We are IntechOpen, the world's leading publisher of Open Access books Built by scientists, for scientists



185,000

200M



Our authors are among the

TOP 1% most cited scientists





WEB OF SCIENCE

Selection of our books indexed in the Book Citation Index in Web of Science™ Core Collection (BKCI)

Interested in publishing with us? Contact book.department@intechopen.com

Numbers displayed above are based on latest data collected. For more information visit www.intechopen.com



Transradial Approach for Coronary Interventions: The New Gold Standard for Vascular Access?

Antoine Guédès CHU Mont-Godinne, University of Louvain Belgium

1. Introduction

The perfect cardiac catheterization technique, including good diagnostic and therapeutic qualities, without risk and with no recovery time for the patient, does not exist. Obtaining initial access to the arterial circulation is the first and most frequent catheterization difficulty encountered by the interventional cardiologist during the procedure. Often, it is also the only difficult part of the exam for the patient because it may cause a vagal reaction or painful spasm. These procedural problems inevitably increase catheterization time and are sometimes the underlying causes of more significant complications. Arterial access is a crucial step of percutaneous cardiac procedures and therefore requires special attention.

Today, percutaneous coronary intervention (PCI) are usually performed via the femoral or radial arteries (a brachial approach may occasionally be required as third choice vascular access). Since the first demonstration of transradial approach feasibility in 1989, by Lucien Campeau, many studies have confirmed this initial experience and especially its safety and performances compared to transfemoral route. Nevertheless, a recent study reports that less than 2% of percutaneous coronary interventions were performed by a transradial approach in the United States between 2004 and 2007(1). The persistent discrepancy between current practice in vascular access site choice and known advantages of a radial access needs to be clarified, enlightened by recent data.

2. Short overview of complications related to arterial access site choice for PCI

Over the last three decades, advances in percutaneous coronary interventions techniques and contemporary pharmacotherapy have made these procedures safer and more reliable in a wide range of patients, often older and sicker than before.

2.1 Bleeding after percutaneous coronary interventions

In routine clinical practice, bleeding complications are a frequent non-cardiac outcome of therapy for acute coronary syndromes even in the case of an adequate arterial puncture technique. Aggressive antithrombotic regimens used in this setting even if highly powerful

in reducing ischemic events, also expose patients to a higher rate of bleeding (related or not to the vascular access site).

More than two thirds of all bleeding complications involve the arterial access site and range from a local non significant hematoma to life-threatening bleeding (Fig. 1). The most common origins of bleedings not related to arterial access are gastrointestinal followed by cardiac tamponade and intracranial haemorrhage (2,3).

Retroperitoneal haemorrhage is more difficult to classify because of its double potential aetiology (often linked to manipulations related to a femoral approach but rarely occurring spontaneously in the case of anticoagulation and/or antiplatelet therapy). Retroperitoneal bleeding leading to a major bleed is reported to occur in approximately 0.1% to 0.3% of patient treated by a femoral access but is maybe an underestimate (2,4).

Risk factors for such complications are now well identified and could be divided in four categories (see Table 1).

Clinical Factors	 Advanced age Female gender Low body weight/obesity Prior bleeding Severe hypertension Heart failure Peripheral vascular disease Acute coronary syndrome
Biochemical Factors	- Renal insufficiency - Anemia - Diabetes
Procedural Variations	 Femoral Access (versus Radial Access) Increased sheath / Catheter size Prolonged sheath time after procedure Intra aortic Balloon Pump Concomitant venous sheath Need for repeat intervention
Treatment Combinations	 Antiplatelet therapy (dosage, efficacy, timing, duration) Overdose of anticoagulants (+/- GP IIb/IIIa inhibitors) Crossover / combinations of anticoagulants Thrombolytic agents

Table 1. Factors associated with a higher bleeding risk (5-10)

Large randomized trials and registries with "real world" populations of patients have clearly identified clinical characteristics conferring a higher risk of bleeding: advanced age, female gender, obesity, low body weight, chronic renal disease, peripheral vascular disease and a previous history of bleeding. Procedural predictors for an increased bleeding risk include faulty puncture technique, sheath size, prolonged sheath time, use of glycoprotein (GP) IIb/IIIa inhibitors, vascular closure devices, intensity/duration of anticoagulation with heparin, but also vascular access strategy using femoral rather than radial artery(3,9,11-17).

The main difficulty encountered when comparing trials which study the true incidence of haemorrhagic events linked to vascular access options remains the lack of a precise definition for this complication (18-20) or at least of a consensus taking into account main parameters in order to establish a bleeding severity score (clear identification of bleeding site, haematocrit /haemoglobin drop, hemodynamic consequences, treatments required...).

Even if some authors (21) report a significant reduction in the incidence of major femoral bleeding complications over time (from 8.4 % in 1995 to 3.5 % in 2005), the single effective way to reduce majors bleeding related to a coronary angiography or intervention procedure, according to recent data, is to use radial access (2,11,22-24). In experts hands, this strategy allows a 50 to 75 % reduction in major bleeding events (24) with the greatest absolute benefit for obese patients and in the setting of acute myocardial infarction (primary or rescue coronary angioplasty). Therefore, radial access should be promoted as the preferential access site for percutaneous coronary interventions. Nevertheless the keys to preventing bleeding complications are well known: good knowledge and recognition of predisposing factors, meticulous examination of the access site before the puncture follow by a careful sheath placement in the artery without forceful manoeuvre and discontinuation of heparin at the end of the procedure.



Fig. 1. Large right groin and forearm hematomas.

2.2 Other frequent complications related to arterial access site

Other significant access site related complications encountered after a catheterization procedure are pseudoaneurysm, arterio-venous fistula, femoral laceration, femoral thrombosis with or without distal embolization, and any need for a surgical exploration or repair. Less frequently groin infection (puncture site abscess), neural damage and venous thrombosis are observed.

2.2.1 Pseudonaneurysm

A pseudoaneurysm is defined as an encapsulated hematoma or cavity (contained by surrounding tissues) communicating with the lumen of an artery because of a localized disruption of the media (Fig. 2). It mainly occurs after an inadequate artery compression

following sheath withdrawal. Predisposing factors for this iatrogenic arterial trauma are impaired hemostasis and factors known to be associated with difficult and prolonged procedures (peripheral vascular disease, large sheath use, aggressive anticoagulation and/or fibrinolytic therapy, prolonged sheath and anticoagulation times) and in case of a femoral approach the concomitant use of an intra aortic balloon pump and an early ambulation after catheterization. The reported incidence for femoral access seems to be around 1% (maybe higher), and is lower in the case of radial access (≤ 0.2 %) (2,25-28).

An adequate recognition of this complication, which may occur more than one year after the catheterization procedure, is mandatory because of the risk of rupture estimated at approximately 4 % for large pseudoaneurysms (> 3cm) (29-31).

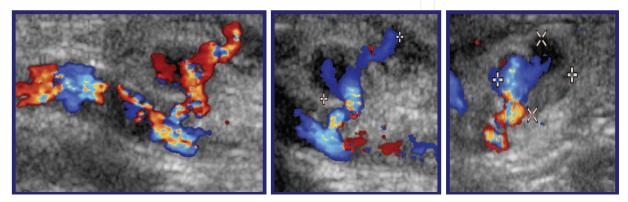


Fig. 2. Pseudoaneurysm of the radial artery (2D color-Doppler flow imaging)

2.2.2 Arteriovenous fistula

An arteriovenous fistula results from an overlying vein puncture during femoral artery catheterization, creating a communication between the two vessels after sheath removal. A high velocity and continuous jet originating from the artery and going into the vein lumen, is often easily demonstrated by color flow Doppler examination if clinical manifestations exist at the access site. The reported incidence is low in recent trials studying patients after a coronary angiography or intervention by femoral approach (0.1-2.2%) and extremely rare for radial approach (< 0.1%) (2,4,26).

By femoral approach, the occurrence of arteriovenous fistula and pseudonaneurysm is reported to be significantly higher if the puncture site is located distal to the division of the deep and superficial femoral arteries (25).

2.2.3 Arterial wall dissection

Arterial wall dissection is probably frequently unrecognized especially in cases of local dissection although its true incidence is hard to establish. Regarding published and already historical data for recognized dissection, the incidence of this arterial wall injury varies from 0.01% to 0.5% (32,33). However, when considering the fact that, as demonstrated by angiographic studies, 25% of patients admitted for a catheterization procedure had common femoral artery atherosclerotic plaques determining at least a 20% stenosis, it is easy to understand that all intravascular foreign body as a needle or catheter may easily deflect off some of these plaques.

4

2.2.4 Arterial thrombosis

Due to the increasing number of percutaneous cardiac procedures performed annually and to the worldwide operator preference for this vascular access, most arterial thromboses occur in the common femoral artery. Nevertheless the incidence of this serious adverse event remains very low after coronary intervention (<0.5%) probably because of the widespread use of high dose multi-drug antithrombotic therapy for percutaneous interventions (2,4).

The common femoral artery being the unique blood supply to the leg, an urgent diagnostic of this complication followed by immediate heparinization and mechanical or surgical thrombectomy are usually required. On the contrary, radial artery thrombosis is a relatively frequent asymptomatic condition (incidence: 3-6 %). It is a benign issue, with nearly no clinical sequelae observed after occlusion of this vessel, because of the double blood supply to the hand insured by the palmar arch. Many of these radial occlusions (40-60%) are spontaneously recanalized after one month (11,34). This specific point will be discussed later in the chapter.

2.3 Impact of vascular closure devices on vascular access site complications

Today, closure devices are widely used to obtain a rapid hemostasis after percutaneous transfemoral approach but their safety remains largely controversial. Marginal evidences concerning the effectiveness of these devices are derived from pooled analyses of a heterogeneous group of small randomized trials, many of poor methodological quality (26,35).

All of the approved arterial closure devices have proven their efficacy in obtaining immediate hemostasis after sheath removal, in allowing early ambulation, and in improving patient comfort (36). However, there is no report showing a clear reduction of access site complications related to their use (compared to efficacy of manual compression) especially after diagnostic angiography. In the setting of percutaneous coronary interventions, meta-analysis of randomized trials only showed a trend towards less access site related complications with some of these devices but also an increased risk with others (26,35). Additionally, four separate prospective studies have found that bleeding complications were more frequent with transfemoral access and closure device than with transradial access (up to 3.7% versus less than 0.7%, respectively) (37-40).

There are still matters of concern about the use of these devices. For example they may increase the risk of hematoma and pseudoaneurysm formation (26,35,36,41-43). Moreover, early device failure rates and their impact on vascular access site complications are not always clearly reported in these trials but may decrease after the initial learning curve. Recently, data with the last generation of vascular closure devices suggest that their use may decrease vascular complications but these points had to be confirmed once again by large randomized trials because it maybe simply reflects a better patient selection and operator experience with these devices over time (4,42,44).

When an arteriotomy closure device is used, some specific complications may occur in addition to those previously described for manual compression. A higher rate of access site infections (0.3% versus 0.05 % with manual compression) and more episodes of acute or late

limb ischemia (0.4% versus 0.1% for manual compression) are reported. The need for surgery, in case of device failure, is not commonly reported with details in the great majority of previous published trials. Nevertheless, surgery for partial embolization, to remove trapped components of these devices or after vessel laceration is uncommon(4,35).

Given the remaining uncertainty about their true impact on vascular complications and the difficulty to assess costs induced by specific vascular access complications, the widespread adoption of these devices following endovascular interventions is still controversial and needs to be clarified in the future (4,45).

2.4 Conclusions

All vascular access techniques, even if perfectly handled by the interventional cardiologist are linked with a minimal but inevitable rate of complications arising because materials enter atherosclerotic vessels. To avoid more serious clinical consequences for the patients, it is particularly important to give meticulous attention to the access site not only before the puncture but also in the hours following the procedure and to recognize predisposing factors for such complications.

3. Anatomical considerations and technical aspects of a transradial approach

3.1 Favorable anatomical characteristics of the radial artery

Differences observed in terms of vascular complications after radial and femoral percutaneous interventions are mainly based on favorable anatomical characteristics of the radial artery (compared to those describe for the common femoral artery) (Table 2 and Fig. 3).

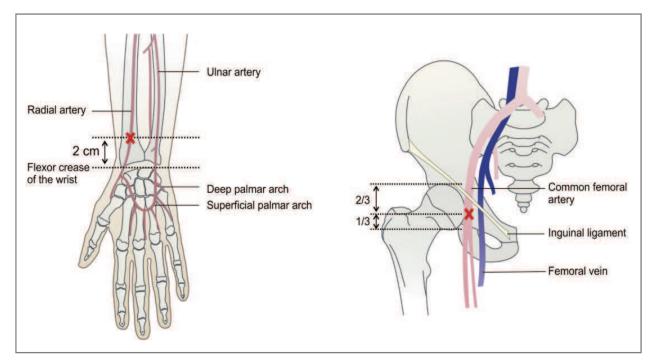


Fig. 3. Landmarks for vascular access (48,50,51)

Common Femoral Artery (CFA)	Radial Artery (RA)
 CFA is relatively deep. The ideal site of puncture may be hard to identify especially in obese patients. The inguinal crease is an unreliable landmark in more than two thirds of patients. The strongest femoral pulse correctly identified the mid-CFA in 90 % of cases 	 Distal RA had a superficial course, This artery is easy to palpate even in obese patients At the level of the puncture site, the artery lies just under skin and fascias
 Puncture site is over the hip joint The most reliable landmark is probably the junction between the middle and the lower third of the femoral head (radiographic landmark) 	 Puncture site is not over a joint The most reliable landmark is ideally 2-3 cm proximal to the flexor crease of the wrist (clinical landmark)
 Compression of the CFA may be hard No hard and fixed structures behind the artery 	 RA can easily be compressed with minimal pressure At the puncture site, radial bone is just beneath the artery
CFA lies just near a major vein (Femoral Vein) and nerve (Femoral Nerve) CFA is the unique blood supply to the leg	RA is separated from median nerve and major veins Double blood supply to the hand insured by the palmar arch

Table 2. Comparison of access site characteristics (46-48)

Its superficial course makes this artery easily accessible to puncture and, after the procedure, more amenable to compression (because of bone support beneath), even in obese patients. The puncture site is not over a joint, so compression devices are always stable and effective to ensure good hemostasis after sheath removal. Also wrist movements are not impaired after a transradial percutaneous intervention, which facilitates rapid recovery and makes an outpatient strategy feasible. Moreover, the radial artery is separated from median nerve and major veins of the forearm making post-catheter injuries of these structures rare. Lastly, the double blood supply to the hand makes hand ischemia an almost impossible complication if the presence of functional collaterals between the radial and the ulnar arteries, as judged by the Modified Allen's Test (49) or alternative tests, has been assessed.

3.2 Learning curve and prerequisite conditions for a safe technique conversion

The same catheterization laboratory set up and patient preparation as for femoral procedures can be used for the radial approach and only minor adaptations to improve patient and operator comfort, especially for the puncture, are required. A good arm support system is the only inescapable element needed and a pulse oximeter (finger plethysmography) may be required to perform alternative tests in case of an abnormal modified Allen's test (50,51).

Transradial access is known to be technically more demanding and time consuming, especially during the early learning curve (52).

7

The small caliber (2-3.5 mm in diameter) and the alpha–adrenergic innervations of the artery make the puncture task the key point of a successful transradial procedure.

When the accurate site of puncture has been correctly identified, the most critical step of the radial catheterization procedure begins. Different puncture techniques exist but the most commonly used today by experienced radial operators is the over-the-needle technique (50,51).

As described in many papers dedicated to transradial approach (53) puncture remains, for beginners, the cornerstone of the learning curve and it takes time to develop all the skills required, even for experienced interventionalists. Obtaining arterial access by a single or a limited number of puncture attempts is probably the best way to avoid difficulties linked to a refractory spasm following a difficult puncture.

This is the reason why, it is strongly recommended to take extra time to prepare and realize the puncture and to keep in mind that gentle and cautious manipulations will always pay off later. Failure of the puncture task (inability to puncture or to wire the artery) accounts for more than 50 % of transradial approach failures. Even if it takes approximately 200-300 cases to overcome initial difficulties, several studies confirms the reality of a long learning curve (53). During the beginner's phase of radial access experience, good patient selection with a readily palpable radial pulse is necessary to help perfect all the skills needed for this elegant technique. Weak radial pulses, small radial arteries, old patients, patients with known peripheral vascular disease or post CABG surgery should be avoided at this time. All these elements, required to identify patients with the most difficult access, are given by the bedside clinical evaluation of the patient, even if puncture is frequently less difficult than anticipated.

During the procedure, inability to cross forearm, arm or intra thoracic vasculature difficulties accounts for 10 % of transradial approach failures, inability to reach a coronary or graft ostia due to difficulties in rotating and manipulating the catheters for 10% and the remaining failures are related to the inability to reach a contra-lateral mammary graft.

An access site crossover, related to failure of initial strategy, is required in 6-7% of transradial procedures compared to less than 2% in case of femoral approach (including PCI procedures). For high volume radial operators or centers, lower crossover rates are reported (4-6%) (2,11,24,53). Once again, these data confirm the importance of experience and expertise when interventionalists are dealing with this approach.

In these conditions, with growing experience and state of the art materials, and if there is a systematic use of the contra-lateral radial artery in case of puncture failure on the initial side (the same technique is applied for femoral access) a very high success rate can be expected by this technique, approximately 98 % or more, with no significant differences among subgroups of patients (53).

After a while, when experience and confidence in the technique has grown, more adequate catheter choice and skills in their manipulations will ensure similar clinical results as in the femoral approach (2,11).

Indeed, PCI success rate is similar for the two approaches. The RIVAL study, the largest randomized trial comparing radial and femoral access for acute coronary syndromes,

8

demonstrates the equivalence of the two techniques in terms of complications at the level of the coronary tree (2). The number of guiding catheters required for the procedure, the rate of abrupt coronary closure, no reflow, dissection with reduced flow, perforation, catheter thrombus and stent thrombosis were similar in the two arms of the study. These observations had already emerged from the meta-analysis performed by Agostoni in 2004 (11), which did not show statistically significant differences in terms of procedural failure for studies performed after 1999. Similarly, no differences were shown in PCI procedural time and contrast volumes used for the procedures.

3.3 Difficult cases by transradial approach and limits of the technique

Transradial approach is considered to be a difficult approach, first because of the puncture task but also for the frequent occurrence of spasm, difficult catheter selection or inability to overcome difficult radial or vascular anatomy, especially during the learning curve.

Spasm is usually related to prolonged or excessive catheter manipulation but may already occur during puncture or after sheath insertion. By using adequate doses of spasmolytic drugs (intra-arterial verapamil) at the beginning and during the procedure and small catheter size (5 French), refractory spasm becomes rare (1,1% versus 4,8% with 6 French catheters) (54). Interestingly, spasm more frequently occurs where difficulties are encountered in advancing the wire or the catheter and not only at the level of the radial artery (it can also be seen at the level of the upper limb or of the brachio-cephalic trunk). For experienced radial operators, spasm is not reported as a pertinent cause of radial approach failure during percutaneous coronary interventions (11,53). However, when resistance occurs, it is strongly recommended to perform an angiogram to adequately define the anatomy, spasm level or rarely stenosis or occlusion levels. Several studies have shown that intra-arterial verapamil and nitroglycerine are the most effective medications to prevent or to relieve spasms. Moreover, selective angiograms of the left and right coronary arteries (as well as left ventriculography) are possible with only one catheter by transradial approach (Optitorque TIG[™] catheter, Terumo corp.). Thus, there should not be a need for three different catheter exchanges, which also helps in reducing the occurrence of spasm. In the same way, sheath-induced spasms are minimized and far less frequent when hydrophilic-coated materials are used. Hydrophilic coating also helps to reduce patient discomfort and facilitates sheath withdrawal (55). Finally, a higher incidence of radial artery thrombosis is documented in patients with periprocedural spasm (56).

Beginners frequently evoke loops, tortuosities and anatomic variants as one other major hurdle to overcome during learning curve. These unpredictable abnormalities are quite rare in current practice but the most challenging ones may require an alternative vascular access site. Tips and tricks, state of the art materials (especially hydrophilic wire and 0.014" PTCA guidewires) are helpful in overcoming these difficulties in a large majority of these cases. Solutions that work are often those associated with gentle wire and catheter manipulations in order to prevent vascular injury and perforation.

Another frequently advanced argument against transradial intervention is inadequate guiding support. Randomized trials performed after 2000 do not advocate this point when procedural success is compared to those reported for transfemoral PCI studies, especially when dedicated radial materials are used (2,11,37,57). Most radial arteries have a lumen

large enough to accommodate 6 French catheters and some large radial arteries are able to eventually accept 7 French catheters or larger, but these sizes are not often required.

Large lumen 6 French guiding catheters with dedicated radial shapes give good back up support and allow to perform a wide range of the most complex intracoronary procedures (ostial or bifurcation lesions, left main stenosis, chronic total occlusions, thrombectomy, rotational atherectomy, saphenous vein graft lesions, acute coronary syndromes and ST-elevation myocardial infarction) (2,58-63) but standard curves designed for femoral approach also work well in most cases.

Nevertheless, in routine clinical practice, 5 French guiding catheters make direct stenting easily feasible in the great majority of procedures. In a randomized comparison study, Dahm had even shown a trend in favor of the superiority of 5 French guiding catheters over 6 French guiding catheters in terms of procedural (95.4 versus 92.9 %, p =0,097) and clinical success (93.1 versus 90.5 %, p=0,097) (54).On the other hand, today, with larger sheathless guiding catheter technology, coronary techniques only accessible by a femoral way are far less numerous than before (64,65). For example, sheathless 7.5 French guiding catheters, by transradial approach but had smaller outer diameters than 6 French radial introducer sheaths.

As with the femoral approach, the ideal sizing and shape of guiding catheters is still, and will stay a matter for debate.

The side to choose for the first radial approach in a given patient also remains a controversial issue with no clear answer. In most centers, transradial coronary interventions are performed through the right radial artery, because this side offers a more comfortable working position for the operator, but on a technical point of view there is some evidence that catheter manipulation could be easier by a left-sided approach, because of similar sensations compared to a femoral way and perhaps offering more back-up support for guiding catheters. In the TALENT study, a randomized comparison of right versus left radial approach for diagnostic procedures, the left approach was associated with lower fluoroscopy time and radiation dose, reflecting an easier procedure, particularly in older patients (> 70 years) and for operators in training (66). The absence of a radial artery pulse or a negative Modified Allen's Test on one side, as well as the need to selectively cannulate a mammary bypass graft also frequently influence the choice. Today, long catheters allow to easily reach the infradiaphragmatic arterial system (renal, mesenteric, iliac, femoral or lower limb arteries but also for example a gastro-epiploic bypass graft). If these catheters are not available, a left radial approach saves ten centimeters of catheter length (by this route, catheters do not cross the arch of aorta).Similarly, the cerebrovascular pathology (carotid and vertebral arteries) can be imaged and eventually treated by transradial approach.

In routine clinical practice, the control of bypass grafts is also a frequent request. Angiography of the left internal mammary artery is easy to perform by the left radial approach (as for a right internal mammary artery by the right radial approach). In case of a bilateral mammary artery bypass graft, a right radial approach should be preferred but left internal mammary artery opacification by the right radial remains challenging even for

10

skilled operators (53,67). A successful selective opacification of the contra-lateral mammary artery can be expected in 50% of these particular cases if performed by an experienced operator using dedicated catheters (53). In our institution, we mainly use for this purpose the OutlookTM 4 French diagnostic catheter (Terumo corp.). To reach saphenous vein grafts, either left or right radial approaches can be chosen, with a similar success rate using standard catheter curves (63). Sometimes, a bilateral radial approach, during the same procedure, is necessary to obtain adequate images of the grafts.

Finally, there are only a few relative contraindications to a transradial approach: patients with a negative Allen test in both hands, patients with end-stage renal disease (just before the creation of an arteriovenous fistula for haemodialysis) and patients with known severe obstructive atherosclerotic disease at the level of the innominate, subclavian or upper limb arteries. Finally, some patients may have had previous coronary artery bypass surgery using a radial artery as a conduit which precludes radial access by this side.

3.4 Conclusions

One challenge encountered with radial access is the steep learning curve, but this hurdle can be more easily overcome by following an educational program dedicated to this approach and addressed to interventionalists and fellows in training. The widespread diffusion of the technique in teaching centers as well as the growing interest of major cardiovascular societies and device industry for this approach will also progressively ensure its greater penetration in the interventional cardiologists' community.

4. Specific complications of transradial approach

Despite a proven safety profile leading to a drastic reduction of vascular access site bleeding, the transradial approach is not totally free of complications. Catheterizers must be aware of some rare complications, which are often minor and localized if recognized without any delay.

4.1 Post procedural radial artery thrombosis: The main pitfall of transradial approach?

Although radial artery thrombosis is still a matter of concern after a transradial approach, this complication is usually benign because of the double blood supply to the hand insured by the two forearm arteries inter-connected at the level of the palmar arch. Moreover, hand-threatening ischemia, with necrosis or clinical sequelae, has not been reported after a transradial procedure to this day.

As shown by studies that have planned post catheterization Doppler ultrasound examinations, the incidence of radial artery thrombosis ranges, in general, from 3% to 6% but one study reports a rate of 9.5% (34,56,68-71). A loss of radial pulse is reported in up to 9% of patients in other studies.

The occlusion rate increases with the size of catheters used for the procedure (54,72) and is more precisely related to the ratio between the inner radial artery diameter and the sheath outer diameter (73). The incidence of occlusion is 4% if the ratio is higher than 1 and rises dramatically to 13% in patients with a ratio of less than 1.

Other factors have been found to affect occlusion rate. Repeat cannulation (74) and older age are known to be predisposing factors but heparinization is effective in reducing its occurrence as well as the use of hydrophilic materials. For transradial procedure, adequate anticoagulation is extremely important and should be immediately started in all patients after sheath insertion; at least 5000 units of intra-arterial heparin are recommended. In patients receiving only 1000 units for a diagnostic coronary angiography, the incidence of radial occlusion climbs up to 30% (34). Intra-arterial or intravenous heparin administration provide comparable efficacy in preventing radial artery occlusion (75).

Nearly 50% of the patients in whom the radial artery is shown occluded at hospital discharge may expect a spontaneous recanalization of the vessel in the first month after procedure. Therefore, the true definitive incidence of radial artery thrombosis is probably between 2 and 3% (34).

Short procedure duration and immediate sheath removal at the end of the procedure, whatever the dose of heparin or the use of GP IIbIIa inhibitors, also contribute in maintaining radial permeability. In the same way, it seems to be relevant to avoid prolonged post-procedure compression times, especially if a mechanical device applying high pressures is used. Moreover, with some of these compression devices, a fine pressure adjustment, in order to always maintain blood flow in the radial artery during the compression, is feasible and may contribute to radial artery protection (76). In the PROPHET trial, guided compression that allowed antegrade flow, using the Barbeau's test to document radial artery patency at time of hemostasis, was shown to be highly effective in preventing radial artery occlusion (incidence decreased by 75% at 30 days after radial access) when compared to usual care (1.8% versus 7%, p<0.05) (77).

Nevertheless, even if radial occlusion is a fairly infrequent outcome of transradial approach, the radial artery patency should be checked in all patients after the procedure. Bernat et al. have shown recently that an early and short (1-hour) ipsilateral ulnar artery compression using TR bandTM (Terumo corp.) could be an effective and safe non-pharmacologic method for the treatment of acute radial artery occlusion (78).

4.2 Post-procedural non-occlusive radial artery injury

As demonstrated by several studies, permanent radial artery damage without occlusion may sometimes follow transradial procedure.

In a first study, ultrasound examinations of the radial artery showed no significant difference in the mean radial artery internal diameter between pre and early post-procedure measurements (at 1 day). Conversely, after a mean follow up of 4.5 months, internal diameter significantly decreased from 2.63 ± 0.35 to 2.51 ± 0.29 mm (p = 0.01). Moreover the mean radial artery diameter was smaller and the radial occlusion rate higher (2.6% versus 0%; p = 0.01) in patients undergoing repeat transradial approach as compared to a first-time procedure (79).

Further intravascular ultrasound (IVUS) studies have explained that this progressive narrowing is secondary to an intima-media thickening (hyperplasia), especially in the distal radial artery, presumably induced by trauma from sheath or catheter insertion (80,81). Sanmartin et al. reported that soon after a transradial catheterization the vasoreactivity is

12

impaired, but generally recovers as early as 1 month after the procedure (82). Edmunson et al. have also demonstrated that the vessel vasoreactivity was maintained despite the fact that post procedural non occlusive radial artery injury was a quiet common observation after transradial interventions (80). Therefore, the main underlying process of this permanent arterial wall injury is certainly catheter-based.

4.3 Forearm hematoma

Radial artery perforation, if not early recognized and managed, can lead to severe forearm hematoma and compartment syndrome. Prompt detection of the complication and precise localization of the bleeding source are of prime importance to adequately manage the problem with a pressure bandage dressing or a blood pressure sphygmomanometer inflated just over systolic pressure and placed over the bleeding area (83,84). In the great majority of cases this maneuver permits an easy, rapid and effective hemostasis. Afterwards, a careful observation of the forearm is required especially if the procedure is completed with the same initial access.

The most common etiology of hematoma is radial or small side branch perforation by the guidewire during sheath insertion or loops crossing especially in patients receiving multiple antiplatelet therapies (85).

Inadequate catheter manipulations or forceful maneuvers during guidewire or catheter advancement can also cause small radial side branch avulsions or dissections leading to hematomas. Hydrophilic guidewires easily entering these small arteries should always be advanced carefully because of their high perforation risk profiles.

Delayed recognition of a quiet but prolonged bleeding may lead to a large hematoma formation and sometimes to a compartment syndrome by pressure induced occlusion of the two major forearm arteries (ulnar and radial) (83,86).This severe complication must be treated by urgent fasciotomy and hematoma drainage to prevent ischemic injuries (Fig. 4). Fortunately, this very infrequent complication more often occurs during the learning curve of the technique and can be partially avoided by adequate nursing staff education and training.

4.4 Miscellaneous complications

Radial artery eversion or rupture during sheath removal or when catheters are drawing back, are due to a severe and refractory spasm of the radial artery blocking material retrieval (87). This complication should never occur by using hydrophilic-coated sheaths/catheters and with gentle manipulations.

Extremely rare cases of axillary, infraclavicular or even mediastinal hematomas due to perforation of a small arterial branch have also been reported (88).Late rebleeding occurring several hours or days after the procedure, as well as pseudo-aneurysms and arterio-venous fistula are quiet rare after transradial approach (see below paragraph 2.2).

Causalgia (uncommon) is secondary to nerve injury during arterial puncture or sometimes secondary to aggressive haemostatic compression (50). Residual pain is often transient but may be permanent. Similarly, but with a more severe clinical pattern, instances of chronic regional pain syndrome are described at the whole arm level (89).



Fig. 4. Rare case of compartment syndrome (The same patient before and after urgent fasciotomy)

4.5 Conclusions

Long term consequences of radial artery occlusion or injury have to be further investigated, not only in patients requiring repeated percutaneous coronary interventions but also for patients in whom a radial conduit may be used for a surgical myocardial revascularization or the creation of an arterio-venous fistula.

To defend the use of radial access for coronary interventions, the conclusions of some recent major trials do not advocate the superiority of the radial artery over venous conduits for CABG surgery in terms of usefulness as well as for short or long-term patency (90). Nevertheless a retrospective study has shown a reduced early graft patency (77% versus 98%, p=0.017) in patients who had experienced a previous radial procedure before radial artery harvesting but without early clinical impact (91).

5. Clinical results and outcomes with transradial approach

5.1 Drastic reduction of periprocedural bleeding complications with transradial approach potentially drives reduction in mortality

Initially based on limited observational studies, followed by small single center or limited multicenter randomized studies, data concerning the safety of transradial approach and the

lack of severe access site bleeding when compared to transfemoral approach are now supported by large registries (22), several meta-analyses (11,24) and more recently by a large, randomized and multicenter trial (2). According to these data, when compared with the transfemoral approach, a 27% (2) to 80% (11) reduction of entry-site bleeding complications may be expected with transradial approach.

As a result of these observations and of the progressive widespread endorsement of guidelines related to antithrombotic therapies for coronary procedures, attention has progressively turned to periprocedural bleeding complications and how to reduce the risk. If post-PCI bleeding events not related to the arterial access site are more difficult to anticipate, current literature, as Rao et al. have written, provides more and more data suggesting that the choice of the radial rather than the femoral access is associated with comparatively larger reductions in bleeding risk than those ever achieved with any anticoagulant strategy (92).

In parallel, according to several important studies, major bleeding events occurring after percutaneous coronary interventions have been shown to be independently associated with a marked increased risk of death and recurrent ischemic events in patients with an acute coronary syndrome or undergoing an elective revascularization (13,15,17,21,24,93). More precisely, bleeding in the 30 days after a percutaneous coronary intervention is strongly associated with mortality as late as 1 year after the procedure. This bleeding in the first 30 days after the procedure is comparatively as strong as the 30-day occurrence of other events such as post-procedural myocardial infarction and the need for an urgent revascularization. Not only major but also minor bleedings have been shown to be associated with late mortality (15). Before these observations, the composite endpoint of efficacy and safety used to assess PCI procedures was, traditionally, the combined incidence of death, myocardial infarction and urgent repeat revascularization of the target vessel at 30-days. To take into account post PCI bleeding impact on mortality, the "quadruple endpoint" that includes 30days incidence of death, myocardial infarction, urgent revascularization and major bleeding has been recently introduced and should be promoted for the assessment of outcome after PCI.

Finally, as expected, a link between the reduction of bleeding complications with transradial interventions and a potential mortality reduction had recently emerged from data analysis. In the MORTAL study, Chase et al. found, by data linkage of three databases collecting clinical and procedural outcomes of 38,872 PCI patients of the British Columbia Cardiac Registry, that patients treated by transradial approach had a significantly lower rate of post-procedural blood transfusions (1.4% versus 2.8% for femoral, p<0.01) and a significant reduction in 30-day and 1-year mortality, odds ratio = 0.71 [95% CI 0.61 to 0.82] and 0.83 [95% CI 0.71 to 0.98], respectively (all p<0.001). In this study, the absolute increase in risk of death at 1 year associated with receiving a transfusion was 6.78% and the number needed to treat was 14.74 (prevention of 15 transfusions required to "avoid" one death). Therefore, transradial approach could potentially save one life for one thousand percutaneous coronary interventions performed by this way rather than by transfemoral approach (22). A large international registry provided similar results and demonstrated that transradial approach was independently associated with a lower risk of death or myocardial infarction

after PCI (odds ratio = 0.52 [95% CI 0.31 to 0.89]) (94). Subsequently, the PRESTO ACS vascular substudy, including patients with non-ST-elevation acute coronary syndromes, also showed significant reduction in bleedings with the radial approach (0.7% versus 2.4% for femoral, p=0.05) and for the combined endpoint of 1-year mortality or re-infarction (4.9% versus 8.3%, p=0.05)(95). In patients suffering ST-segment elevation myocardial infarction (STEMI), the meta-analysis conducted by Vorobcsuk demonstrated a significant mortality reduction with transradial PCI (2.04% versus 3.06% for femoral, odds ratio= 0.54 [95% CI 0.33-0.86], p=0.01) (96). In the meta-analysis conducted by Jolly et al., despite the confirmation of a dramatic reduction of major access site bleedings with the transradial approach (0.05% versus 2.3% for femoral, odds ratio= 0.27 [95% CI 0.16, 0.45], p < 0.001), no significant association between this approach and a reduced 1-year mortality was found (24). In the same way, in the RIVAL study including patients with acute coronary syndromes, radial access did not reduce the primary outcome of death, myocardial infarction, stroke or non-CABG-related major bleeding compared with femoral approach even if radial access significantly reduced vascular access complications and insured similar procedural success rates (but patients presented with cardiogenic shock, known severe peripheral vascular disease precluding a femoral approach or previous coronary bypass surgery using the two internal mammary artery were ineligible for this trial). Nevertheless when the results of the RIVAL study ,restricted to centers with the highest radial tertile in this study, are included in an updated meta-analysis of all randomized trials conducted by known radial experts, the composite of death, myocardial infarction, or stroke was lower in the radial group than in the femoral group (2.3% versus 3.5%, p=0.005) (2). These observations suggest that the effectiveness of radial access might be linked to operator's or center's expertise in transradial PCI.

5.2 Does transradial approach influence the occurrence of silent cerebral injuries or post-procedural strokes?

Stroke is also a subject that people are worried about with the radial approach but previous studies have never demonstrated higher rates of TIAs or strokes with this technique even if used in higher risk subgroups of patients, such as the octogenarians (2,24,27).

Lund et al. and more recently Jurga et al. raised concern about the possibility that transradial access may induce subclinical solid cerebral microemboli at a higher extent than the transfemoral approach (97,98). As assessed by magnetic resonance imaging, 15% of patients suffered embolization toward the brain when the catheter passed from the right arm to the aorta in those examined with transradial access compared with none in the transfemoral group (p=0.567)(98). Transcranial Doppler showed that significantly more microemboli passed the right middle cerebral artery with right radial access than with the femoral (for radial median number of microemboli was 10 (1-120) and 6 (1-19) for femoral) (97).

Nevertheless, these two small studies have to be interpreted with caution for many reasons. The limited number of patients, the not so well reported operators experience for transradial approach but also the restricted use of the right radial artery may have negatively influenced the results. The clinical implications of these observations and the risk of cognitive impairment have not been explored further.

16

5.3 What about operator and patient radiation exposure during a transradial approach?

Interventional cardiology is known to be one of the professions with the greatest exposure to radiation. This is currently a growing problem for the cardiologist's health. Therefore, data regarding transradial technique are of great interest.

When interventional cardiologists, or fellows during their training, are dealing with a new technique they are often confronted with a higher level of radiation. When skills improve, catheter manipulations are more efficient and procedures are shortened which finally helps minimize radiation exposure.

For the transradial approach the problem is the same but, being technically more demanding, this technique is associated with a longer learning curve. However, in current literature, radial access is consistently associated, when compared to femoral, with longer procedural and fluoroscopic times which slightly but significantly increase occupational radiation exposure for operators but also irradiation for patients (1,2,11,24,99). In the RIVAL study, median fluoroscopy time was higher in the radial group than in the femoral group (9.8 min versus 8.0 min, p<0.0001) and these results were similar to those reported by Agostoni et al. (8.9 min versus 7.8 min, p< 0.001) or Rao et al. (13.5 versus 11.3 min, p<0.01).Jolly et al. have reported a mean difference of 0.4 minutes of fluoroscopy between the two techniques ([95% CI 0.3-0.5], p<0.001). The main limitation of previous observations is the significant variability among operators' performances. Some other confounding factors have to be discussed.

First of all, fluoroscopy time does not always correlate well with radiation dose received by operators (100). Secondly, many centers used classic catheter curves (Judkins, Amplatz, etc) for either diagnosis or intervention but the use of a dedicated radial catheter (Optitorque TIG[™] catheter, Terumo corp.) may have influenced total fluoroscopic time. Indeed, radial operators have to take advantage of the possibility to complete a full coronary and left ventricular study with only one catheter to reduce radiation exposure (which is a significant difference compared to the femoral technique). Third, the exact puncture site is not always clearly reported in these trials. As mentioned before, a recent randomized trial, designed to evaluate safety and efficacy of left radial approach compared with right radial approach for coronary diagnostic and interventional procedures, showed that the left side was associated with slight but significantly lower fluoroscopy time and radiation dose adsorbed by patients. The left radial access advantages were particularly seen in older patients and for operators in training (66). These results are encouraging and future trials may further explore the potential advantages of a systematic left radial approach with the use of dedicated radial catheters to reduce the amount of fluoroscopy and finally the gap with femoral approach in terms of radiation exposure.

In addition, impact of operator ability in catheters or X-Ray tube manipulations (beam collimation, adequate tube angulations and operator position), as well as the use of radiation protection devices (low leaded flaps, upper mobile leaded glass, lead shields, lead aprons) are not often evaluated. The procedural setting (coronary angiography versus angioplasty, ad-hoc versus staged or urgent coronary interventions) may also influence measurements. Moreover many of these studies have been performed in centers (or by operators) with

limited experience in transradial approach and results have not been corrected for probable improvements with greater expertise.

Finally, even if differences in terms of radiation dose beneath the lead apron are minimal between these approaches, their clinical impact in the long term is not known and operators should always apply all efforts to reduce the radiation dose in their daily practice.

5.4 Conclusions

Concerning many points, the debate is not closed and future randomized trials, if correctly powered to demonstrated differences in primary outcomes between the two vascular approaches and designed to avoid confounding factors, will be useful to confirm these findings. However, all the previous authors agree with the fact that clinicians may choose radial access for percutaneous coronary interventions because of its similar performances and above all, its reduced vascular complications.

6. Transradial approach: The perspectives

6.1 Outpatient strategy is feasible with transradial approach

Ad-hoc percutaneous coronary interventions, performed immediately after diagnostic angiography, have been shown to have equivalent short and long term safety when compared to elective interventions (101-105). In current clinical practice, ad-hoc PCI represents the majority of elective coronary interventions in most countries. PCI programs with same day discharge are therefore conceivable.

In accordance with the known benefits of transradial interventions, including less bleeding complications, better quality of care and earlier ambulation after the procedure, it was natural to test the feasibility and safety of an ambulatory discharge strategy in selected patients undergoing transradial coronary procedures. Numerous international studies are now available and even if not always randomized, they have validated this strategy after uncomplicated transradial percutaneous coronary interventions (106-112). No more access site complications are observed and the majority of events occurring 24 hours after discharge would not have been avoided by traditional next-day discharge. Bertrand et al. have also shown in a selected high risk population of patients (two thirds of patients presented with unstable angina and approximately 20% presented with high-risk acute coronary syndrome prior to the procedure) that same-day home discharge after uncomplicated transradial coronary stenting and administration of a bolus of abciximab is not clinically inferior to the standard overnight hospitalization with a bolus of abciximab followed by a 12-hour infusion. The primary composite end point of this study was the 30day incidence of any of the following events: death, myocardial infarction, urgent revascularization, major bleeding, repeat hospitalization, access site complications, and severe thrombocytopenia. The incidence of the primary end point was 20.4% in the sameday discharge group and 18.2% in the overnight hospitalization group (P=0.017 for noninferiority).No death occurred and the rate of major bleeding in both groups was extremely low at 0.8% and 0.2%, respectively (106).

Interestingly, similar feasibility and safety data are far less numerous to date for femoral approach, even if the same strategy may likewise be amenable by this access. Previous trials

18

have demonstrated a higher incidence of local vascular complications either with or without the use of a vascular closure device and despite an optimal post-PCI recumbency depending on the vascular access management strategy chosen by the operator. Moreover, patients undergoing a transfemoral access, even if receiving closure devices, more frequently need to be reassured regarding early ambulation compared to those with a transradial approach and an unrestricted post-catheterization ambulation (109).

6.2 Reductions of hospitalizations stays and costs

Several dedicated costs analyses have shown a significant reduction in hospital costs with transradial access compared to other arterial access sites .The economic benefits of the transradial approach are mainly derived from its known advantages: a reduced incidence of vascular access site complications and immediate ambulation after the procedure (45).

A lower rate of access site complications also means decreased length of stay and costs compared with those observed in case of an adverse event (1,113,114). A vascular complication inevitably drives additional charges related to its careful medical evaluation using different diagnostic vascular imaging techniques and because of treatments required. Red blood cell or platelet transfusions (preceded by numerous laboratory tests), thrombin injections or operating room charges for surgical repair rapidly increase hospitalization costs. These adverse outcomes inevitably prolong hospitalization but indirect costs linked with an increased nursing and staff workload must also be considered even if they are more difficult to appreciate. Several authors have evaluated the negative economic impact of vascular access complications and the incremental costs ranged from \$ 4000 for minor complications up to \$ 14 000 for major events (114-116). Cooper et al. have showed, in a single center randomized study, that transradial access for diagnostic cardiac catheterization led to significant reductions in hospital costs when compared to femoral access (\$ 2010 versus \$2299 respectively, p< 0.001). Lower bed costs, mainly, taking into account nursing workload, but also pharmacy explain the median cost reduction of 289 \$ per procedure (117). In the same way, Roussanov et al. have shown that a femoral access with or without the use of a closure device also failed to reduce total hospitalization costs as compare to radial access even in case of similar recovery times (radial =369.5 \$ ± 74.6, femoral= 446.9 \$ ± 60.2 and femoral with closure device 553.4 ± 81.0 ; p < 0.001) (118).

Immediate ambulation, in addition to showing radial approach safety, provides additional cost reductions through different mechanisms. First, transradial approach provides shorter length of stay .A systematic review and meta-analysis of randomized trials showed that radial access reduced hospital stay by a mean of 0.4 days [95% CI 0.2-0.5], p=0.0001) which also means an expedited room turn-over (24).Secondly, as reported by Amoroso et al, nursing workload can be significantly reduced inside (86 min versus 174 min for femoral access) as well as outside the catheterization laboratory (386 min versus 720 min for femoral access) when the radial way is systematically used for a catheterization procedure (119).An increased catheterization laboratory throughput can also be expected with radial access because less time is spent for sheath removal. Third, it has been shown that same day home discharge after an uncomplicated transradial percutaneous intervention results in a 50% relative reduction in post-PCI medical costs. In the EASY trial, at 30-day follow-up, the mean cumulative medical cost per outpatient was \$1,117 \pm \$1,554 versus \$2,258 \pm \$1,328 for overnight-stay patients (Canadian dollars). The mean difference of \$1,141[95% CI: \$962 to \$1,320] was mainly due to the extra night for overnight hospital stay (120). Finally, with

shorter length of stay and fewer vascular access site complications, a more rapid return to professional activities is insured for working patients.

Dedicated radial equipments (such as micropuncture kits and catheters) are still a little bit more expensive than those used for femoral access. However, the RIVAL study reported the use of a lower mean number of diagnostic catheters per procedure with transradial access and similarly the same number of guiding catheters per PCI for the two techniques (2). Economic implications of these observations are not yet quantified, especially during the early adoption of the radial technique, which is often associated with increased catheter usage because of frequent inadequate choices.

7. Conclusions

Over the last two decades, major improvements have been achieved in pharmacotherapy and device technology making percutaneous coronary interventions safer, despite the increasing complexity of clinical and anatomic conditions treated during these procedures. Numerous trials are now available and show undoubtedly the superiority of the transradial approach with respect to the incidence of vascular access site complications, especially bleeding, and this despite the fact that all transradial procedures are performed immediately after an initial bolus of heparin to prevent radial artery thrombosis. Moreover, transradial percutaneous interventions can be performed with the same success rate as procedures by femoral approach and have shown their capacities to shorten hospitalization duration and offer the possibility for an outpatient strategy. In addition, transradial access has the potential of reducing medical costs and increasing hospital bed utilization without jeopardizing patient safety. The transradial approach also increases peri-procedural patient comfort and is now strongly preferred by patients for subsequent procedures (2,117). All these advantages are maybe a part of the solution to reduce pressure on limited hospital resources facing rising demands. Nevertheless, even if the transradial approach is extremely safe and occlusion of the artery without any clinical consequences, further studies are needed to search for materials minimizing physiological and anatomical changes in the cannulated radial artery. Radial experts underscore the need for other large randomized trials to confirm that radial approach has a favourable impact on the incidence of post procedural ischemic events and cuts mortality as compared to femoral approach. In this case, guidelines relative to percutaneous coronary interventions should be updated and the worldwide practice changed but transradial access is already an essential tool for the interventional cardiologist.

8. Acknowledgments

The author would like to thank Caroline Lepiece, MD, for her expert assistance in the revision of the manuscript and also Vincent Dangoisse, MD, Patrick Chenu, MD, and Erwin Schroeder, MD, my teachers in interventional cardiology.

9. References

[1] Rao SV, Ou FS, Wang TY, et al. Trends in the prevalence and outcomes of radial and femoral approaches to percutaneous coronary intervention: a report from the National Cardiovascular Data Registry. JACC Cardiovasc Interv 2008;1:379-86.

20

- [2] Jolly SS, Yusuf S, Cairns J, et al. Radial versus femoral access for coronary angiography and intervention in patients with acute coronary syndromes (RIVAL): a randomised, parallel group, multicentre trial. Lancet 2011;377:1409-20.
- [3] Kinnaird TD, Stabile E, Mintz GS, et al. Incidence, predictors, and prognostic implications of bleeding and blood transfusion following percutaneous coronary interventions. Am J Cardiol 2003;92:930-5.
- [4] Resnic FS, Arora N, Matheny M, Reynolds MR. A cost-minimization analysis of the angio-seal vascular closure device following percutaneous coronary intervention. Am J Cardiol 2007;99:766-70.
- [5] Geisler T, Gawaz M, Steinhubl SR, Bhatt DL, Storey RF, Flather M. Current strategies in antiplatelet therapy--does identification of risk and adjustment of therapy contribute to more effective, personalized medicine in cardiovascular disease? Pharmacol Ther 2010;127:95-107.
- [6] Gunasekaran S, Cherukupalli R. Radial artery perforation and its management during PCI. J Invasive Cardiol 2009;21:E24-6.
- [7] Mannucci PM, Franchini M. Mechanism of hemostasis defects and management of bleeding in patients with acute coronary syndromes. Eur J Intern Med 2010;21:254-9.
- [8] Ndrepepa G, Keta D, Byrne RA, et al. Impact of body mass index on clinical outcome in patients with acute coronary syndromes treated with percutaneous coronary intervention. Heart Vessels 2010;25:27-34.
- [9] Ndrepepa G, Keta D, Schulz S, et al. Characterization of patients with bleeding complications who are at increased risk of death after percutaneous coronary intervention. Heart Vessels 2010;25:294-8.
- [10] Wijns W, Kolh P, Danchin N, et al. Guidelines on myocardial revascularization. Eur Heart J 2010;31:2501-55.
- [11] Agostoni P, Biondi-Zoccai GG, de Benedictis ML, et al. Radial versus femoral approach for percutaneous coronary diagnostic and interventional procedures; Systematic overview and meta-analysis of randomized trials. J Am Coll Cardiol 2004;44:349-56.
- [12] Doyle BJ, Rihal CS, Gastineau DA, Holmes DR, Jr. Bleeding, blood transfusion, and increased mortality after percutaneous coronary intervention: implications for contemporary practice. J Am Coll Cardiol 2009;53:2019-27.
- [13] Eikelboom JW, Mehta SR, Anand SS, Xie C, Fox KA, Yusuf S. Adverse impact of bleeding on prognosis in patients with acute coronary syndromes. Circulation 2006;114:774-82.
- [14] Moscucci M, Fox KA, Cannon CP, et al. Predictors of major bleeding in acute coronary syndromes: the Global Registry of Acute Coronary Events (GRACE). Eur Heart J 2003;24:1815-23.
- [15] Ndrepepa G, Berger PB, Mehilli J, et al. Periprocedural bleeding and 1-year outcome after percutaneous coronary interventions: appropriateness of including bleeding as a component of a quadruple end point. J Am Coll Cardiol 2008;51:690-7.
- [16] Osten MD, Ivanov J, Eichhofer J, et al. Impact of renal insufficiency on angiographic, procedural, and in-hospital outcomes following percutaneous coronary intervention. Am J Cardiol 2008;101:780-5.
- [17] Rao SV, O'Grady K, Pieper KS, et al. Impact of bleeding severity on clinical outcomes among patients with acute coronary syndromes. Am J Cardiol 2005;96:1200-6.

- [18] An international randomized trial comparing four thrombolytic strategies for acute myocardial infarction. The GUSTO investigators. N Engl J Med 1993;329:673-82.
- [19] Chesebro JH, Knatterud G, Roberts R, et al. Thrombolysis in Myocardial Infarction (TIMI) Trial, Phase I: A comparison between intravenous tissue plasminogen activator and intravenous streptokinase. Clinical findings through hospital discharge. Circulation 1987;76:142-54.
- [20] Stone GW, McLaurin BT, Cox DA, et al. Bivalirudin for patients with acute coronary syndromes. N Engl J Med 2006;355:2203-16.
- [21] Doyle BJ, Ting HH, Bell MR, et al. Major femoral bleeding complications after percutaneous coronary intervention: incidence, predictors, and impact on longterm survival among 17,901 patients treated at the Mayo Clinic from 1994 to 2005. JACC Cardiovasc Interv 2008;1:202-9.
- [22] Chase AJ, Fretz EB, Warburton WP, et al. Association of the arterial access site at angioplasty with transfusion and mortality: the M.O.R.T.A.L study (Mortality benefit Of Reduced Transfusion after percutaneous coronary intervention via the Arm or Leg). Heart 2008;94:1019-25.
- [23] Cox N, Resnic FS, Popma JJ, Simon DI, Eisenhauer AC, Rogers C. Comparison of the risk of vascular complications associated with femoral and radial access coronary catheterization procedures in obese versus nonobese patients. Am J Cardiol 2004;94:1174-7.
- [24] Jolly SS, Amlani S, Hamon M, Yusuf S, Mehta SR. Radial versus femoral access for coronary angiography or intervention and the impact on major bleeding and ischemic events: a systematic review and meta-analysis of randomized trials. Am Heart J 2009;157:132-40.
- [25] Hirano Y, Ikuta S, Uehara H, et al. Diagnosis of vascular complications at the puncture site after cardiac catheterization. J Cardiol 2004;43:259-65.
- [26] Koreny M, Riedmuller E, Nikfardjam M, Siostrzonek P, Mullner M. Arterial puncture closing devices compared with standard manual compression after cardiac catheterization: systematic review and meta-analysis. Jama 2004;291:350-7.
- [27] Louvard Y, Benamer H, Garot P, et al. Comparison of transradial and transfermoral approaches for coronary angiography and angioplasty in octogenarians (the OCTOPLUS study). Am J Cardiol 2004;94:1177-80.
- [28] Waksman R, King SB, 3rd, Douglas JS, et al. Predictors of groin complications after balloon and new-device coronary intervention. Am J Cardiol 1995;75:886-9.
- [29] Corriere MA, Guzman RJ. True and false aneurysms of the femoral artery. Semin Vasc Surg 2005;18:216-23.
- [30] Graham AN, Wilson CM, Hood JM, Barros D'Sa AA. Risk of rupture of postangiographic femoral false aneurysm. Br J Surg 1992;79:1022-5.
- [31] Kazmers A, Meeker C, Nofz K, et al. Nonoperative therapy for postcatheterization femoral artery pseudoaneurysms. Am Surg 1997;63:199-204.
- [32] Sherev DA, Shaw RE, Brent BN. Angiographic predictors of femoral access site complications: implication for planned percutaneous coronary intervention. Catheter Cardiovasc Interv 2005;65:196-202.
- [33] Tavris DR, Gallauresi BA, Dey S, Brindis R, Mitchel K. Risk of local adverse events by gender following cardiac catheterization. Pharmacoepidemiol Drug Saf 2007;16:125-31.

- [34] Stella PR, Kiemeneij F, Laarman GJ, Odekerken D, Slagboom T, van der Wieken R. Incidence and outcome of radial artery occlusion following transradial artery coronary angioplasty. Cathet Cardiovasc Diagn 1997;40:156-8.
- [35] Nikolsky E, Mehran R, Halkin A, et al. Vascular complications associated with arteriotomy closure devices in patients undergoing percutaneous coronary procedures: a meta-analysis. J Am Coll Cardiol 2004;44:1200-9.
- [36] Chevalier B, Lancelin B, Koning R, et al. Effect of a closure device on complication rates in high-local-risk patients: results of a randomized multicenter trial. Catheter Cardiovasc Interv 2003;58:285-91.
- [37] Mann T, Cowper PA, Peterson ED, et al. Transradial coronary stenting: comparison with femoral access closed with an arterial suture device. Catheter Cardiovasc Interv 2000;49:150-6.
- [38] Louvard Y, Ludwig J, Lefevre T, et al. Transradial approach for coronary angioplasty in the setting of acute myocardial infarction: a dual-center registry. Catheter Cardiovasc Interv 2002;55:206-11.
- [39] Morice MC, Dumas P, Lefevre T, Loubeyre C, Louvard Y, Piechaud JF. Systematic use of transradial approach or suture of the femoral artery after angioplasty: attempt at achieving zero access site complications. Catheter Cardiovasc Interv 2000;51:417-21.
- [40] Sciahbasi A, Fischetti D, Picciolo A, et al. Transradial access compared with femoral puncture closure devices in percutaneous coronary procedures. Int J Cardiol 2009;137:199-205.
- [41] Dangas G, Mehran R, Kokolis S, et al. Vascular complications after percutaneous coronary interventions following hemostasis with manual compression versus arteriotomy closure devices. J Am Coll Cardiol 2001;38:638-41.
- [42] Dauerman HL, Applegate RJ, Cohen DJ. Vascular closure devices: the second decade. J Am Coll Cardiol 2007;50:1617-26.
- [43] Meyerson SL, Feldman T, Desai TR, Leef J, Schwartz LB, McKinsey JF. Angiographic access site complications in the era of arterial closure devices. Vasc Endovascular Surg 2002;36:137-44.
- [44] Arora N, Matheny ME, Sepke C, Resnic FS. A propensity analysis of the risk of vascular complications after cardiac catheterization procedures with the use of vascular closure devices. Am Heart J 2007;153:606-11.
- [45] Caputo RP. Transradial Arterial Access: Economic Considerations. J Invasive Cardiol. 2009;21:18-20.
- [46] Fitts J, Ver Lee P, Hofmaster P, Malenka D. Fluoroscopy-guided femoral artery puncture reduces the risk of PCI-related vascular complications. J Interv Cardiol 2008;21:273-8.
- [47] Grier D, Hartnell G. Percutaneous femoral artery puncture: practice and anatomy. Br J Radiol 1990;63:602-4.
- [48] Safian RD, Freed M. The manual of interventional cardiology: Physicians' Press, 2001.
- [49] Barbeau GR, Arsenault F, Dugas L, Simard S, Lariviere MM. Evaluation of the ulnopalmar arterial arches with pulse oximetry and plethysmography: comparison with the Allen's test in 1010 patients. Am Heart J 2004;147:489-93.
- [50] Hamon M, Mc Fadden E. Trans-radial approach for cardiovascular interventions: ESM, 2003.
- [51] Patel T. Patel's Atlas of Transradial Intervention: The Basics: Seascript Company, 2007.

- [52] Sciahbasi A, Romagnoli E, Trani C, et al. Evaluation of the "learning curve" for left and right radial approach during percutaneous coronary procedures. Am J Cardiol 2011;108:185-8.
- [53] Guédès A, Dangoisse V, Gabriel L, et al. Low rate of conversion to transfemoral approach when attempting both radial arteries for coronary angiography and percutaneous coronary intervention: a study of 1,826 consecutive procedures. J Invasive Cardiol 2010;22:391-7.
- [54] Dahm JB, Vogelgesang D, Hummel A, Staudt A, Volzke H, Felix SB. A randomized trial of 5 vs. 6 French transradial percutaneous coronary interventions. Catheter Cardiovasc Interv 2002;57:172-6.
- [55] Kiemeneij F, Fraser D, Slagboom T, Laarman G, van der Wieken R. Hydrophilic coating aids radial sheath withdrawal and reduces patient discomfort following transradial coronary intervention: a randomized double-blind comparison of coated and uncoated sheaths. Catheter Cardiovasc Interv 2003;59:161-4.
- [56] Rathore S, Stables RH, Pauriah M, et al. Impact of length and hydrophilic coating of the introducer sheath on radial artery spasm during transradial coronary intervention: a randomized study. JACC Cardiovasc Interv 2010;3:475-83.
- [57] Saito S, Tanaka S, Hiroe Y, et al. 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.
- [58] Chodor P, Krupa H, Kurek T, et al. RADIal versus femoral approach for percutaneous coronary interventions in patients with Acute Myocardial Infarction (RADIAMI): A prospective, randomized, single-center clinical trial. Cardiol J 2009;16:332-40.
- [59] Egred M. Feasibility and Safety of 7-Fr Radial Approach for Complex PCI. J Interv Cardiol 2011.
- [60] Hamon M, Sabatier R, Zhao Q, Niculescu R, Valette B, Grollier G. Mini-invasive strategy in acute coronary syndromes: direct coronary stenting using 5 Fr guiding catheters and transradial approach. Catheter Cardiovasc Interv 2002;55:340-3.
- [61] Ochiai M, Isshiki T, Toyoizumi H, et al. Efficacy of transradial primary stenting in patients with acute myocardial infarction. Am J Cardiol 1999;83:966-8, A10.
- [62] Rathore S, Hakeem A, Pauriah M, Roberts E, Beaumont A, Morris JL. A comparison of the transradial and the transfemoral approach in chronic total occlusion percutaneous coronary intervention. Catheter Cardiovasc Interv 2009;73:883-7.
- [63] Rathore S, Roberts E, Hakeem AR, Pauriah M, Beaumont A, Morris JL. The feasibility of percutaneous transradial coronary intervention for saphenous vein graft lesions and comparison with transfemoral route. J Interv Cardiol 2009;22:336-40.
- [64] Mamas MA, Eichhofer J, Hendry C, et al. Use of the Heartrail II catheter as a distal stent delivery device; an extended case series. EuroIntervention 2009;5:265-71.
- [65] Mamas MA, Fath-Ordoubadi F, Fraser DG. Atraumatic complex transradial intervention using large bore sheathless guide catheter. Catheter Cardiovasc Interv 2008;72:357-64.
- [66] Sciahbasi A, Romagnoli E, Burzotta F, et al. Transradial approach (left vs right) and procedural times during percutaneous coronary procedures: TALENT study. Am Heart J 2011;161:172-9.

- [67] Cha KS, Kim MH. Feasibility and safety of concomitant left internal mammary arteriography at the setting of the right transradial coronary angiography. Catheter Cardiovasc Interv 2002;56:188-95.
- [68] Benit E, Missault L, Eeman T, et al. Brachial, radial, or femoral approach for elective Palmaz-Schatz stent implantation: a randomized comparison. Cathet Cardiovasc Diagn 1997;41:124-30.
- [69] 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.
- [70] Mann JT, 3rd, Cubeddu MG, Schneider JE, Arrowood M. Right Radial Access for PTCA: A Prospective Study Demonstrates Reduced Complications and Hospital Charges. J Invasive Cardiol 1996;8 Suppl D:40D-44D.
- [71] Plante S, Cantor WJ, Goldman L, et al. Comparison of bivalirudin versus heparin on radial artery occlusion after transradial catheterization. Catheter Cardiovasc Interv 2010;76:654-8.
- [72] 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 Invasive Cardiol 2000;12:605-9.
- [73] 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.
- [74] Sakai H, Ikeda S, Harada T, et al. Limitations of successive transradial approach in the same arm: the Japanese experience. Catheter Cardiovasc Interv 2001;54:204-8.
- [75] Pancholy SB. Comparison of the effect of intra-arterial versus intravenous heparin on radial artery occlusion after transradial catheterization. Am J Cardiol 2009;104:1083-5.
- [76] Sanmartin M, Gomez M, Rumoroso JR, et al. Interruption of blood flow during compression and radial artery occlusion after transradial catheterization. Catheter Cardiovasc Interv 2007;70:185-9.
- [77] Pancholy S, Coppola J, Patel T, Roke-Thomas M. Prevention of radial artery occlusionpatent hemostasis evaluation trial (PROPHET study): a randomized comparison of traditional versus patency documented hemostasis after transradial catheterization. Catheter Cardiovasc Interv 2008;72:335-40.
- [78] Bernat I, Bertrand OF, Rokyta R, et al. Efficacy and safety of transient ulnar artery compression to recanalize acute radial artery occlusion after transradial catheterization. Am J Cardiol 2011;107:1698-701.
- [79] Yoo BS, Lee SH, Ko JY, et al. Procedural outcomes of repeated transradial coronary procedure. Catheter Cardiovasc Interv 2003;58:301-4.
- [80] Edmundson A, Mann T. Nonocclusive radial artery injury resulting from transradial coronary interventions: radial artery IVUS. J Invasive Cardiol 2005;17:528-31.
- [81] Wakeyama T, Ogawa H, Iida H, et al. Intima-media thickening of the radial artery after transradial intervention. An intravascular ultrasound study. J Am Coll Cardiol 2003;41:1109-14.
- [82] Sanmartin M, Goicolea J, Ocaranza R, Cuevas D, Calvo F. Vasoreactivity of the radial artery after transradial catheterization. J Invasive Cardiol 2004;16:635-8.

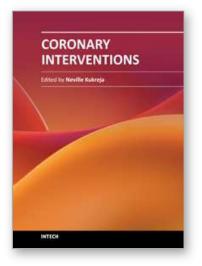
- [83] Bazemore E, Mann JT, 3rd. Problems and complications of the transradial approach for coronary interventions: a review. J Invasive Cardiol 2005;17:156-9.
- [84] Tizon-Marcos H, Barbeau GR. Incidence of compartment syndrome of the arm in a large series of transradial approach for coronary procedures. J Interv Cardiol 2008;21:380-4.
- [85] Louvard Y, Lefevre T. Loops and transradial approach in coronary diagnosis and intervention. Catheter Cardiovasc Interv 2000;51:250-2.
- [86] Rathore S, Morris JL. The radial approach: is this the route to take? J Interv Cardiol 2008;21:375-9.
- [87] Dieter RS, Akef A, Wolff M. Eversion endarterectomy complicating radial artery access for left heart catheterization. Catheter Cardiovasc Interv 2003;58:478-80.
- [88] Park KW, Chung JW, Chang SA, Kim KI, Chung WY, Chae IH. Two cases of mediastinal hematoma after cardiac catheterization: A rare but real complication of the transradial approach. Int J Cardiol 2008;130:e89-92.
- [89] Papadimos TJ, Hofmann JP. Radial artery thrombosis, palmar arch systolic blood velocities, and chronic regional pain syndrome 1 following transradial cardiac catheterization. Catheter Cardiovasc Interv 2002;57:537-40.
- [90] Goldman S, Sethi GK, Holman W, et al. Radial artery grafts vs saphenous vein grafts in coronary artery bypass surgery: a randomized trial. Jama 2011;305:167-74.
- [91] Kamiya H, Ushijima T, Kanamori T, et al. Use of the radial artery graft after transradial catheterization: is it suitable as a bypass conduit? Ann Thorac Surg 2003;76:1505-9.
- [92] Rao SV, Cohen MG, Kandzari DE, Bertrand OF, Gilchrist IC. The transradial approach to percutaneous coronary intervention: historical perspective, current concepts, and future directions. J Am Coll Cardiol 2010;55:2187-95.
- [93] Manoukian SV, Feit F, Mehran R, et al. Impact of major bleeding on 30-day mortality and clinical outcomes in patients with acute coronary syndromes: an analysis from the ACUITY Trial. J Am Coll Cardiol 2007;49:1362-8.
- [94] Montalescot G, Ongen Z, Guindy R, et al. Predictors of outcome in patients undergoing PCI. Results of the RIVIERA study. Int J Cardiol 2008;129:379-87.
- [95] Sciahbasi A, Pristipino C, Ambrosio G, et al. Arterial access-site-related outcomes of patients undergoing invasive coronary procedures for acute coronary syndromes (from the ComPaRison of Early Invasive and Conservative Treatment in Patients With Non-ST-ElevatiOn Acute Coronary Syndromes [PRESTO-ACS] Vascular Substudy). Am J Cardiol 2009;103:796-800.
- [96] Vorobcsuk A, Konyi A, Aradi D, et al. Transradial versus transfemoral percutaneous coronary intervention in acute myocardial infarction Systematic overview and meta-analysis. Am Heart J 2009;158:814-21.
- [97] Jurga J, Nyman J, Tornvall P, et al. Cerebral microembolism during coronary angiography: a randomized comparison between femoral and radial arterial access. Stroke 2011;42:1475-7.
- [98] Lund C, Nes RB, Ugelstad TP, et al. Cerebral emboli during left heart catheterization may cause acute brain injury. Eur Heart J 2005;26:1269-75.
- [99] Brasselet C, Blanpain T, Tassan-Mangina S, et al. Comparison of operator radiation exposure with optimized radiation protection devices during coronary angiograms and ad hoc percutaneous coronary interventions by radial and femoral routes. Eur Heart J 2007.

- [100] Sciahbasi A, Romagnoli E, Trani C, et al. Operator radiation exposure during percutaneous coronary procedures through the left or right radial approach: the TALENT dosimetric substudy. Circ Cardiovasc Interv 2011;4:226-31.
- [101] Chung WJ, Fang HY, Tsai TH, et al. Transradial approach percutaneous coronary interventions in an out-patient clinic. Int Heart J 2010;51:371-6.
- [102] Feldman DN, Minutello RM, Gade CL, Wong SC. Outcomes following immediate (ad hoc) versus staged percutaneous coronary interventions (report from the 2000 to 2001 New York State Angioplasty Registry). Am J Cardiol 2007;99:446-9.
- [103] Good CW, Blankenship JC, Scott TD, Skelding KA, Berger PB, Wood GC. Feasibility and safety of ad hoc percutaneous coronary intervention in the modern era. J Invasive Cardiol 2009;21:194-200.
- [104] Krone RJ, Shaw RE, Klein LW, Blankenship JC, Weintraub WS. Ad hoc percutaneous coronary interventions in patients with stable coronary artery disease--a study of prevalence, safety, and variation in use from the American College of Cardiology National Cardiovascular Data Registry (ACC-NCDR). Catheter Cardiovasc Interv 2006;68:696-703.
- [105] Shubrooks SJ, Jr., Malenka DJ, Piper WD, et al. Safety and efficacy of percutaneous coronary interventions performed immediately after diagnostic catheterization in northern new england and comparison with similar procedures performed later. Am J Cardiol 2000;86:41-5.
- [106] Bertrand OF, De Larochelliere R, Rodes-Cabau J, et al. A randomized study comparing same-day home discharge and abciximab bolus only to overnight hospitalization and abciximab bolus and infusion after transradial coronary stent implantation. Circulation 2006;114:2636-43.
- [107] Gilchrist IC, Nickolaus MJ, Momplaisir T. Same-day transradial outpatient stenting with a 6-hr course of glycoprotein IIb/IIIa receptor blockade: a feasibility study. Catheter Cardiovasc Interv 2002;56:10-3.
- [108] Heyde GS, Koch KT, de Winter RJ, et al. Randomized trial comparing same-day discharge with overnight hospital stay after percutaneous coronary intervention: results of the Elective PCI in Outpatient Study (EPOS). Circulation 2007;115:2299-306.
- [109] Jabara R, Gadesam R, Pendyala L, et al. Ambulatory discharge after transradial coronary intervention: Preliminary US single-center experience (Same-day TransRadial Intervention and Discharge Evaluation, the STRIDE Study). Am Heart J 2008;156:1141-6.
- [110] Silber S, Albertsson P, Aviles FF, et al. Guidelines for percutaneous coronary interventions. The Task Force for Percutaneous Coronary Interventions of the European Society of Cardiology. Eur Heart J 2005;26:804-47.
- [111] Slagboom T, Kiemeneij F, Laarman GJ, van der Wieken R. Outpatient coronary angioplasty: feasible and safe. Catheter Cardiovasc Interv 2005;64:421-7.
- [112] Slagboom T, Kiemeneij F, Laarman GJ, van der Wieken R, Odekerken D. Actual outpatient PTCA: results of the OUTCLAS pilot study. Catheter Cardiovasc Interv 2001;53:204-8.
- [113] Cohen DJ, Lincoff AM, Lavelle TA, et al. Economic evaluation of bivalirudin with provisional glycoprotein IIB/IIIA inhibition versus heparin with routine

glycoprotein IIB/IIIA inhibition for percutaneous coronary intervention: results from the REPLACE-2 trial. J Am Coll Cardiol 2004;44:1792-800.

- [114] Rao SV, Kaul PR, Liao L, et al. Association between bleeding, blood transfusion, and costs among patients with non-ST-segment elevation acute coronary syndromes. Am Heart J 2008;155:369-74.
- [115] Kugelmass AD, Cohen DJ, Brown PP, Simon AW, Becker ER, Culler SD. Hospital resources consumed in treating complications associated with percutaneous coronary interventions. Am J Cardiol 2006;97:322-7.
- [116] Pinto DS, Stone GW, Shi C, et al. Economic evaluation of bivalirudin with or without glycoprotein IIb/IIIa inhibition versus heparin with routine glycoprotein IIb/IIIa inhibition for early invasive management of acute coronary syndromes. J Am Coll Cardiol 2008;52:1758-68.
- [117] Cooper CJ, El-Shiekh RA, Cohen DJ, et al. Effect of transradial access on quality of life and cost of cardiac catheterization: A randomized comparison. Am Heart J 1999;138:430-6.
- [118] Roussanov O, Wilson SJ, Henley K, et al. Cost-effectiveness of the radial versus femoral artery approach to diagnostic cardiac catheterization. J Invasive Cardiol 2007;19:349-53.
- [119] Amoroso G, Sarti M, Bellucci R, et al. Clinical and procedural predictors of nurse workload during and after invasive coronary procedures: the potential benefit of a systematic radial access. Eur J Cardiovasc Nurs 2005;4:234-41.
- [120] Rinfret S, Kennedy WA, Lachaine J, et al. Economic impact of same-day home discharge after uncomplicated transradial percutaneous coronary intervention and bolus-only abciximab regimen. JACC Cardiovasc Interv 2010;3:1011-9.





Coronary Interventions Edited by Dr. Neville Kukreja

ISBN 978-953-51-0498-8 Hard cover, 244 pages **Publisher** InTech **Published online** 18, April, 2012 **Published in print edition** April, 2012

How to reference

In order to correctly reference this scholarly work, feel free to copy and paste the following:

Antoine Guedes (2012). Transradial Approach for Coronary Interventions: The New Gold Standard for Vascular Access?, Coronary Interventions, Dr. Neville Kukreja (Ed.), ISBN: 978-953-51-0498-8, InTech, Available from: http://www.intechopen.com/books/coronary-interventions/transradial-approach-tra-for-coronary-interventions-the-new-gold-standard-for-vascular-access-

INTECH

open science | open minds

InTech Europe

University Campus STeP Ri Slavka Krautzeka 83/A 51000 Rijeka, Croatia Phone: +385 (51) 770 447 Fax: +385 (51) 686 166 www.intechopen.com

InTech China

Unit 405, Office Block, Hotel Equatorial Shanghai No.65, Yan An Road (West), Shanghai, 200040, China 中国上海市延安西路65号上海国际贵都大饭店办公楼405单元 Phone: +86-21-62489820 Fax: +86-21-62489821 © 2012 The Author(s). Licensee IntechOpen. This is an open access article distributed under the terms of the <u>Creative Commons Attribution 3.0</u> <u>License</u>, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

IntechOpen

IntechOpen