Interventional Cardiology

Novel insights on spontaneous coronary artery dissection

"Our study suggested that in patients with spontaneous coronary artery dissection a 'conservative' medical management (watchful waiting strategy) provides an excellent clinical and angiographic outcome."

Spontaneous coronary artery dissection (SCAD) remains an elusive and challenging clinical entity of unknown etiology eight decades after its initial pathological recognition [1]. Coronary angiography has been classically used for the diagnosis of these patients [2–6]. A radiolucent intimal flap, separating the true lumen from the false lumen, has been considered as the hallmark of the disease [2–6]. Multiple case reports and small retrospective series with limited clinical follow-up have been published but the total number of patients with SCAD reported to date is less than 700 [2–6]. This largely explains the limited information currently available on prevalence, predisposing conditions, pathophysiology, diagnosis, management and prognosis of patients with SCAD [2–6].

Spontaneous coronary artery dissection is a rare disease with a prevalence ranging from 0.1 to 1% in most angiographic series [2–6]. A young female without coronary risk factors presenting with typical chest pain represents the classical clinical scenario. From a pathophysiological standpoint it is accepted that in most patients an intimal tear constitutes the initiating event, leading to intramural bleeding with progressive separation between the true and false lumens. Eventually, pressure-driven compression of the true lumen precipitating myocardial ischemia occurs [2–6]. Alternatively, in other cases the intima remains intact. In these patients disruption of the *vasa vasorum* causes an intramural hematoma that may also compress the coronary lumen [2–6]. Triggers (including exercise and cocaine, among others) and a pathological

underlying anatomic substrate (cystic medial necrosis) are frequently reported in patients suffering from with SCAD [2–6]. In fact, a never-ending list of pathological conditions has been associated with SCAD. Systemic connective tissue disorders (e.g., Ehlers-Danlos syndrome) and the peripartum period are frequently highlighted in classical series [2–6]. Most patients with SCAD present as an acute coronary syndrome although cases presenting as sudden death or ventricular arrhythmias are also reported. The treatment of choice for patients with SCAD remains unsettled [2–6]. Most investigators favor a management similar to that used in patients with acute coronary syndromes secondary to atherosclerotic coronary artery disease. Revascularization, however, is specially challenging in this scenario and both percutaneous techniques and coronary surgery provide suboptimal results due to the friable – already disrupted – coronary vessel wall [2–6]. Therefore, a conservative approach has been advocated for stable patients with SCAD. Despite a significant acute morbidity patients tend to stabilize after the acute episode and long-term prognosis is largely favorable. All of the above summarize the 'classical knowledge' on this unique condition which has remained unchanged for decades [2–6].

Recently, however, major advances have occurred in our understanding of the pathophysiology of the condition [5–11]. Importantly, the widespread use of early coronary angiography in patients presenting with an acute myocardial infarction (including young females) together with an increased

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clinical suspicion has enhanced recognition on this disease [5]. In addition, the use of new sophisticated intracoronary imaging techniques has revolutionized our diagnostic accuracy [5,12,13]. Finally, recent studies, including relatively large series of patients studied in a highly comprehensive manner and systematically followed-up, have shed a new light on this elusive clinical entity [11,14–16].

Association with fibromuscular dysplasia

Many underlying pathological conditions have been classically associated with the occurrence of SCAD. The common substrate entails a 'vulnerable vessel wall' prone to disruption and to SCAD. Recently, Canadian investigators proposed the association of SCAD with fibromuscular dysplasia (FMD) [8–11]. FMD is a non-inflammatory, nonatherosclerotic, vascular disease of unknown etiology that involves large arteries and typically affects young females [7]. Pathologically, FMD presents as arterial stenosis, aneurysms, dissection or thrombosis, involving renal, carotid and iliac arteries. Medial fibroplasia is the most common underlying substrate and is responsible for the classical 'string-of-beads' angiographic appearance [7]. FMD tends to be clinically silent and is often detected incidentally [7]. The group from Vancouver [8–11] reported a series of perimenopausal women with acute myocardial infarction, diffuse coronary lesions and coincidental renal FMD [8–10]. More recently the same group reported on 50 patients with SCAD that were systematically screened for FMD with invasive or noninvasive angiography in three different vascular territories (renal, iliac and cerebrovascular) [11]. FMD was identified in most cases and, accordingly, these investigators proposed the possibility of a causative link. This association has also been confirmed by other groups. A study from the Mayo Clinic [16] confirmed that external iliac FMD was present in half of the patients with SCAD undergoing iliofemoral angiography. Another recent report from the same institution using CT-angiography demonstrated the presence of FMD in two-thirds of patients with SCAD [17]. All together currently available evidence suggests that FMD in large arteries is frequently demonstrated in patients with SCAD. Further studies are warranted to elucidate if this unique association actually represents causation.

Diagnosis by optical coherence tomography

Until now the diagnosis of SCAD relied on the demonstration of a radiolucent intimal 'flap' on coronary angiography [2–6]. However, angiography fails to visualize the vessel wall and only detects lumen compromise or indirect signs of coronary wall disruption. In many cases the angiographic narrowing caused by an intramural hematoma impinging into the lumen is misinterpreted as atherosclerotic coronary artery disease. In other patients a confined intramural hematoma causes no lumen compromise. A long confined lesion in a young patient with smooth appearance in the remaining coronary vessels should always raise the clinical suspicious of an underlying intramural hematoma [2–6].

> "Optical coherence tomography is also of major help in patients with spontaneous coronary artery dissection requiring coronary interventions."

Tomographic techniques, including intravascular ultrasound and, more recently, optical coherence tomography (OCT) have been able to provide novel diagnostic insights in patients with SCAD [12,13]. Interestingly, OCT has an unsurpassed axial resolution (15 μm, that is, ten-times superior to that obtained with intravascular ultrasound) and therefore provides unique insights on the underlying anatomic substrate of these patients [13]. OCT readily visualizes the diseased segment along the entire vessel. This technique nicely depicts the length of the dissecting membrane, the occurrence of two lumens (true and false) and the presence of intramural hematoma [13]. The circumferential and longitudinal extent of the disease is well visualized. In addition, the presence of thrombi in the true lumen or false lumen thrombosis may be recognized. Moreover, the superb resolution of OCT is ideally suited to identify the intimal tear. In addition, OCT is able to accurately measure the thickness of the dissecting membrane. Notably, in most patients a relatively 'thick' membrane is visualized corresponding to the intima and the inner part of the medial layer. The take-off and involvement of affected side branches is nicely depicted [13].

OCT is also of major help in patients with SCAD requiring coronary interventions [13]. Before stenting, OCT is critical to confirm the correct guidewire location within the true lumen. Stent length may be selected according to the true longitudinal extension of the disease. Furthermore, OCT ensures that the entry door has been completely sealed by the stent. Finally, stent expansion and apposition can be determined. Of interest, residual abluminal intramural hematoma and residual distal dissections are frequently detected after stenting. However, aggressive attempts to fully compress the intramural hematoma or to tackle distal dissections are not justified. As compared with intravascular ultrasound OCT enables a better visualization of the intimomedial membrane and allows a precise identification of the site of intimal tear [12,13].

However, on OCT severe thrombosis produces intense dorsal shadowing whereas attenuation caused by large hematomas may prevent visualization of the entire vessel that is much better appreciated using intravascular ultrasound [12,13].

Although intracoronary techniques provide striking images and allow an accurate diagnosis of this entity they should be used with great care in patients with SCAD in order to avoid any additional injury on the already disrupted vessel wall [5,13].

New evidences from large series of patients

Until very recently our knowledge on this rare condition was based on multiple single case reports and rather small retrospective series [2–6]. Recently, however, new evidence coming from larger series of patients with systematic late clinical follow has enriched our understanding of the disease [11,14–16]. We studied a relatively large series of patients with SCAD using a prospective protocol that aimed to determine clinical, angiographic and prognostic findings [14]. The protocol suggested a conservative initial management strategy for patients presenting with SCAD and revascularization was only indicated for patients with ongoing or recurrent ischemia. A high level of clinical suspicion was maintained during the study and the use of intracoronary imaging was recommended for patients with unclear angiographic findings. Furthermore, in selected cases, clinical follow-up was complemented by angiographic follow-up [14]. A total of 45 consecutive patients with SCAD were included (incidence 0.27% of patients undergoing coronary angiography). Interestingly, mean age was 53 years, only 58% were female and 40% had SCAD associated with coronary artery disease. Coronary risk factors were common and only one patient was in the peripartum period. Revascularization was only required in a third of patients (14 patients coronary stenting, two coronary surgery) either at the time of diagnosis or due to recurrent ischemia. The event-free survival at 3 years was 92% and was similar for patients with isolated SCAD and SCAD associated with coronary artery disease. Notably, at 9-month angiography, the image of SCAD spontaneously resolved or improved in most patients [14]. Our study suggested that in patients with SCAD a 'conservative' medical management (watchful waiting strategy) provides an excellent clinical and angiographic outcome [14].

Another large series of 50 patients with SCAD was reported from the Vancouver General Hospital [11]. Mean age was 51 years and only one case was postpartum. Revascularization was only needed in nine patients (18%) and no patient died during hospitalization. Again, an excellent clinical outcome was obtained with a watchful waiting strategy in stabilized patients. Finally, Tweet *et al.*, reported findings from 87 consecutive patients with SCAD seen at the Mayo Clinic [15,16]. Mean age was 43 years and all patients showed an angiographic flap on angiography. Predisposing factors involved extreme exertion (44% of males) and postpartum status (18% of females). Most patients presented with a myocardial infarction but 14% presented with severe ventricular arrhythmias. Although two-thirds of patients underwent coronary revascularization the results of these procedures were far from optimal. Indeed, success of percutaneous coronary interventions was only obtained in 65% of cases. Likewise, although initial surgical results were satisfactory eventually most grafts were occluded at late follow-up [16]. Again this series suggests that revascularization is very challenging in these patients.

> "A conservative stenting approach should be favored avoiding a 'full-metal-jacket' strategy."

When percutaneous revascularization is indicated care should be taken to ensure optimal results and minimize complications. In this regard intracoronary imaging may be of value to guide the procedure [5,13]. Direct stenting should be considered to cover the entry door and the segment showing severe lumen compromise. Covering the edges of the disease may prevent propagation of an intramural hematoma. A conservative stenting approach should be favored avoiding a 'full-metal-jacket' strategy [13,14]. Residual distal dissection should be left untreated when they do not cause significant residual stenosis and when coronary flow is normal [13,14] as these tend to disappear at follow-up [14]. Disease in small distal vessel should not be treated. The use of drug-eluting stents in this setting remains controversial but they are very attractive when long segments should be treated [14]. Very recently, the use of cutting balloon to fenestrate the membrane has been suggested [18]. Likewise, the use of bioresorbable vascular scaffolds appears very attractive in these patients as complete vessel restoration frequently occurs at late follow-up.

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