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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).

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

### 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.
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)

<table>
<thead>
<tr>
<th><strong>Common Femoral Artery (CFA)</strong></th>
<th><strong>Radial Artery (RA)</strong></th>
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<tbody>
<tr>
<td>CFA is relatively deep.</td>
<td>Distal RA had a superficial course,</td>
</tr>
<tr>
<td>• The ideal site of puncture may be hard to identify especially in obese patients.</td>
<td>• This artery is easy to palpate even in obese patients</td>
</tr>
<tr>
<td>• The inguinal crease is an unreliable landmark in more than two thirds of patients.</td>
<td>• At the level of the puncture site, the artery lies just under skin and fascias</td>
</tr>
<tr>
<td>• The strongest femoral pulse correctly identified the mid-CFA in 90% of cases</td>
<td></td>
</tr>
<tr>
<td>Puncture site is over the hip joint</td>
<td>Puncture site is not over a joint</td>
</tr>
<tr>
<td>• The most reliable landmark is probably the junction between the middle and the lower third of the femoral head (radiographic landmark)</td>
<td>• The most reliable landmark is ideally 2-3 cm proximal to the flexor crease of the wrist (clinical landmark)</td>
</tr>
<tr>
<td>Compression of the CFA may be hard</td>
<td>RA can easily be compressed with minimal pressure</td>
</tr>
<tr>
<td>• No hard and fixed structures behind the artery</td>
<td>• At the puncture site, radial bone is just beneath the artery</td>
</tr>
<tr>
<td>CFA lies just near a major vein (Femoral Vein) and nerve (Femoral Nerve)</td>
<td>RA is separated from median nerve and major veins</td>
</tr>
<tr>
<td>CFA is the unique blood supply to the leg</td>
<td>Double blood supply to the hand insured by the palmar arch</td>
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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).
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,
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 open the way for the most complex PCI techniques, in nearly all patients, 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
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 Outlook™ 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 band™ (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
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).
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 30-days 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.
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 30-day 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 same-day discharge group and 18.2% in the overnight hospitalization group (P=0.017 for non-inferiority). 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
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 compared 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 ± $1,554 versus $2,258 ± $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.

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