane cross-sectional area (EEMcsa), maximum intimal thickness (IT-max), minimum intimal thickness (ITmin), vessel diameter and minimum lumen diameter (MLD). Common calculations include the percent plaque burden (%PB) or the percent cross-sectional narrowing (%CSN), the intimal index, the eccentricity index and diameter stenosis (DS) (37).

Diagnostic and interventional applications of IVUS: Although coronary angiography is considered the reference standard for coronary artery imaging, it detects only arterial disease that impinges on the luminal column of contrast medium. It has limited ability to detect plaque content or the disease process itself. In contrast, intravascular ultrasonography (IVUS) provides tomographic assessment analogous to histologic cross-sections and provides information about plaque morphology, vessel wall structure, and luminal and vessel area. IVUS offers the following advantages over angiography:

• Clarification of angiographically equivocal or intermediate lesions. This is especially helpful with left main lesions, which can be difficult to quantitate with angiography.

• Assessment of coronary stenoses before and after catheter-based coronary interventions. IVUS has proven useful in determining true vessel size prior to stent implantation and appropriate stent strut apposition after stent implantation.

• In cardiac transplant recipients, coronary artery disease is best studied by IVUS because of the diffuse nature of atherosclerosis that develops after transplantation

TRANSRADIAL ACCESS FOR CORONARY AND PERIPERAL INTERVENTIONS

1. **Transradial coronary angioplasty in STEMI**

In the treatment of patients with unstable angina and acute myocardial infarction PCI plays a crucial role. Aggressive antithrombotic therapy is a cornerstone of contemporary PCI in order to limit the occurrence of thrombotic complications during and after the procedure. However, access site complications occur more frequently using this aggressive adjunctive pharmacological therapy. The transradial way for coronary angioplasty and stenting was first published by Kiemeneij and Laarman (38). The rationale for the TR approach has been to attempt to reduce the incidence of bleeding complications and the vascular access site and the necessity for prolonged bed rest. Being able to avoid local complications of TR coronary angioplasty is mainly determined by the favourable anatomic relations of the radial artery to its surrounding structures. A number of studies have confirmed its applicability and potential advantages over the TF approach in elective and acute procedures (39-42).

2. Transradial angioplasty in carotid artery stenting

Stenting of the internal carotid artery has gained wide acceptance in the treatment of occlusive disease of the extracranial cerebral arteries (43,44). The results are constantly improving because of the introduction of new embolic protection devices and small caliber catheter and stenting systems. The conventional way to access the common carotid artery during endovascular interventions is through the femoral artery; however, this approach is not always possible because of vessel pathology or aberrant anatomy in the iliofemoral arteries and the aortic arch. A transbrachial or a direct transcervical approach can be employed as an alternative when femoral access is not possible. We have performed carotid artery stenting (CAS) in our hospital since 2001. We initially utilized the transcervical approach if femoral access was not possible. We decided to start using transradial access (TRA) for carotid stenting following the performance of several successful cerebral angiographies via radial artery access.

3. Transradial angioplasty in renal artery stenosis

Fibromuscular dysplasia, which affects mostly young females, is the underlying disease in 10 percent of all renal artery (RA) stenosis. The remaining 90 percent are caused by atherosclerotic narrowing of the renal artery. The incidence of RA stenosis increases with age and is higher among those with diabetes and patients with known aortoiliac occlusive disease, coronary artery disease, and hypertension (45). Percutaneous transluminal intervention is a balloon dilation method, used either alone or with stent implantation. The open surgical procedure may be an anatomical (aortorenal) or an extra-anatomical bypass (bypass from the

celiac or mesenteric artery), a procedure that has recently been preferred at some centres. Percutaneous transluminal intervention is usually performed through the femoral or brachial artery. There are only a few reports on RA stenting using the radial artery as an access site (46).

OPEN ISSUES IN THE ELUSIVE CLINICAL QUEST OF CORONARY ANGIOGRAPHY AND TRANSFEMORAL INTERVENTION

Pitfalls of Coronary Angiography: Most of the pitfalls in coronary angiography involve errors of omission whereby stenoses or anomalies are not appreciated. The most common angiographic pitfalls are: *Unrecognized LMCA stenosis*. The LMCA should be viewed in several projections with the vessel unobscured by the spine. Catheter pressure damping (a result of "wedging" into a stenosed vessel causing a damped waveform) and the absence of contrast reflux into the aorta suggest the presence of ostial LMCA disease. Several factors make adequate assessment of ostial LM stenosis challenging; they include the inherent difficulty of assessing aorto-ostial disease, vulnerability to catheter- induced vasospasm (see below), the high degree of interobserver variability of LMCA stenosis severity, and the prognostic significance of over- or underestimating LMCA lesion severity. *Too few projections.* Eccentric lesions and those obscured by overlap will go unnoticed unless additional projections are made. Detection of eccentric stenosis requires that the short axis of the stenotic lumen is projected. *Inadequate opacification.* Inadequate opacification can result in streaming and give the impression of ostial stenosis, missing side branches, thrombus, and stenosis over- or under-estimation. Properly sized catheters and injection rates avoid this problem. *Aorto-ostial lesions.* If an aorto-ostial lesion is suspected by partial ventricularization or pressure damping, injecting during withdrawal of the catheter from the ostium may be useful. *Failure to recognize occlusions.* Occlusions at branch origins tend to escape detection and may be recognized only by late filling of the distal segment by collateral circulation. *Catheter tip-induced spasm.* Catheter tip-induced spasm can occur at or within 1 cm of the catheter tip. It is caused by mechanical irritation and reflex contraction of the artery. Intracoronary or sublingual nitroglycerin should be given before the injection is repeated.

Transfemoral interventions in acute coronary syndromes:

Aggressive antithrombotic therapy is very important in order to limit the occurrence of thrombotic complications during and after the procedure. Nevertheless, during transfemoral

PCI this aggressive antithrombotic treatment is associated with a high risk of access site complications. Kiemenej *et al.* compare the results of transradial approach with the brachial and femoral approaches in randomized study (ACCESS study) (39). They found that although the vascular access site complication rate was not significantly lower after the transradial approach (0%) than the transfemoral (2%) or brachial approaches (2%) ($p = 0.05$), however in patients treated with the platelet GP IIb/IIIa inhibitor the missing major access site bleeding complications in the radial group, proved to be significantly less to the five occurrence (7%) in the femoral group ($p = 0.04$) (4). Despite the improvement of access site management after transfemoral intervention with the advent of vascular closure devices, bleeding complication remains a great challenge (47).

Transfemoral interventions for carotid artery stenting:

Stenting of the internal carotid artery has gained wide acceptance in the treatment of occlusive disease of the extracranial cerebral arteries (48). The results are constantly improving because of the introduction of new embolic protection devices and small caliber catheter and stenting systems. The conventional way to access the common carotid artery during endovascular interventions is through the femoral artery; however, this approach is not always possible because of vessel pathology or aberrant anatomy in the iliofemoral arteries and the aortic arch. Specifically, for cases performed viathe femoral route, potential complications include the formation of a hematoma, frank hemorrhage, retroperitoneal bleeding, pseudoaneurysm or arteriovenous fistula formation, or even the loss of peripheral pulses with associated leg ischemia (49). The most common underlying cause for local complications remains the anatomically incorrect arteriotomy site (too high above the inguinal ligament, or too low in one of the femoral artery branches) but there are also other patient-related risk factors, such as female sex, advanced age, a high systolic blood pressure, and even the inappropriate use of closure devices. In addition, the introduction of more potent antiplatelet and anticoagulant regimens (low molecular weight heparins, glycoprotein (GP) IIb/IIIa inhibitors,high doses of clopidogrel, direct thrombin inhibitors,etc.) has contributed to significant reductions in the ischemic complications of PCI, at the expense, however, of persistently high local complication rates (with the exception of the recently introduced direct thrombin inhibitors, specifically bivalirudin) (50-52). Specifically,while a recent meta-analysis demonstrated a 90% reduction in emergency coronary artery bypass operations in patients undergoing PCI over a ten-year period,7 in another recent meta-analysis including almost 13,898 PCIs the

rates of local complications, even in contemporary practice, still remain high with an overall incidence of 3.4% (53). In recent years, a number of closure device systems have been introduced with the purpose of reducing immobilization times post PCI and the hope of reducing the frequency of local complications. Large clinical trials have indeed demonstrated the patients' preference for the use of these closure devices compared to the long bed rest associated with the more traditional manual compression. However, in these studies reductions in local complications associated with the use of these devices were not demonstrated.

THE PRIMARY GOALS OF THE DISSERTATION

The main objective of the present thesis was to examine the role of transthoracic and transoesophageal echocardiography in the detection of proximal epicardial stenosis and to determine the applicability of transradial artery access in percutaneous coronary, carotid and renal artery stenting.

To achieve this, the followings have been analyzed:

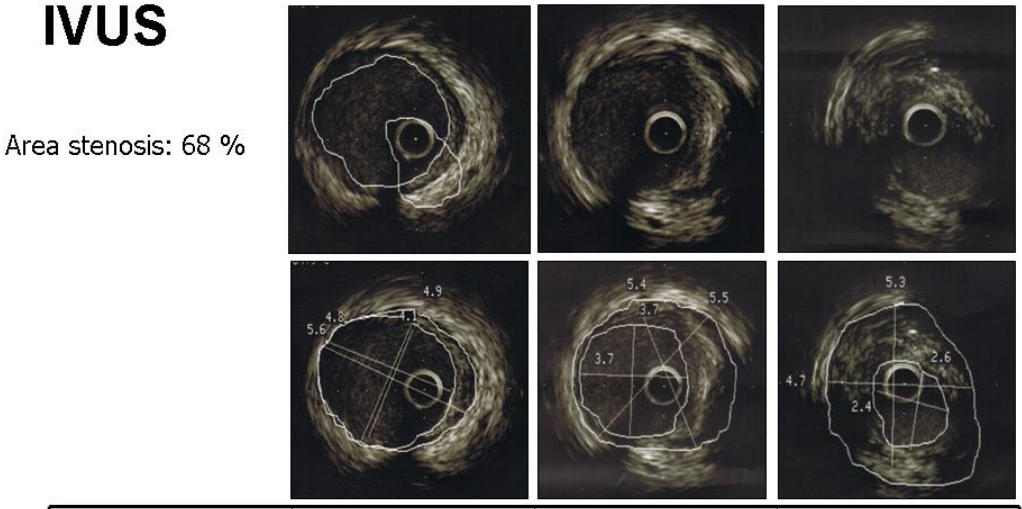
1. Comparative study between IVUS, quantitative coronary angiography and transthroracal Doppler echocardiography and an additional case report in a patient with borderline left main stenosis.
2. Evaluation of borderline stenosis severity in the proximal section of the LAD with , quantitative coronary angiography, intravascular ultrasound and CFR measured by transesophageal echo.
3. The purpose of the study was to evaluate the outcome, device consumption and the rate of vascular complications during transradial angioplasty in ST segment elevation myocardial infarction compared to the transfemoral access.
4. We report our early experience with transradial access for carotide artery stenting and in a case report for renal artery stenting.

METHODS

Coronary angiography and quantitative angiography: All patients underwent standard angiography, at the beginning of which intracoronary nitroglycerine (0.2 mg) was administered to achieve maximum vasodilatation. Measurements were then taken from two orthogonal views. Data were recorded on CD-ROM to allow offline assessment. The edge-detection technique developed by Reiber, et al. (CMS, Medis) was used for QCA assessment An empty guiding catheter was used for calibration, and diameter stenosis (%) was

determined using a computer quantitative analysis (General Electrics) program. Stenosis was considered significant if QCA showed diameter stenosis greater than 70%.

Intravascular ultrasound: IVUS and coronary angiography were performed at one sitting using an Atlantis Plus 40 MHz catheter (Boston Scientific). After guided catheter cannulation of the LMCA, a 0.014" guidewire was introduced into the distal LAD and the IVUS catheter was placed into the distal position. The IVUS catheter was withdrawn at 0.25 mm/s by automated pullback, while IVUS measurements were recorded on super VHS. Quantitative measurements were taken according to the IVUS standards of the American Society of Cardiology. In each case we measured minimum lumen diameter (MLD, mm), minimum lumen cross-sectional area (LCSA, mm^2), and external elastic membrane cross-sectional area (EEM-CSA, mm^2). A physician, who was experienced in IVUS, but independent of the study, measured vessel diameter at its narrowest region. LAD stenosis was considered significant if LCSA was smaller than 4 mm2, while values less than 7.5 mm^2 indicated significant left main stenosis (37).



	Ostium	Mid Shaft	Distal shaft
Lumen diameter 1	4.1 mm	3.5 mm	2.4 mm
Lumen diameter 2	4.8 mm	3.7 mm	2.6 mm
Lumen CSA	17.4 mm^2	11.5 mm^2	5.5 mm^2
EEM CSA	20.9 mm^2	22.6 mm^2	23.8 mm^2
Plaque burden %	16.8 %	49.7 %	77.1 %

3.

Transthoracic echocardiography for LM assessment: TTDE studies were performed with a Vivid 8 ultrasound equipment (General Electric, New York, USA) using a 3.5 MHz transducer with harmonic imaging. All TTDE studies were carried out by an experienced sonographer blinded to the angiographic and IVUS findings. B-mode image was used to

identify the LM and pulsatile Doppler to measure the flow velocity in diastole. Imaging plane was oriented in parallel with short-axis view of the aortic root slightly above the aortic valve. Sample images were stored digitally for subsequent analysis analysis.

Transoesophageal echocardiography: TEE was performed one day before IVUS in each case, using a Toshiba Power vision 8000 system with a high frequency (5-12 MHz) transducer. Patients received local lidocaine and IV midazolam. After LAD visualization and flow visualization with colour Doppler, flow velocity in the proximal LAD was measured using pulsatile Doppler first at rest, proximal to the lesion, then at peak dipyridamole effect (6 min after initial dipyridamole infusion, 0.56 mg in 4 min). Blood pressure and heart rate were monitored during the examination. The position of the transducer remained unchanged during dipyridamole infusion in order to maintain identical positions when measuring the resting and hyperaemic flow. CFR value was calculated from the ratio of the peak and resting diastolic velocities; values lower than two were considered pathologic. Diaphylline was administered at the end of the study to antagonize the effects of dipyridamole. Each measurement was recorded on super VHS, and digital pictures were stored for subsequent offline analysis.

Transradial angioplasty in acute coronary syndromes

Anticoagulant regimen. All patients were treated before the procedure with aspirin and clopidogrel (300 mg oral loading dose, then 75 mg PO for 6 months). A bolus of intracoronary Na-heparine (5000 U) was administered after sheath placement. Tirofiban – (Aggrastat) (180 mcg/kg iv. bolus plus 2.0 mcg/kg/min iv. infusion) or eptifibatide (Integrilin) (10 mcg/kg iv. bolus plus 0.15 mcg/kg/min iv. infusion) was administered before or during the procedure. **Vascular access and procedure (Table 1).** For the radial approach, an ischaemic Allen test contraindicated the procedure. After local anaesthesia (2% Xylocaine) modified Seldinger method was used for cannulating the radial artery with a 21-gauge needle, and a 0.021 inch straight wire was advanced in the radial artery. For cannulation of the radial artery a 6F dedicated transradial sheath (10 cm) was used (Cordis, Transradial Kit). Intraarterial vasodilators (2,5 mg verapamil, 5000 IU heparin sodium, 250 mcg nitroglycerine) were injected directly in the radial artery through the sheath. After the procedure the sheath was removed immediately and haemostasis was achieved with a tourniquet for 6 hours. We did not apply a dedicated haemostatic device. Despite radial artery access the patient was immobilised in the ICU for 24 for hours. For the femoral approach after local anaesthesia the femoral artery was punctured with a 19- gauge needle through

which a J wire was advanced in the femoral artery. A 6F sheath was introduced in all cases, but in case of a true bifurcational lesion it was replaced for 7F allowing for use of 7F guiding catheter for “kissing technique”. In transradial cases 6F guiding catheter was used routinely for „kissing technique” due to the size of the radial artery. The arterial access sheaths were removed 4 hours after the procedure, and after mechanic compression a pressure bandage was used for 12 hours.

Table 1 Technical descriptions of procedures

		Transradial	Transfemoral
Drugs	**Pre-procedural**	· Aspirin · Clopidogrel	· Aspirin · Clopidogrel
	Peri-procedural	NaHeparin 50 U/kg	NaHeparin 100 U/kg
	Antispasmolitic cocktail	· 2,5 mg Verapamil · 200 µg NTG · 5000 IU of Heparin	
Puncture		· 19 gauge needle · 0.022” straight wire or · 0.035” J wire with straight tip · 6-7 F short or long sheath · Modified Seldinger technique	· 19 gauge needle · 0.035” J wire · Modified Seldinger technique
Cannulation of the coronary arteries		LM: JL, EBU, AL RCA: JR, ART, SCR, MP	LM: JL, EBU, AL RCA: JR, ART, SCR
Guidewire		Depends on the lesion	Depends on the lesion
Sheath removal		Immediately after the procedure	4 hours after the procedure (ACT <200)
Pressure bandage		Elastic torniquet for 6 hours (not occlusive bandage !)	Elastic torniquet for 6-12 hours
Mobilisation		Very early (6-12 h)	24 h after the procedure

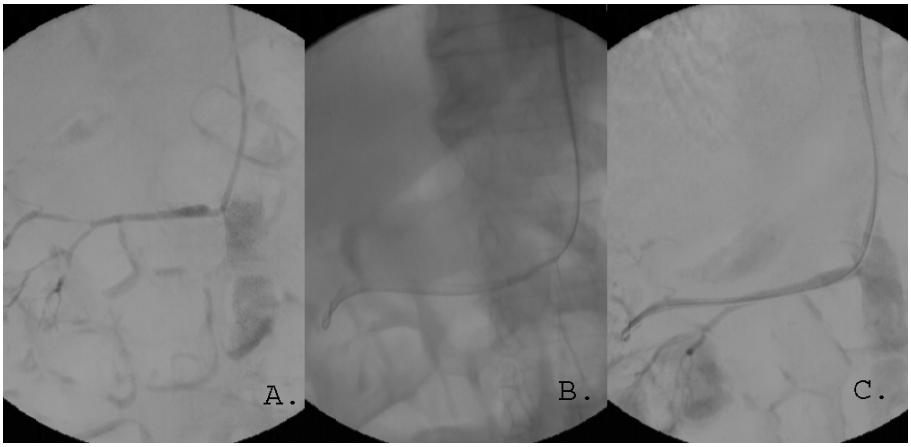
Angiographic analysis / angioplasty procedure. Angioplasty was performed according to the standard clinical practice. According to the guidelines, bare metal stents were used, we avoided application of drug-eluting stents. All angiograms were evaluated after ic. administration of nitrates. The vessels and the lesions were analysed by using a computerized quantitative analysis system (Siemens Hicor). Measurements were obtained with digital calliper method.

Transradial access for carotid artery stenting: Prior to TRA, every patient has an Allen’s test performed. The test is considered as normal (negative Allen’s test) if the palm colour returns to normal within 10 seconds. The right arm of the patient is positioned on an arm holder, abducted 45 °. The wrist is hyper extended over a gel pad and the arm is prepped and draped to the axilla. After access is gained, the arm can be left in an abducted position for left-handed operators, or, placed parallel to the body to facilitate catheter manipulations for right-handed operators. Local anaesthesia is infiltrated along the distal radial pulse. The artery is

punctured with a Check-Flo™ micro puncture radial artery access-set (Cook®) and a 5 Fr short sheath is introduced. Systemic unfractionated heparin is administered intravenously to achieve an activated clotting time (ACT) > 250 s, and a "spasmolytic cocktail" (200µg Nitro-glycerine, 2.5mg Verapamil) is given intra-arterially through the side arm of the sheath in order to prevent spasm secondary to vessel manipulation. It is necessary to use multiple views to optimize visualization of the carotid anatomy. We use variable projections and patient head positions to obtain the widest angle at the carotid origin. The right or left common carotid artery (CCA) is cannulated with an appropriately shaped diagnostic catheter and hydrophilic guide wire. We prefer to use the Internal Mammary Artery (IMA), Simmons 1 or Bernstein catheter configurations for cannulation of the right CCA (all selective catheters are Imager ™ II from Boston Scientific). For cannulation of the left CCA in patients with bovine arch anatomy, we use the Bernstein or JB1 catheter (Imager ™ II from Boston Scientific) configurations. For cannulation of the left CCA in patients with standard (normal) aortic arch anatomy we prefer to use the Simmons 2 (Imager ™ II) selective diagnostic catheter. The catheter is then advanced just proximal to the carotid bifurcation and an Amplatz Super Stiff ™ (Boston Scientific) wire is positioned in the external carotid artery (ECA) to provide support for the subsequent sheath exchange. In cases of angulated, tortuous aortic branch vessels, where access with the Super Stiff ™ wire is unable to be maintained, we resort to use of a "telescope" technique. For the "telescope" technique, a hydrophilic 0.035" Terumo® Glidewire (260 cm) is utilized to advance a diagnostic angiography catheter into the distal CCA. The selected guiding sheath is then advanced over the catheter – wire combination just proximal to the carotid bulb. We use a 6 Fr or 7 Fr, 90cm hydrophilic guide sheath; either a Terumo® Destination ™ carotid guiding sheath or a Shuttle SL Flexor ™ with a Tuohy-Borst side-arm from Cook®. The size of the guide sheath must accommodate both the carotid stent platform (which is usually 5 Fr or 6 Fr) and allow for continuous flushing with heparinised saline, as well as adequate contrast administration during the procedure. We have found that using matched French sizes for the guide sheath and the carotid stent, limits our ability to perform adequate flushing and contrast injections, thus we oversize the guide sheath by one French size in relation to the carotid stent system that is utilized. Road map angiography is performed to confirm that the degree of stenosis is 60% or greater. The degree of angiographic carotid artery stenosis is calculated according to NASCET criteria (48). Beneficial effect of carotid endarterectomy in symptomatic patients with high-grade carotid stenosis. The embolic protection device is deployed in the usual fashion and after administration of 1 mg intravenous Atropine, predilatation of the carotid stenosis with a small

diameter (3.0 or 3.5 mm) angioplasty balloon (Ultrasoft™ SV, Boston Scientific) is performed if necessary to facilitate positioning of the carotid stent. The carotid stent is deployed and post-dilated with a 5.0 mm diameter angioplasty balloon (Ultrasoft™ SV, Boston Scientific) if necessary. We prefer to use the Zilver Stent (Zilver® 518, Cook®) because of the very low profile (5 Fr), but we have also used 6 Fr systems such as the Carotid Wallstent™ Monorail™ (Boston Scientific) or Precise Stent (Precise™ RX, Cordis Corporation, Miami, USA). After completion angiography, the protection system and the sheath are removed without reversal of anticoagulation. The puncture site is compressed by hand for 5 minutes. We then use a 5-mL syringe with both ends cut off that has been wrapped with gauze to maintain pressure on the radial artery puncture site for six hours. The syringe is positioned longitudinally along the course of the distal radial artery and held in place with a non-circumferential elastic tape. The patient is moved to the postoperative care unit for 2 hours and then sent to the ward. The patient's neurologic status is evaluated by the interventionalist at the completion of the procedure, at removal of the bandage, prior to discharge and at 30-day follow-up. If a neurological deficit is observed, then a neurologist is consulted to evaluate the patient. Patients are allowed to ambulate and eat without restrictions. They are kept for observation for one night in the hospital and discharged home on the first postoperative day. The radial pulse is palpated and the adequacy of the hand's blood supply is evaluated clinically when the dressing is removed, at the time of discharge and at 30-day follow-up.

Transradial access for renal artery angioplasty: After successful cannulation of the radial artery, the renal artery was cannulated with a 90-cm 7F Mach1 MP catheter then the distal vessel with a 0.014-inch extra support guide wire (Boston Scientific; Natick, MA) (Figure 1). Following pre-dilation with a 3×20-mm Phantom balloon (PanMedical, Gloucestershire, United Kingdom), a 6x18- mm Express SD stent (Boston Scientific; Natick, MA) was implanted with 10 atm. The proximal 1–2 mm of the stent was left to protrude into the aorta. Finally, a balloon postdilation of the stent at the aortic end was performed. Control angiography showed no residual narrowing.



STUDY PROTOCOLS

1. COMPARISON BETWEEN TRANSTHORACAL, INTRAVASCULAR ULTRASOUND AND CORONARY ANGIOGRAPHY: Consecutive patients with angiographically documented borderline LM stenosis (30 to50%) (n =26, mean age: 64±8 years, 19 males) were enrolled in the present study. Following coronary angiography, LM has been evaluated by IVUS and TTDE in all patients. Exclusion criteria were hemodynamic instability, acute myocardial infarction, hypertrophic cardiomyopathy, severe obesity (BMI >35 kg/m^2), known congenital heart disease. Patients were informed about the study itself, its proceedings, and possible adverse events. The study satisfied with Declaration of Helsinki and was approved by ethical committee of University of Szeged.

2. COMPARISON BETWEEN TEE-CFR, INTRAVASCULAR ULTRASOUND AND CORONARY ANGIOGRAPHY: The only inclusion criterion was that the patient had coronarography-confirmed borderline lesion of the proximal LAD. Following coronarography, the LAD was examined by IVUS and TEE-CFR was performed. Exclusion criteria were severe left ventricular hypertrophy (because of the CFR-decreasing effect of hypertrophy), myocardial infarction within one month, significant left main and ostial LAD stenosis confirmed by angiography, and contraindication to dipyridamole (second or third degree AV block, sinus node dysfunction, severe chronic obstructive pulmonary disease, bronchospasm). Nine patients were excluded from the study due to significant left main or ostial LAD lesions because these types of lesions could limit TEE-CFR assessment. Patients refrained from taking food or drink containing theophylline or xanthine 24 hours before TEE, and they were not given any coronary drugs. Patients were informed about the study itself, its proceedings, and possible adverse events. The study satisfied the Helsinki Declaration and it was approved by the ethical committee of the University of Szeged.

3. TRANSRADIAL ANGIOPLASTY IN ACUTE CORONARY SYNDROMES: The clinical and angiographic data of 582 consecutive STEMI patients undergoing primary or rescue PCI were reviewed retrospectively, and evaluated. All of the patients with STEMI (n =582) was labelled into transradial (TR, n =167) or transfemoral (TF, n =415) group. The

transradial interventions were performed by experienced (>300 TR procedures previous to the study period) operators. Several parameters were applied to evaluate the potential advantages or drawbacks of TR access: access site cross over, rate of access site complications, major adverse cardiac events (MACE) at 1-month and consumption of angioplasty equipment. Selection of the access site was made by the operator's preference. The patients with rescue PCI and cardiogenic shock were excluded from the study. Criteria for the diagnosis of STEMI were chest pain lasting at least 30 minutes not responsive for nitrates and ST segment elevation on the electrocardiogram of at least 0.2 mV in 2 or more contiguous precordial leads or 0.1 mV in 2 or more extremity leads or non-diagnostic electrocardiogram (left bundle-branch block, ST-segment depression or T wave inversion). Rescue PCI was defined as PCI within 12 hours after failed fibrinolysis for patients with continuing or recurrent myocardial ischemia. The clinical criteria of cardiogenic shock were hypotension (a systolic blood pressure of <90 mm Hg for at least 30 minutes or the need for supportive measures to maintain a systolic blood pressure of ≥90 mm Hg) and end-organ hypoperfusion (cool extremities or a urine output of <30 ml per hour, and a heart rate of ≥60 beats per minute).

Endpoints and definitions. The following parameters were applied to evaluate the potential advantages of TR access:

- *Primary endpoint:* MACE, rate of access site complications
- *Secondary endpoints:* angiographic outcome of the PCI, and consumption of angioplasty equipment and cross over to another puncture site.

A successful angioplasty met three criteria: no more than 50 percent post-intervention stenosis, improvement of at least 20 percent in the degree of stenosis, and a flow of Thrombolysis in Myocardial Infarction (TIMI) grade II or III. Access site bleeding was defined as major if associated with haemoglobin loss of at least 2 mmol/l, administrations of blood transfusions, vascular repair and prolonged hospitalisation, and minor if bleeding at vascular access site only resulted in hematoma formation and did not require specific therapy. Major adverse cardiac events (MACE) were assessed as the composite of death, nonfatal acute myocardial infarction, and repeated revascularization of the target vessel by PCI or coronary artery bypass graft operation) during the hospital stay and at 30-day.

4. TRANSRADIAL ANGIOPLASTY IN CAROTIDE ARTERY STENTING:

There were 46 patients treated with carotid stents during the study period (March 2006 – December 2006). This study is a retrospective review of twenty patients who had CAS performed using TRA. The transradial approach was utilized only by the first (LP) and senior

authors (RK) in the institution. All patients underwent carotid stenting because they were considered high risk for open carotid endarterectomy. Grade of carotid stenosis was determined by use of preoperative duplex ultrasonography, computer tomographic angiography (CTA) or magnetic resonance angiography (MRA), but degree of stenosis was always verified by intra-operative angiography. All carotid stenting procedures were performed in the operating room using a portable C-arm (OEC 9800 Plus, General Electric). All patients provided informed consent prior to performance of any intervention. The major complications (within 30 days) evaluated were perioperative myocardial infarction, stroke or TIAs and death. Technical success, peripheral nerve injury, access site hematoma, radial artery occlusion or digital ischemia, as well as, pain and early ambulation were also evaluated.

RESULTS

1. COMPARISON BETWEEN TTE, INTRAVASCULAR ULTRASOUND AND CORONARY ANGIOGRAPHY:

Clinical and demographic patient data are demonstrated in Table 1. All study patients underwent positive Treadmill test or had ST segment depression under chest pain. Eight patients were presented with troponin negative acute coronary syndrome (33%).

Table 1. Clinical characteristics of study population

Parameters		n (%)
Age (year)		64 ± 8
Male gender (%)		18 (75)
Systemic hypertension (%)		16 (67)
Hypercholesterolemia (%)		14 (58)
Current smoker (%)		8 (33)
Diabetes mellitus (%)		7 (29)
Canadian angina classification:		
- I.	0 (0)	
- II.	5 (21)	
- III.	11 (46)	
- IV.	8 (33)	
Previous myocardial infarction (%)		9 (37.5)
Previous coronary bypass surgery (%)		0 (0)

Transthoracic echocardiography: Interpretable Doppler signal could be obtained in 24 patients (88 % feasibility). Mean resting peak diastolic Doppler velocity was 140 ± 58.5 cm/s in the LM.

Quantitative coronary angiography: Mean LM diameter stenosis was 36.5 ± 9.6 %, area stenosis was 58.15±12.25 %, MLD was 2.6 ± 0.7 mm and lesion length was 7.2 ± 3.2 mm.

Intravascular ultrasound: Clear IVUS images were obtained in all cases and no complications occurred during the recordings. IVUS revealed significant LM stenosis in 17 patients (71%) Fourteen patients with significant LM stenosis underwent percutaneous coronary intervention (PCI), 3 patients were referred for bypass surgery (12.5%), while 7 patients were considered having haemodynamically non-significant lesions, and therefore were recommended for further medical treatment and follow up (29%). Decision was made by intravascular ultrasound. Mean MLA in the LM was 7.1 ± 2.7 mm^2, mean MLD was 2.75 ± 0.7 mm and mean plaque burden was 52.8 ± 21.8 %.

Table 2. Quantitative coronary angiography, IVUS and TTDE findings

- **QCA**
  - MLD (mm) 2.6 ± 0.7
  - Diameter stenosis (%) 36.5 ± 9.6
  - Area stenosis (%) 58.15 ± 12.25
  - Reference diameter (mm) 4.10 ± 1.10
  - Lesion length (mm) 7.2 ± 3.2
- **IVUS**
  - **Quantitative analysis**
    - **LM MLA site**
      - MLA (mm^2) 7.1 ± 2.7
      - MLD (mm) 2.75 ± 0.7
      - Plaque burden (%) 52.8 ± 21.8
- **TTDE**

Correlations between angiographic, IVUS and echocardiographic parameters: There was no significant correlation between TTDE and QCA (r= 0.19, p=ns, figure 1.). TTDE measured PDV correlated significantly with IVUS-derived MLA (r= -0.46, p<0.05, figure 2.) and plaque burden (r=0.51, p<0.05, figure 3.). According to the ROC analysis the best cut off for PDV was 112 cm/s (sensitivity, 92.%; specificity, 62%) (figure 4.).

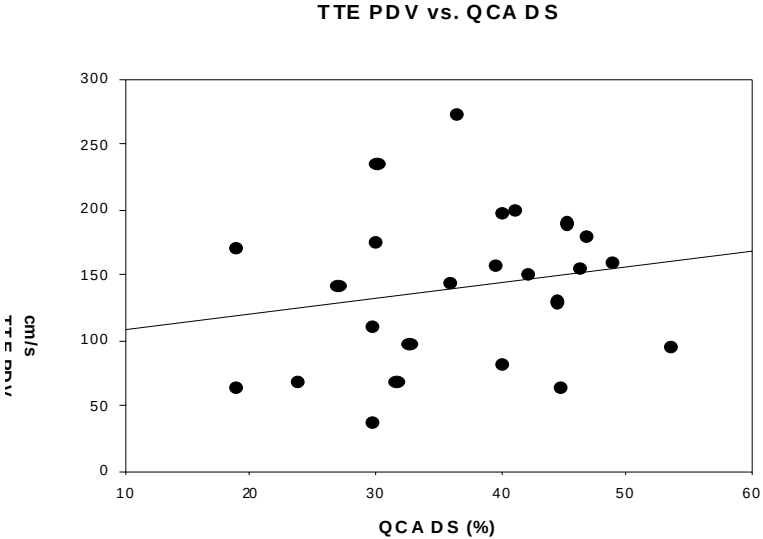


Figure 1. Comparison of peak diastolic velocity (TTDE) and diameter stenosis (QCA) show no significant correlation (R=0.19, p= ns).

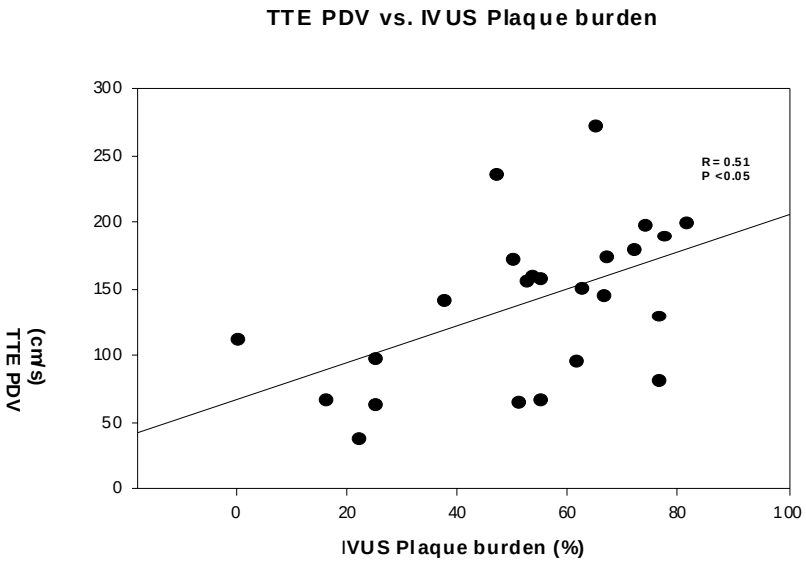


Figure 2. Comparison of peak diastolic velocity (TTDE) and minimum lumea area (IVUS) show significant correlation (R= -0.46, p <0.05).

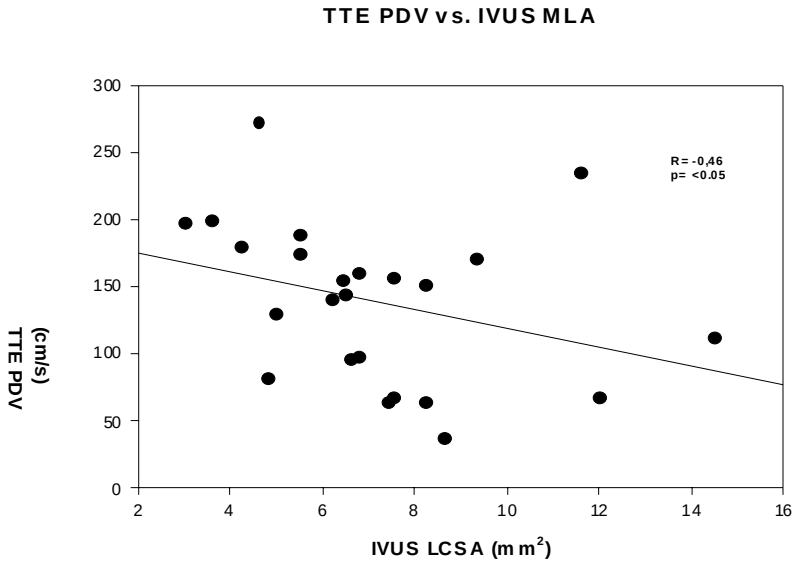


Figure 3. Comparison of peak diastolic velocity (TTDE) and plaque burden (IVUS) show significant correlation (R= 0.51, p <0.05).

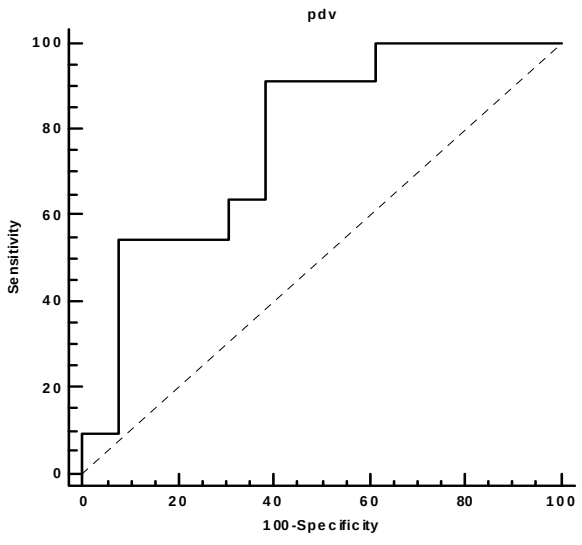


Figure 4. ROC analysis of peak diastolic velocity (TTDE) and minimum lumen area (IVUS)

2. COMPARISON BETWEEN TEE-CFR, INTRAVASCULAR ULTRASOUND AND CORONARY ANGIOGRAPHY:

Clinical and echocardiographic patient data are listed in Table 1. We performed percutaneous coronary intervention (PCI) for all patients with significant LAD stenosis revealed by IVUS (n = 25); no major cardiac events occurred.

Table I: Demographic data and risk factors

	N= (%)
• Age (year)	62±10
• Men	17 (51)
• Smoking	12 (36)
• Hypertension	27 (82)
• Hyperlipidemia	28 (85)
• Diabetes	5 (15)
• Obesity	11 (33)
• Peripheral obliterative disease	8 (24)

Transesophageal echocardiography: Proper Doppler signal was obtained for all examined patients (n = 42, 100%). CFR assessments were performed without complications in all cases. Mean resting Doppler velocity was 54.79 ± 21.44 cm/s in the proximal LAD, and it increased to 94.56 ± 25.86 cm/s ($p < 0.05$) after dipyridamole infusion. The mean CFR was 1.92 ± 0.42. CFR remained lower than 2 in 19 cases; these cases were considered significantly pathological.

Quantitative coronarography: The average diameter stenosis in our patients was 37.92 ± 10.81%.

Intravascular ultrasound: Clear IVUS pictures were obtained in each case and no complications occurred during recording. IVUS revealed significant left main or ostial LAD stenosis in nine patients; these patients were excluded from the study. The remaining patients had an average minimum lumen diameter of 1.97 ± 0.42 mm and an average cross-sectional

area of 3.66 ± 1.39 mm^2. LAD stenosis was considered significant if LCSA was smaller than 4 mm^2 (37), while stenosis less than 7.5 mm^2 indicated significant LM stenosis (55,56).

Correlation analysis:

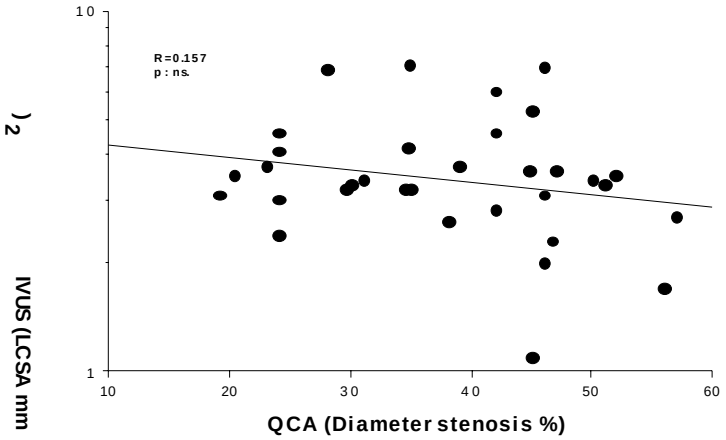


Figure 1.: Comparison of diameter stenosis by QCA and minimum lumen area by IVUS

QCA diameter stenosis versus IVUS-LCSA: We analysed the correlation between diameter stenosis measured after coronarography and the IVUS-defined lumen cross-sectional area using regression analysis and found no significant relationship (r = 0.157, p = ns; Figure 1).

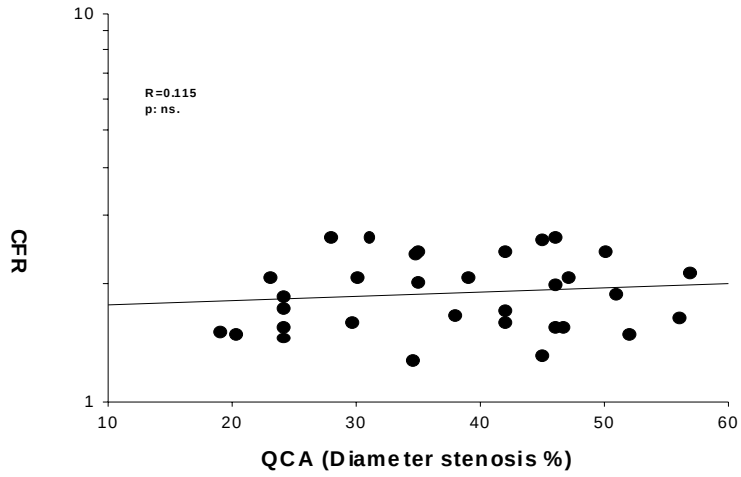


Figure 2.: Comparison of coronary flow reserve by TEE and diameter stenosis by QCA

QCA diameter stenosis versus TEE-CFR: No significant correlation was found between the diameter stenosis and TEE-CFR using linear regression analysis (r = 0.115, p = ns; Figure 2).

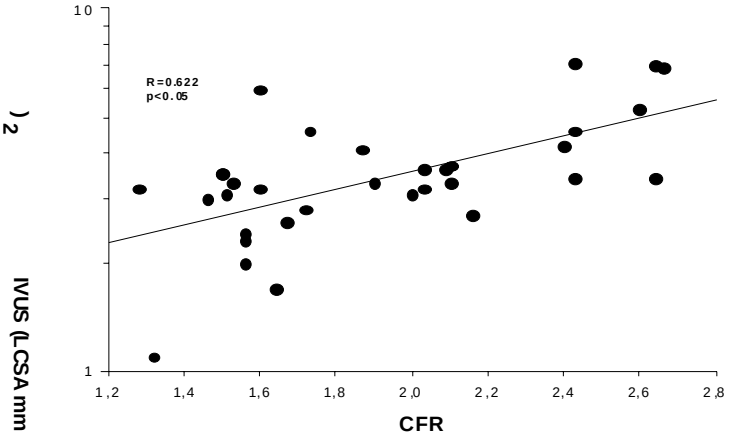


Figure 3.: Comparison of coronary flow reserve by TEE and minimum lumen area by IVUS

IVUS-LCSA versus TEE-CFR: Linear regression analysis showed a significant correlation between the IVUS-defined LCSA and the value of TEE-CFR (r = 0.622, $p < 0.05$; Figure3)

3. TRANSRADIAL ANGIOPLASTY IN ACUTE CORONARY SYNDROMES: Baseline demographic and clinical characteristics of study population are shown in Table 1. Most of the demographic data did not differ between the two groups, the only exception proved to be the incidence of peripheral obliterative disease, which was significantly higher in the transradial group (26% vs 9%, p<0.05). Previous CABG was performed in 12 patients (17%) in TR group and in 17 patients (8%) in TF group (p =0.02). Previous PCI had been performed in 12 patients (17%) in TR group and in 25 patients (11%) in TF group (p =ns).

Table 1. Baseline clinical characteristics of the study patients

		Radial group (n =167)	Femoral group (n =372)
Demographic data	Age (years)	62 ± 9	64 ± 8
	Male (%)	120 (72)	273 (74)
	Hypertension (%)	92 (61)	219 (59)
	Dyslipidaemia (%)	59 (35)	122 (33)
	Smokers (%)	35 (20)	46 (13)
	Diabetes mellitus (%)	43 (25) (IDDM: 3 and NIDDM: 40)	66 (18) (IDDM: 11 and NIDDM: 55)
	Severe obesity (%)	24 (14)	31 (8) *
*p <0.05 vs radial group	Peripheral obliterative disease (%)	27 (16)	33 (9) *
Cardiac history	Previous MI (%)	19 (28)	49 (13)
	Previous PTCA (%)	10 (6)	21 (6)
	Previous CABG (%)	4 (2)	10 (3)
GP IIb/IIIa blocking agents	Eptifibatide or Tirofoban (%)	45 (27)	110 (30)

Vascular access (see Table 2): From TR group 156 interventions were performed from the right (93%) and 11 (7%) procedures from the left radial artery. The preferred site of TR access in our cathlab is the right one, the indication of left radial access was a small diameter

right radial artery in 7 patients (63%) and a negative Allen test in 4 patients (36%). From the femoral group 43 patients (11%) were excluded due to cardiogenic shock and rescue PCI. The TF interventions were performed in 357 patients (96%) from right femoral access and in 15 patients (4%) from left femoral access. In the TR group the cross over rate to femoral artery was 8 (5%). The of cross over was a severe radial artery spasm in 2 patients, brachial artery tortuosity in 5, and an inadequate guiding catheter back up in 1 case. In the TF group the procedure was finished via radial artery in 3 patients (1%) due to severe iliac artery tortuosity. The cross over rate proved to be significantly more frequent from the radial than from the femoral artery ($p<0.05$).

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Table 2. Angiographic and clinical characteristics

		Radial group (n =167)	Femoral group (n =372)
Crossover to other access site (%)		8 (5)	3 (1)
Access	Right (%)	156 (94)	357 (96)
	Left (%)	11 (7)	15 (4)
Guide catheter / procedure		203 (1.22)	431 (1.16)
Stent used / procedure		1.12	1.14
GP IIb/IIIa inhibitors (%)		45 (27)	110 (30)
Distal protection device (%)		7 (4)	0 (0)
Thrombus aspiration (%)		15 (9)	54 (14)
Successfull procedure (%)		167 (100)	370 (99)
Vascular closure device (%)		0 (0)	20 (5) *

*p <0.05 vs radial group

Coronary angioplasty success: The procedure was successful in all patients in TR group (100%) and in 370 patients (99%) in TF group.

Consumption of equipments: The consumption of guiding catheters, guide wires, balloon catheters and coronary stents proved to be the same for the two groups.

Complications (see Table 3): The MACE rate was 7 (4%) in TR group and 41 (11%) in TF group ($p <0.05$). The MACE-rate at 1-month was found to be 11% in the TF group and 4% in the TR group ($p <0.05$). In the TR group the myocardial infarction occurred due to a side branch occlusion in 1 case and due to stent thrombosis in another case. In the TF group Re-PCI was due to stent-thrombosis 5 case and acute myocardial infarcion was due to side branch occlusion. The cause of death was cardiogenic shock in all cases due to no-reflow phenomenon.

Rate of access site complications: GP IIb/IIIa receptor blocking agent was used in 45 patients (27%) after TR interventions and in 110 patients (30%) after TF interventions (p =ns). Major entry site complications were encountered in 19 patients (5%) (2 false aneurysm requiring vascular repair, 17 haematomas (requiring blood transfusion in 9 cases and prolonged hospitalisation in another 8 cases) in the TF group. There was no major entry site complication in the TR group. Minor entry site complications were encountered in 35 patients (9%) in the TF group (small hematomas) and 6 patients (small hematoma) (4%) in the TR group (p <0.05). The lower arm hematoma was treated with local cooling, anti-inflammatory drugs. There was no occurance of compartment syndrome in the TR group.

Table 3. Complications

			Radial group (n =167)	Femoral group (n =372)	p value
MACE	Death (%)		2 (1)	15 (4)	NS
	AMI (%)		3 (2)	16 (4)	NS
	Urgent CABG (%)		0 (0)	2 (1)	NS
	Re PCI (%)		2 (1)	8 (2)	NS
	Summary (%)		7 (4)	41 (11)	<0.05
Access site	Major	Transfusion (%)	0 (0)	6 (2)	NS
		Vasular repair (%)	0 (0)	3 (1)	NS
		Prolonged hospitalisation (%)	0 (0)	10 (3)	NS
		Summary (%)	0 (0)	19 (5)	<0.05
	Minor	Haematoma (%)	6 (4)	35 (9)	NS
	Summary (%)		6 (4)	54 (15)	<0.01

4. TRANSRADIAL ANGIOPLASTY IN CAROTIDE ARTERY STENTING: The mean age of patients treated was 72 years. There were 14 males and 6 females. Seven patients were symptomatic (transient ischemic attacks (TIAs) and / or stroke and > 60% stenosis). Thirteen patients were asymptomatic but had high grade stenosis (> 80%) on computed tomographic angiography (CTA), magnetic resonance angiography (MRA) or conventional duplex ultrasonography. We did not exclude patients from TRA based on preoperative imaging. The patients had the following comorbidities: 65% were smokers, 30% were diabetic, 70% were hypertensive, 45% had coronary artery disease and 40% were hypercholesterolemic. (Table 1) Twelve patients had disease in the right carotid bifurcation. Eight patients also had a bovine arch. We had 16 patients with type I arch anatomy and 4 patients with type II arch anatomy.

We were able to successfully complete the carotid stenting procedure using transradial access in 18 out of 20 patients (90% technical success rate). The mean procedure time was 67 minutes. We used one diagnostic catheter in 15 patients and 2 diagnostic catheters in 3. The mean fluoroscopy time was 17 minutes. One patient developed intense radial artery vasospasm that precluded passage of the guiding sheath. This patient was a seventy year old, diabetic male, who in retrospect, had calcinosis of the radial artery. After removal of the 7 Fr sheath, we were unable to palpate a radial pulse proximal to the puncture site, but, there was a Doppler signal in the palmar arch and no sign of hand ischemia. In the other patient, the left CCA was not able to be cannulated. This patient had a type I arch and despite three catheter exchanges we were unable to cannulate the orifice of the left CCA thus aborting the procedure. There were no peri-operative myocardial infarctions, strokes or TIAs or deaths (0/20). (Table 2) In the case, where radial artery spasm prevented completion of the procedure, the radial artery occluded postoperatively but the patient remained asymptomatic. All other patients had patent access arteries, clinically, at the time of discharge and at 30-day follow-up None of the patients developed access site haematoma requiring surgical evacuation. One patient had incapacitating pain requiring intravenous analgesia and all patients were ambulatory within two hours of intervention. There were no instances of peripheral nerve injury or digital ischemia. All patients were discharged home on the first postoperative day.

	(N)	(%)
Symptomatic	7	35
Asymptomatic	13	65
Smoking	13	65
Diabetes	6	30
Hypertension	14	70
Coronary artery disease	9	45
Hypercholesterolemia	8	40
Right Carotid artery disease	12	60
Left Carotid artery disease	8	40
Bovine arch	4	20
Type I arch	16	80
Type II arch	4	20

Table 1. Patient demographic data

	N	(%)
Stroke/TIA	0	0
Acute myocardial infraction	0	0
Radial artery occlusion	1	5
Incapacitating pain	1	5
Surgical haematoma	0	0
Mobilization in 2 hours	20	100

Table 2. Postoperative outcomes

CONCLUSION

SELECTION OF A TEST TO IDENTIFY SIGNIFICANT CORONARY STENOSIS

1. CORONARY ANGIOGRAPHY FOR LM AND PROXIMAL LAD ASSESSMENT

In many cases, the planar 2D silhouette of the arterial lumen may be unable to accurately define the severity of coronary stenosis, regardless of whether visual or quantitative methods are used. LM has unique anatomical features, which influences the visual and angiographic assessment of lesion severity (54-56). LM is a relatively short vessel, and diffuse disease (tubular lesions) often precludes identification of a normal reference segment, leading to underestimation of lesion severity by angiography. Furthermore, the LM is relatively large vessel, therefore non-parallel catheter alignment may lead to an apparent ostial lesion due to

contrast streaming, while the overlap of the left anterior descending and left circumflex ostia may obscure the LM bifurcation. Additionally, haziness is often the result of an eccentric plaque seen en face rather than in profile, leading to a reduced volume of contrast dye at the lesion site without producing a stenosis that is quantifiable angiographically. Several studies have shown a poor correlation between IVUS and QCA-derived lumen dimensions in patients with angiographically detected LM stenosis, demonstrating significant intraobserver as well as interobserver variability in the angiographic assessment of the LM (57).

2. TTE RESTING DOPPLER VELOCITY

Assessing borderline coronary stenosis is an ongoing challenge in invasive cardiology. The optimal techniques are IVUS and FFR measurements, however these techniques are extremely expensive, not widely available, and require special training. Non-invasive techniques like TEE or TTDE using a high frequency transducer are useful for noninvasive evaluation of flow velocity dynamics in the LM (25-28). Doppler-TTE is a simple, widely-used, and noninvasive procedure that does not require lengthy preparation and post-examination observation, therefore can be used for routine screening of patients with known ambiguous LM as adjunct to other invasive or non-invasive diagnostic modalities. The cut-off value of 112 cm/sec determined by the ROC analysis demonstrated a good sensitivity of PDV in recognizing hemodynamically significant (determined by IVUS) LM disease, however the specificity of the method was rather low. This can still generate further unnecessary invasive testing’s, therefore at this point the PDV cannot considered a standalone method in the evaluation process of the borderline LM narrowing’s. A possible clinical algorithm is given in figure 1 and a typical borderline LM case is presented in figure 2. Further, large scale studies are needed to establish the exact cut-off value of PDV for routine clinical application.

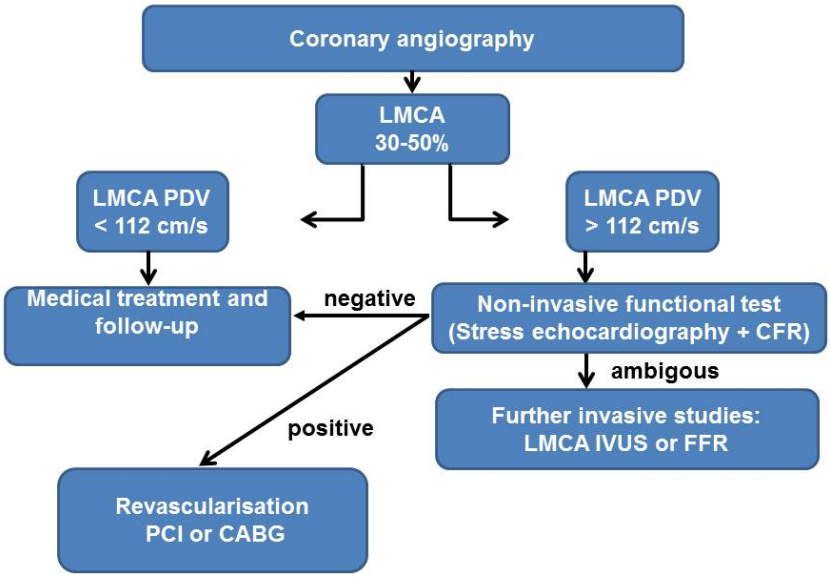


Figure 1. Left main coronary disease: diagnostic flow chart which incorporates the Doppler echocardiographic parameters.

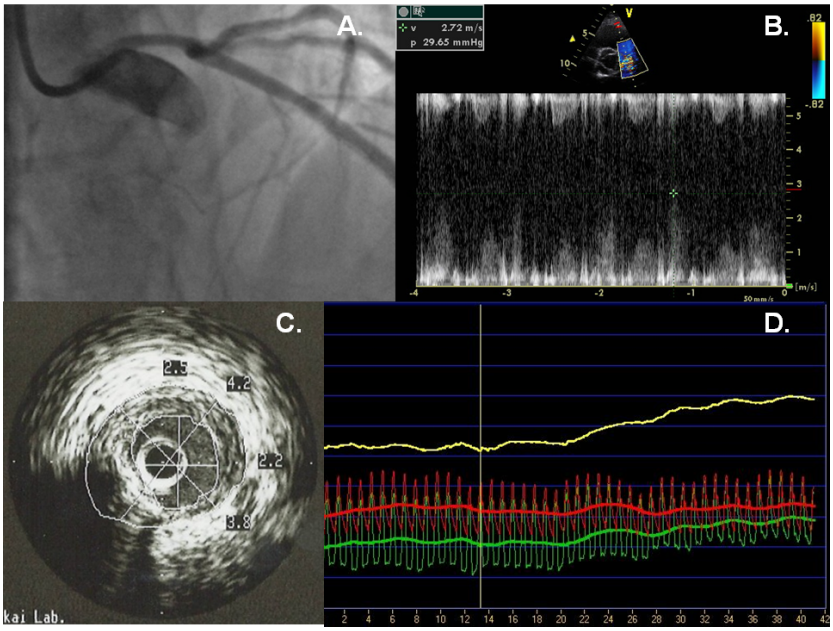


Figure 2. The imaging sequel of a 64-year old male patient with ambiguous angiography result. Coronary angiography revealed a tubular 30% stenosis of the LM, and non significant stenosis of the left and right coronary artery (panel A). However, the clinical presentation (severe angina, Canadian classification III-IV) did not corroborate with the angiographical findings, therefore the patient was sent to TTDE, which confirmed very high (272 cm/s) LM resting PDV (panel B). IVUS and FFR were performed, which both confirmed the severity of the LM stenosis (FFR=0.72; IVUS plaque burden: 65 % and LCSA: 4.6 mm2) (panel C-D)

SELECTION OF THE ACCESS FOR CORONARY AND PERIPHERAL INTERVETION

1. CORONARY ANGIOPLASTY FOR STEMI

The primary purpose of this study was to justify the safety and efficacy of transradial approach for PCI in STEMI patient subset. Louvard *et al*. reported the results of nonrandomized comparison of the radial and femoral approaches for primary PCI (58). The study included 1214 patients treated in two European centers; 267 patients (22%) were treated via a transradial approach; 947 patients were treated via the femoral approach with use of vascular closure system (Perclose) in 889 patients and manual compression in the remaining 58 patients. Overall procedure time, procedural outcome and the rate of TIMI III flow (88-91%) did not differ between the transradial and transfemoral approach. Conversion to a femoral approach was necessary in 2% of patients. Overall local bleeding complications only occured in patients treated via the femoral approach, whether or not the Perclose system was used: transfusion or surgery were required in 12 out of 947 (1%) patients. Saito *et al.* compared the TR and TF routes for primary PCI in a randomized study that included 77 patients (59). Cardiogenic shock was present in 6 % of patients. The procedural success rate in the radial group (96%) did not differ from that in the femoral group (97%). In no patient from radial to a femoral approach required cross-over. Some studies have confirmed the applicability and potential advantages of TR access in this patient subset with good procedural outcome and low vascular complication rate (60-63). This study demonstrates that transradial PCI in ACS subset was safe and the primary success rate was the same, regardless of whether the procedure was performed from the femoral or radial approach. The most important difference between our TF and TR groups is that while the incidence of major access site complications was considerably high in the TF group (5%), we could not detect any of them following TR access. Cross over rate to femoral apporach was 5% in TR group due to 2 severe radial artery spasm, 5 brachial artery tortuosity, 1 inadequate guiding back up. Aggressive antithrombotic therapy is very important in order to limit the occurrence of thrombotic complications during and after the procedure. Nevertheless, during transfemoral PCI this aggressive antithrombotic treatment is associated with a high risk of access site complications. Kiemenej *et al.* compare the results of transradial approach with the brachial and femoral approaches in randomized study (ACCESS study) (39). They found that although the vascular access site complication rate was not significantly lower after the transradial approach (0%) than the transfemoral (2%) or brachial approaches (2%) ($p = 0.05$), however in

patients treated with the platelet GP IIb/IIIa inhibitor the missing major access site bleeding complications in the radial group, proved to be significantly less to the five occurrence (7%) in the femoral group (p =0.04) (62). Despite the improvement of access site management after transfemoral intervention with the advent of vascular closure devices, bleeding complication remains a great challenge (63) The radial artery is a superficial and compressible vessel that allows for effective hemostasis. The avoidance of site related complication in the TR group is extremely important in the ACS patient subset. Patient comfort is increased due to the ability to sit up and ambulate immediately after procedure.

Limitations of TR access. The major limitations of TR technique is that the absence of radial pulse or an ischaemic Allen test must be considered as absolute contraindications. The radial artery spasm is a common problem and in most cases can be prevented with intra-arterial vasodilators and/or hydrophilic guidewires. Following the intra-arterial spasmolytic cocktail the occurance of the radial artery was infrequent in our patient cohort. Forearm compartment syndrome can be a serious complication, however with experienced access of the radial artery we can prevent it, and if it occurs, with a lower arm bandage can be treated effectively, and surgery is not necessary in the vast majority of the cases. Forearm compartement sysndrome was not observed in our study population despite aggressive anticoagulation of this study population. Radial artery occlusion is a rare complication but it has no clinical importance if the Allen test is positive (64). With a non occlusive pressure bandage after transradial intervention the occurace of the radial artery occlusion can be minimaized (65). The anatomic variations of the radial artery (radial artery loop, tortuous radial artery, small radial artery) can be clarified before the intervention with forearm echo examination but in this population, particularly in STEMI patients there is not enough time to rule out the anatomical variations. Our data suggests that despite this potential anatomical problems with a careful guidewire insertion, with a low threshold of performing radial angiography, and in selected cases passing these anatomical obstacles with long hydrophilic sheath and hydrophilic wire we can solve these problems, and the routine echo examination is not neccessary (66). The small internal diameter of 6F catheters does not allow the use of some devices: debulking devices, embolic protective devices and the first-generation thrombus aspiration systems, but the 6F sheath can be changed to 7F or even 8F without any vascular complication (67). The recently used balloon catheters are compatible with 6F guiding catheters for kissing technique, however, in bifurcation lesions we can replace the 6F sheath with a 7F device, if necessary. Although the cannulation of the coronary arteries is easy from the right radial artery, an adequate backup support and coaxial alignment from the contralateral aortic wall is a

prerequisite for difficult situations. With using long-tip catheters such as AL, Voda we can solve difficult situations, as well. The learning curve is very important in patients with ACS, because more technical difficulties are associated with this approach. For this reason, patient selection is an important issue particularly for beginners who should select first time stable patients with good anatomical properties. With larger experience, operators could extend the indications of transradial access progressively to patients with unstable angina or with myocardial infarction. **Study limitations.** An important limitation of the study is the lack of the randomisation between the femoral and radial approach in consequence of the retrospective nature of the analysis. Another limitation is the lack of ultrasonic assessment of the radial artery before and after the procedure.

2. CAROTIDE ARTERY STENTING

Systematic reviews of observational studies provide considerable data to support the performance of CAS.(68) According to a publication by Burton and Lindsay (69) in which 2992 patients were evaluated in 26 studies from 2002 to 2004, CAS is associated with an adverse event rate of 2.4% ± 0.3%, which is comparable to that of current carotid endarterectomy.(76) Most interventionists prefer to use the transfemoral approach for access. This method provides adequate access in most situations and allows traversal of the arch and negotiation of acute angles at the ostia of the great vessels. Femoral access is not possible in some patients. Extensive atherosclerotic disease in the aortic arch, atypical aortic arch anatomy, dissection of the thoracic aorta, iliofemoral occlusive disease, and infection in the groin are some of the limitations for femoral access. In such cases, alternate access sites need to be considered, such as transcervical, transbrachial, or transradial. The transcervical approach is more invasive because it usually requires a small cervical incision to prevent potentially disastrous access site complications and ensure hemostasis due to the lack of percutaneous carotid puncture closure systems at present. The transbrachial approach may also be difficult to perform and can result in severe complications, including brachial sheath hematoma, compartment syndrome, injury to the median nerve, or ischemia to the hand. (70) Major access site complications were more frequently encountered during coronary artery stenting (CAS) after transbrachial and transfemoral puncture compared with transradial access according to the Access study (39). Significant benefit in favor of transradial access was found in the multicenter randomized Access study comparing transfemoral, transbrachial, and transradial approaches for coronary artery stenting. Radial access was associated with fewer major complications (2.0% for transfemoral, 2.3% for transbrachial, 0% for transradial) and had the same technical success rate (91% to 92%) as transfemoral and transbrachial access.

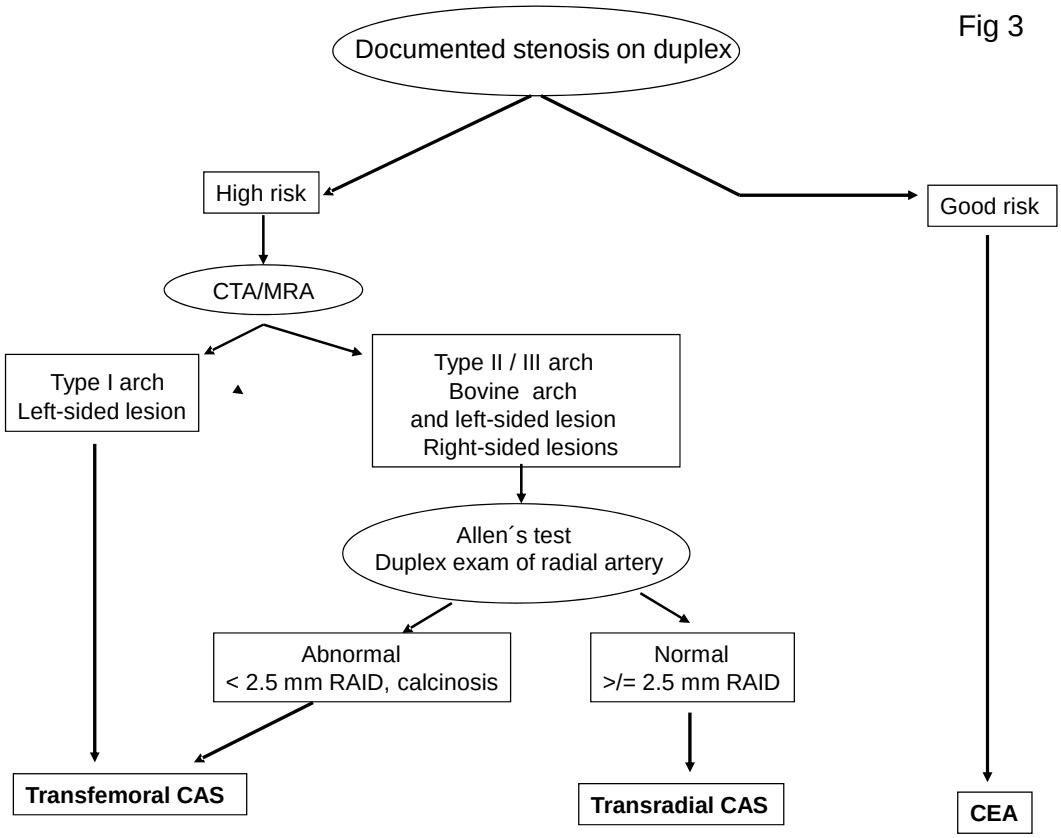
Percutaneous transradial coronary angioplasty led to asymptomatic loss of the radial pulse in approximately 3% of patients. As carotid stenting devices become increasingly more pliable and lower in profile, the percentage of periprocedural radial artery occlusions is expected to decrease. The right transradial approach is particularly efficacious for cannulation of the right CCA or the left CCA in the presence of a bovine arch because it minimizes the risk of particulate embolization. The advantage of the right transradial approach is the avoidance of catheter manipulations in the aortic arch, because there is no need to negotiate the ostia of the arch vessels. The incidence of cerebral embolization during CAS procedures using a transfemoral approach was analyzed by Hammer et al. (71) Their study demonstrated that 40% of the patients had new ischemic lesions in postoperative diffusionweighted MRI, and that 62% of the cases with positive diffusion-weighted MRI had embolic lesions that were found outside the vascular territory of the treated internal carotid artery, thus suggesting embolization from the aortic arch. Cannulation of the left CCA in patients with type I arch anatomy may be more difficult or impossible through the right radial artery. If this is the case, standard femoral access can be used for CAS procedure. We now perform preoperative CTA and MRA to evaluate aortic arch anatomy that might preclude successful transradial access. The use of the transradial approach for coronary angiography was first described by Lucien Campeau in 1989. (72) The safety and feasibility of this approach in coronary angioplasty and stenting have been reported in several studies. (73) As a consequence of these favorable initial results and reduced bleeding risk, despite use of potent antithrombotic and platelet therapy, transradial access for coronary intervention has gained widespread worldwide acceptance. Transradial access provides excellent postoper- ative comfort for the patient, with practically immediate ambulation after the procedure. Researchers have even found a cost reduction in several studies because of the low incidence of complications, no need for a closure devices, and reduced length of stay. Use of transradial access for CAS has been reported in sporadic case reports.(74) Despite excellent results, this method has not gained widespread acceptance. The reasons for the infrequent use of transradial access for CAS may have been the large, inflexible, first-generation stenting systems and sheaths. Devices have quickly been developed, however, that are hydrophilic, flexible, kink-resistant, and that have low profiles (5F to 6F). These technical improvements should facilitate use of TRA access. Further downsizing of carotid stents should theoretically allow most patients to accommodate the procedure through transradial access. Similar to every method in the beginning, the transradial access technique also has a learning curve. The puncture of this relatively small-caliber artery is not always easy. The radial artery is very vasoreactive and tends to spasm; therefore, it is

important to try to achieve entry on the first puncture. The radial artery has a small lumen, but its muscular wall dilates to accommodate 8F diameter sheaths (68). It is very important to administer spasmolytic medication (isosorbide dinitrate, lidocaine, or verapamil) intra-arterially immediately after the puncture. This will decrease the incidence of vasospasm and radial artery occlusion from 60% to 3% (64). Periprocedural pain and paresthesias may be considerably reduced by the use of micropuncture systems to access the radial artery. Complications at the radial artery puncture site are extremely rare owing to the anatomy of the wrist. The median nerve courses apart from the artery in this location; therefore, it is almost impossible to cause an injury to the nerve. The artery lies very superficially on the radius; therefore, it is relatively easy to access and compress. Ease and effectiveness of compressibility are vital for interventions where patients have received anticoagulation medication. In cases of postoperative bleeding after radial access, patients are able to recognize and control the bleeding themselves. Even when the radial artery occludes, the hand is not jeopardized because of the dual blood supply through the ulnar artery and palmar arch. Most patients remained asymptomatic despite radial artery occlusion if they had a negative (normal) Allen's test, and it is notable that the radial pulse had returned to normal at the 1-month follow-up in half of the patients. A properly performed and documented Allen's test is imperative before use of transradial access. The contraindications to use of transradial access are a nonpalpable radial pulse, a positive (abnormal) Allen's test, calcinosis, and need to maintain the radial artery for dialysis access. Radial artery size and degree of calcinosis can be determined by preoperative duplex evaluation. In this pilot study, we did not perform duplex evaluation of our patients' radial arteries; however, after further review of our results and the literature, we now recommend obtaining a duplex study to evaluate size and suitability of the radial artery before sheath insertion. Contrary to public perception, Saito et al (74) have published that there is no relationship between radial artery internal diameter and weight, height, or patient body sur surface area. Stella et al (64) also comment that there is no correlation between gender and postprocedural radial artery occlusion. We perform transradial access in patients with noncalcified arteries sized_2.5 mm duplex because that size will accommodate the outer diameter of a 6F sheath.

CONCLUSIONS: Our early experience with transradial access confirms that CAS can be effectively performed through this approach with acceptable morbidity and with high technical success and patient satisfaction. We propose that transradial access is a safe, ideal alternative to transfemoral access and do not restrict its use just to patients with difficult femoral access. We preferentially perform CAS with transradial access in patients with right-

sided carotid lesions and left-sided carotid lesions in the presence of bovine or type II or III arch anatomy (Fig 3.). We recommend obtaining imaging of the aortic arch and supra-aortic trunks with CTA and MRA, as well as a duplex scan of radial artery before attempting CAS when using transradial access. With this approach, patients with unfavorable aortic arch and radial artery characteristics that impact procedural success can be excluded. A multicenter, randomized, controlled trial is needed to definitively answer whether transradial access can replace transfemoral access routinely during CAS.

Fig 3



3. RENAL ARTERY STENTING

The typical access site for percutaneous angioplasty is the common femoral or brachial artery. We used a 7F sheath because renal artery stents need a 6F guiding sheath or a 7F guiding catheter. It should be noted that the renal artery may not be reached through the radial artery with a 90-cm guiding catheter, so a 120-cm guiding catheter must be used in tall patients

NEW OBSERVATIONS

1. Transthoracal Doppler echocardiography evaluation might be a useful adjunct to other invasive and non-invasive methods in the assessment of borderline left main lesions. LM TTDE gives additional functional information about LM stenosis severity.
2. TEE-CFR measurement is appropriate for the non-invasive functional assessment of proximal LAD stenosis. We have found no significant correlations between angiography- and IVUS-defined stenosis in cases of borderline stenosis. TEE-CFR provides supplementary information on the functional severity of stenosis and its results relate better to the results of IVUS than to those of QCA. Our data also showed that the value of QCA-defined diameter stenosis is not significantly related to either the lumen cross-sectional area or the value of CFR.
3. Transradial access for the treatment of ST elevation myocardial infarction is feasible and safe. The major advantages of the TR technique are the extremely low rate of vascular access complications, an improved comfort for the patient, a short hospitalisation with reduced hospital costs at a not increased procedural cost. Our results demonstrate that TR access for is effective treatment in this population subset and results in significantly less vascular complication rate than TF access. In experienced hands this technique in safe and efficacious. The lack of site related complications, and better patient comfort makes this technique the choice of preference in this high risk population.
4. Early experience with transradial access, confirms that carotid artery stenting can be effectively performed through this approach with acceptable morbidity, as well as high technical success and patient satisfaction. We propose that TRA is a safe, ideal alternative to transfemoral access and do not restrict its use to patients with difficult femoral access.
5. A radial approach can be successfully used for renal artery stenting, yet further studies are needed to assess the long term efficacy of this technique. The radial approach should be preferred in the presence of significant peripheral arterial occlusive disease and if the renal artery points downward.

REFERENCES

1. Topol EJ, Nissen SE. Our preoccupation with coronary luminology. The dissociation between clinical and angiographic findings in ischemic heart disease. Circulation 1995; 92: 2333-42.

2. Tron C, Kern MJ, Donohue TJ, et al. Comparison of quantitative angiographically derived and measured translesion pressure and flow velocity in coronary artery disease. Am J Cardiol. 1995;75:111–117.

3. White, CW et.al., Does visual interpretation of arteriogram predict the physiological importance of a coronary physiological importance of a coronary stenosis, NEJM, 1984; 310: pp 819—24

4. Nissen SE, Gurley JC, Grines CL, Grines CL, Booth DC, McClure R, Berk M, Fischer C, DiMaria AN. Intravascular ultrasound assessment of lumen size and wall morphology in normal subjects and patients with coronary artery disease. Circulation. 1991;84:1087–1099.

5. Briguori C, Anzuini A, Airoldi F, Gimelli G, Nishida T, Adamian M, Corvaja N, Di Mario C, Colombo A. Intravascular ultrasound criteria for the assessment of the functional significance of intermediate coronary artery stenoses and comparison with fractional flow reserve. Am J Cardiol. 2001 Jan 15;87(2):136-41.

6. Pijls NHJ, Van Gelder B, Van der Voort P, Peels K, Bracke FALE, Bonnier JJRM, El Gamal MIH. Fractional flow reserve: a useful index to evaluate the influence of an epicardial coronary stenosis on myocardial blood flow. Circulation. 1995;92:3183–3193.

7. Cameron A, Kemp HG Jr., Fisher LD, et al. Left main coronary artery stenosis: angiographic determination. Circulation.1983;68:484–489.

8. Graham SP, Cohen MD, Hodgson JM. Estimation of coronary flow reserve by intracoronary Doppler flow probes and digital angiography. Cathet Cardiovasc Diagn. 1990;19:214 –221.

9. Doucette JW, Corl PD, Payne HM, et al. Validation of a Doppler guide wire for intravascular measurement of coronary artery flow velocity. Circulation 1992;85:1899 –911.

10. Pijls NH, De Bruyne B, Smith L, et al. Coronary thermodilution to assess flow reserve: validation in humans. Circulation 2002;105:2482–6. 10.

11. Iliceto S, Marangelli V, Memmola C, Rizzon P. Transesophageal Doppler echocardiography evaluation of coronary blood flow velocity in baseline conditions and during dipyridamole-induced coronary vasodilation. Circulation.1991;83:61– 69.

12. Nemes A, Forster T, Pálinkás A, Vass A, Borthaiser A, Ungi I., Thury A, Litvai E, Nádaskay M és Csanády M: A dipyridamol-terheléses transoesophagealis echocardiographia

segítségével számított coronaria-áramlási rezerv klinikai értéke ischaemiás szívbetegségekben. Orv. Hetil. 141.43. 2000. október 22.

13. C. Caiati, N. Zedda, C. Montaldo, R. Montisci and S. Iliceto, Contrast-enhanced transthoracic second harmonic echo Doppler with adenosine. A non-invasive, rapid and effective method for coronary flow reserve assessment, J Am Coll Cardiol 34 (1999), pp. 122–130.

14. T. Hozumi, K. Yoshida and Y. Ogata et al., Non-invasive assessment of significant left anterior descending coronary artery stenosis by coronary flow velocity reserve with transthoracic color-Doppler echocardiography, Circulation 97 (1998), pp. 1557–1562.

15. Hildick-Smith DJ, Maryan R, Shapiro LM. Assessment of coronary flow reserve by adenosine transthoracic echocardiography: validation with intracoronary Doppler. J Am Soc Echocardiogr. 2002 Sep;15(9):984-90.

16. Demer LL, Gould KL, Goldstein RA, Kirkeeide RL, Mullani NA, Smalling RW, Nishikawa A, Merhige ME. Assessment of coronary artery disease severity by positron emission tomography: comparison with quantitative arteriography in 193 patients. Circulation. 1989;79:825– 835

17. Braunwald E: Myocardial oxygen consumption: The quest for its determinants and some clinical fall out. J. Am. Coll. Cardiol. 35:45B, 2000

18. Chilian WM: Coronary microcirculation in health and disease: Summary of an NHLBI workshop. Circulation 95:522-528, 1997.

19. Gould KL, Lipscomb K: Effects of coronary stenosis on coronary flow reserve and resistance. Am J Cardiol 1974, 34:48-55.

20. Uren NG, Melin JA, De Bruyne B, Wijns W, Baudhuin T, Camici GP: Relation between myocardial blood flow and the severity of coronary artery stenosis. N Engl J Med 1994, 330:1782-1788.

21. White CW, Wright CB, Doty DB, Hiratzka LF, Eastham CL, Harrison DG, Marcus ML: Does visual interpretation of the coronary arteriogram predict the physiologic importance of a coronary stenosis? N Engl J Med 1984, 310:819-824.

22. Topol EJ, Nissen SE: Our preoccupation with coronary luminology. The dissociation between clinical and angiographic findings in ischemic heart disease. Circulation 1995,92:2333-42.

23. Uren NG, Melin JA, De Bruyne B, et al. Relation between myocardial blood flow and the severity of coronary-artery stenosis. N Engl J Med 1994;330:1782–1788.

24. Piek JJ, van Liebergen RAM, Koch KT, et al. Clinical, angiographic and hemodynamic predictors of recruitable collateral flow assessed during balloon angioplasty coronary occlusion. J Am Coll Cardiol 1997;29:275–282.

25, Saraste M, Vesalainen RK, Ylitalo A, Saraste A, Koskenvuo JW, Toikka JO, Vaittinen MA, Hartiala JJ, Airaksinen KE. Transthoracic Doppler echocardiography as a noninvasive tool to assess coronary artery stenoses--a comparison with quantitative coronary angiography. J Am Soc Echocardiogr. 2005 Jun;18(6):679-85.

26. Anjaneyulu A, Raghu K, Chandramukhi S, Satyajit GM, Arramraja S, Raghavaraju P, Krishnamraju P, Somaraju B. Evaluation of left main coronary artery stenosis by transthoracic echocardiography. J Am Soc Echocardiogr. 2008 Jul;21(7):855-60. Epub 2008 Mar 6.

27. Palinkas A, Ruzsa Z, Varga A, et al. Feasibility and diagnostic accuracy of transthoracic doppler echocardiography for detection of left main and left anterior descending coronary artery stenosis. European Hear Journal. 24: 566-566 Supplement: 2003

28. Vrublevsky AV, Boshchenko AA, Karpov RS. Diagnostics of main coronary artery stenoses and occlusions: multiplane transoesophageal Doppler echocardiographic assessment. Eur J Echocardiogr. 2001 Sep;2(3):170-7.

29. Holte E, Vegsundvag J, Wiseth R: Direct visualisation of a significant stenosis of the right coronary artery by transthoracic echocardiography. A case report. Cardiovascular Ultrasound 2007, 5:33.

30. Uren NG, et al. Relation between myocardial blood flow and the severity of coronary artery stenosis. N Engl J Med 1994;330:1782.

31. Randall PA. Mach bands in cine coronary arteriography. Radiology 1978;129:65.

32. Piek JJ, van Liebergen RAM, Koch KT, et al. Clinical, angiographic and hemodynamic predictors of recruitable collateral flow assessed during balloon angioplasty coronary occlusion. J Am Coll Cardiol 1997;29:275–282.

33. Rodes-Cabau J, Candell-Riera J, Angel J, de Leon G, Pereztol O, Castell-Conesa J, Soto A, Anivarro I, Aguade S, Vazquez M, Domingo E, Tardif JC, Soler-Soler J. Relation of myocardial perfusion defects and nonsignificant coronary lesions by angiography with insights from intravascular ultrasound and coronary pressure measurements. Am J Cardiol. 2005 Dec 15;96(12):1621-6.

34. Tobis J.M., Mallery J., Mahon D., Intravascular ultrasound imaging of human coronary arteries in vivo. Analysis of tissue characterizations with comparison to in vitro histological specimens. Circulation 1991;83:913-926.

35. Nissen S.E., Gurley J.C., Grines C.L., et al. Intravascular ultrasound assessment of lumen size and wall morphology in normal subjects and patients with coronary artery disease. Circulation 1991;84:1087-1099.

36. Kearney P., Erbel R., Rupprecht H.J., et al. Differences in the morphology of unstable and stable coronary lesions and their impact on the mechanisms of angioplasty. An in vivo study with intravascular ultrasound. Eur Heart J 1996;17:721-730.

37. Mintz GS, Nissen SE, Anderson WD, et al. American College of Cardiology clinical expert consensus document on standards for acquisition, measurement and reporting of intravascular ultrasound studies (IVUS). A report of the American College of Cardiology task force on clinical expert consensus documents. J Am Coll Cardiol 2001;37:1478 –92.

38. Kiemeneij F, Laarman GJ. Percutaneous transradial artery approach for coronary stent implantation. Am Heart J 1995;128:167-74.

39. Kiemeneij F, Laarman GJ, Odekerken D, Slagboom T, van der Wieken R. A randomized comparison of percutaneous transluminal coronary angioplasty by the radial,brachial and femoral approaches: The Access study. J Am Coll Cardiol 1997;29:1269-75.

40. Louvard Y, Ludwig J, Lefevre T, Schmeisser A, Bruck M, Scheinert D, Loubeyre C, Klinghammer L, Morice MC, Flachskampf FA, Daniel WG. Transradial approach for coronary angioplasty in the setting of acute myocardial infarction: a dual-center registry. Catheter Cardiovasc Interv 2002;55:206-11.

41. Saito S, Tanaka S, Hiroe Y, Miyashita Y, Takahashi S, Tanaka K, Satake S. Comparative study on transradial approach vs. transfemoral approach in primary stent implantation for patients with acute myocardial infarction: results of the test for myocardial infarction by prospective unicenter randomization for access sites (TEMPURA) trial. Catheter Cardiovasc Interv 2003;59:26-33.

42. Choussat R, Black A, Bossi I, Fajadet J, Marco J. Vascular complications and clinical outcome after coronary angioplasty with platelet IIb/IIIa receptor blockade. Comparison of transradial vs transfemoral arterial access. Eur Heart J 2000;21:662-7.

43. Levy EI, Kim SH, Bendok BR, Qureshi AI, Guterman LR, Hopkins LN. Transradial stenting of the cervical internal carotid artery: technical case report. Neurosurgery. 2003;53(2):448-51; discussion 451-2.

44. Yoo BS, Lee SH, Kim JY, Lee HH, Ko JY, Lee BK, Hwang SO, Choe KH, Yoon J. A case of transradial carotid stenting in a patient with total occlusion of distal abdominal aorta. Catheter Cardiovasc Interv. 2002 Jun;56(2):243-5.

45. de Mast Q, Beutler JJ. The prevalence of atherosclerotic renal artery stenosis in risk groups: a systematic literature review. J Hypertens. 2009 Apr 10.

46. Kessel DO, Robertson I, Taylor EJ, Patel JV. Renal stenting from the radial artery: a novel approach. Cardiovasc Intervent Radiol. 2003 Mar-Apr;26(2):146-9.

47. Choussat R, Black A, Bossi I, Fajadet J, Marco J. Vascular complications and clinical outcome after coronary angioplasty with platelet IIb/IIIa receptor blockade. Comparison of transradial vs transfemoral arterial access. Eur Heart J 2000;21:662-7.

48. Yadav JS, Wholey MH, Kuntz RE, Fayad P, Katzen BT, Mishkel GJ, Bajwa TK, Whitlow P, Strickman NE, Jaff MR, Popma JJ, Snead DB, Cutlip DE, Firth BG, Ouriel K; Stenting and Angioplasty with Protection in Patients at High Risk for Endarterectomy Investigators. Protected carotid-artery stenting versus endarterectomy in high-risk patients N Engl J Med. 2004 Oct 7;351(15):1493-501.

49. Samal AK, White CJ: Percutaneous management of access site complications. Catheter Cardiovasc Interv 2002; 57: 12-23.

50. Exaire JE, Tcheng JE, Kereiakes DJ, et al: Closure devices and vascular complications among percutaneous coronary interventionpatients receiving enoxaparin, glycoprotein IIb/IIIa inhibitors, and clopidogrel. Catheter Cardiovasc Interv 2005;64: 373-374.

51. Applegate RJ, Grabarczyk MA, Little WC, et al: Vascular closure devices in patients treated with anticoagulation and IIb/IIIa receptor inhibitors during percutaneous revascularization.J Am Cardiol 2002; 40: 78-83.

52. El-Jack SS, Ruygrok PN, Webster MW, et al: Effectiveness of manual pressure hemostasis following transfemoral coronary angiography in patients on therapeutic warfarin anticoagulation.Am J Cardiol 2006; 97: 485-489.

53. Tavris DR, Dey S, Albrecht B, et al: Risk of local adverse events following cardiac catheterization by hemostasis device use - Phase II. J Invasive Cardiol 2005; 17: 644-650.

54. Ayman A. El-Menyar, Jassim Al Suwaidi, David R. Holmes Jr. Left Main Coronary Artery Stenosis: State-of-the-Art. Current Problems in Cardiology, Volume 32, Issue 3, March 2007, Pages 103-193

55. Abizaid AS, Mintz GS, Abizaid A, Mehran R, Lansky AJ, Pichard AD, Satler LF, Wu H, Kent KM, Leon MB. One-year follow-up after intravascular ultrasound assessment of moderate left main coronary artery disease in patients with ambiguous angiograms. J Am Coll Cardiol. 1999 Sep;34(3):707-15

56. Cameron A, Kemp HG Jr, Fisher LD, Gosselin A, Judkins MP,Kennedy JW, Lesperance J, Mudd JG, Ryan TJ, Silverman JF,Tristani F, Vlietstra RE, Wexler LF. Left main coronary artery stenosis: angiographic determination. Circulation 1983;68:484–489.

57. Detre KM, Wright E, Murphy ML, Takaro T. Observer agreement in evaluating coronary angiograms. Circulation 1975;52:979 –986.

58. Louvard Y, Ludwig J, Lefevre T, Schmeisser A, Bruck M, Scheinert D, Loubeyre C, Klinghammer L, Morice MC, Flachskampf FA, Daniel WG. Transradial approach for coronary angioplasty in the setting of acute myocardial infarction: a dual-center registry. Catheter Cardiovasc Interv 2002;55:206-11.

59. Saito S, Tanaka S, Hiroe Y, Miyashita Y, Takahashi S, Tanaka K, Satake S. Comparative study on transradial approach vs. transfemoral approach in primary stent implantation for patients with acute myocardial infarction: results of the test for myocardial infarction by prospective unicenter randomization for access sites (TEMPURA) trial. Catheter Cardiovasc Interv 2003;59:26-33.

60. Vorobcsuk A, Kónyi A, Aradi D, Horváth IG, Ungi I, Louvard Y, Komócsi A. Transradial versus transfemoral percutaneous coronary intervention in acute myocardial infarction
Systematic overview and meta-analysis. Am Heart J. 2009 Nov;158(5):814-21.

61. Louvard Y, Ludwig J, Lefevre T, Schmeisser A, Bruck M, Scheinert D, Loubeyre C, Klinghammer L, Morice MC, Flachskampf FA, Daniel WG. Transradial approach for coronary angioplasty in the setting of acute myocardial infarction: a dual-center registry. Catheter Cardiovasc Interv 2002;55:206-11.

62. Cantor WJ, Puley G, Natarajan MK, Dzavik V, Madan M, Fry A, Kim HH, Velianou JL, Pirani N, Strauss BH, Chisholm RJ. Radial versus femoral access for emergent percutaneous coronary intervention with adjunct glycoprotein IIb/IIIa inhibition in acute myocardial infarction--the RADIAL-AMI pilot randomized trial. Am Heart J. 2005 Sep;150(3):543-9.

63. Choussat R, Black A, Bossi I, Fajadet J, Marco J. Vascular complications and clinical outcome after coronary angioplasty with platelet IIb/IIIa receptor blockade. Comparison of transradial vs transfemoral arterial access. Eur Heart J 2000;21:662-7.

64. Stella PR, Odekerken D, Kiemeneij F, Laarman GJ, Slagboom T, van der Wieken R Incidence and outcome of radial artery occlusion following transradial coronary angioplasty. Cathet Cardiovasc Diagn 1997;40:156-158.

65. Sanmartin M, Gomez M, Rumoroso JR, Sadaba M, Martinez M, Baz JA, Iniguez A. Interruption of blood flow during compression and radial artery occlusion after transradial catheterization. Catheter Cardiovasc Interv 2007;70:185-9.

66. Barbeau G. Radial loop and extreme vessel tortuosity in the transradial approach: Advantage of hydrophilic-coated guidewires and catheters. Cathet Cardiovasc Intervent 2003;59:442-50.

67. Wu SS, Galani RJ, Bahro A, Moore JA, Burket MW, Cooper CJ. 8 French transradial coronary interventions: Clinical outcome and late effects on the radial artery and hand function. J Invas Cardiol 2000;12:605-609.

68. Wholey MH, Kuntz RE, Fayad P, Katzen BT, Mishkel GJ, Bajwa TK, Whitlow P, Strickman NE, Jaff MR, Popma JJ, Snead DB, Cutlip DE, Firth BG, Ouriel K; Stenting and Angioplasty with Protection in Patients at High Risk for Endarterectomy Investigators. Protected carotid-artery stenting versus endarterectomy in high-risk patients N Engl J Med. 2004 Oct 7;351(15):1493-501.

69. Burton KR, Lindsay TF. Assessment of short-term outcomes for protected carotid angioplasty with stents using recent evidence. J Vasc Surg 2005;42:1094-1100.

70. Heenan SD, Grubnic S, Buckenham TM, Belli AM.Transbrachial arteriography: indications and complications.Clin Radiol. 1996;51(3):2059.

71. Hammer FD, Lacroix V, Duprez V, Grandin C, Verhelst R, Peeters A. Cerebral microembolization after protected carotid artery stenting in surgical high risk patients: results of a 2-year prospective study. J Vasc Surg 2005;42:847-853

72. Campeau L. Percutaneous radial artery approach for coronary angioplasty Cathet Cardiovasc Diagn 1989; 16:3-7

73. Levy EI, Kim SH, Bendok BR, Qureshi AI, Guterman LR, Hopkins LN. Transradial stenting of the cervical internal carotid artery: technical case report. Neurosurgery. 2003;53(2):448-51; discussion 451-2.

74. Saito S, Ikei H, Hosokawa G, Tanaka S. Influence of the ratio between radial artery inner diameter and sheath outer diameter on radial artery flow after transradial coronary intervention. Catheter Cardiovasc Interv 1999;46:173-8.

ABBREVIATIONS:

LMCA = Left main coronary artery

LAD = left anterior descending artery

TTE = transthoracal echocardiography

TEE = transoesophageal echocardiography

TTDE = transthoracic Doppler echocardiography

PDV = peak diastolic velocity

CFR = coronary flow reserve

FFR = fractional flow reserve

QCA = quantitative coronary angiography

IVUS = intravascular ultrasound

MLA = minimum lumen area

DS = diameter stenosis

PCI = percutaneous coronary intervention

CTA= computer tomographic angiography

PCI= percutaneous coronary intervention

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ATTACHED RELEVANT, ORIGINAL PUBLICATIONS

Reprints of full papers

I. Cardiologia Hungarica 32(2), 95-96, 2002.

II. Hellenic Journal of Cardiology. 2010; 51: 540-543

III. Cardiologia Hungarica 2008; 38: 1-6

IV. Cardiovascular Ultrasound 2011 Jun 14;9(1):19.

V. Cardiovasc Revasc Med. 2009 Apr-Jun;10(2):73-9.

VI. J Vasc Surg. 2007 Jun;45(6):1136-41.

VII. Cardiologia Hungarica, 2009; 39; 40-42.