Spontaneous coronary artery dissection (SCAD) is an important “zebra” in cardiovascular medicine; it is a relatively rare entity but an important cause of nonatherosclerotic coronary artery disease, particularly in women (1). In this issue of the Journal, Tweet et al. (2) present data from a virtual patient registry that characterized clinical and angiographic features, risk factors, and outcomes among 323 women with SCAD and compared 54 patients with pregnancy-associated SCAD with those who experienced SCAD unrelated to pregnancy (2).

The investigators used a novel study design that allowed for virtual online enrollment of patients, regardless of geographical location, and the ability to be seen at their referral center, which perhaps allowed for recruitment of a more diverse cohort of patients (3). Approximately 50% of the enrolled patients were not seen at Mayo Clinic and participated entirely on a virtual basis. Development of this virtual registry was driven in large part by the efforts of motivated patients who experienced a SCAD event and wished to advance knowledge of this poorly understood condition (3). A key feature of the virtual SCAD registry was the central adjudication of imaging studies, specifically all coronary angiograms (to confirm the diagnosis of SCAD, characterize angiographic features, and procedural outcomes) and available extracoronary vascular imaging studies (to assess for fibromuscular dysplasia and occult aneurysm among other vascular abnormalities).

Although individual case reports and case series of SCAD have been published, as well as a recent analysis of 120 cases of pregnancy-associated SCAD, this paper reported multiple important findings, many of them novel (2,4,5).

DELINEATION OF THE TIME COURSE

Among patients with pregnancy-associated SCAD, most of the events (89%) occurred in the post-partum period, most commonly within the first week (median 5 days) after delivery (2). These were coronary events that would generally have occurred after initial hospital discharge because most patients underwent vaginal deliveries.

PREGNANCY-ASSOCIATED SCAD IS A HIGH-RISK CONDITION WITH AN AGGRESSIVE COURSE

Compared with patients in the virtual registry without recent pregnancy, those with pregnancy-associated SCAD were more likely to present with ST-segment elevation myocardial infarction (57% vs. 36%), had left main (24% vs. 5%) and multivessel coronary involvement (33% vs. 14%) during the index SCAD event, and had lower ejection fraction at diagnosis and follow-up (2). Medical therapy was also more likely to fail in patients with pregnancy-associated SCAD, and patients required subsequent revascularization (2). Importantly, there were no deaths reported during follow-up in either group of patients (2).

IDENTIFICATION OF POTENTIAL NOVEL RISK FACTORS FOR PREGNANCY-ASSOCIATED SCAD

Although only one-half of the patients in the virtual registry underwent extracoronary vascular imaging, among those who did, patients with pregnancy-associated SCAD had a significantly lower prevalence of fibromuscular dysplasia and other vascular lesions.
than patients with SCAD without recent pregnancy (2). Fibromuscular dysplasia has been well established, through the work of these investigators and others, as an underlying pre-disposing condition among all comers with SCAD, which is a somewhat surprising finding (6,7). Other potential factors that may be associated with the development of pregnancy-associated SCAD have been reported, including a higher prevalence of multiparity and of having previously received fertility treatments (2). Single case reports of SCAD associated with β-human chorionic gonadotropin and clomiphene have been reported (8,9). Finally, the investigators reported on 6 of 54 (11%) patients with pregnancy-associated SCAD who developed onset of symptoms of myocardial infarction while breastfeeding (2). This observation is novel and hypothesis-generating, but must be interpreted with caution because of the potential for ascertainment and recall biases.

In addition to these findings, what is remarkable about this study is how it reflects the great progress that has been made in understanding SCAD (pregnancy-associated or not) during the past decade and the rapid evolution of this field. In 1931, SCAD was first described in a single case report of a 42-year-old woman with sudden death (10). For decades, this entity was the subject of dozens (if not hundreds) of case reports and small case series, but there seemed to be little interest in a “deep dive” into understanding this entity beyond reporting and cataloging cases of this cardiology zebra.

The past decade has seen a major shift. Clinical investigators have finally taken this deep dive into the study of SCAD. Investigators at Vancouver General Hospital and Mayo Clinic identified the association between SCAD and fibromuscular dysplasia (6,7,11). Registries in the United States, Canada, and Europe are enrolling patients with SCAD and starting to publish data such as these, on natural history, identification of high-risk patient subsets, and longitudinal outcomes, including the risk of recurrent SCAD (2,3,12,13). Saw et al. (14) have developed and disseminated a diagnostic classification system for SCAD, correlating angiographic findings with the findings of mural hematoma on optical coherence tomography. At my own institution, this work has resulted in increased recognition of SCAD in the catheterization laboratory over a remarkably short period of time. Through international registries, together with single-center studies, investigators have begun to build an evidence base to standardize and optimize care for patients with SCAD, by addressing key issues of medical therapy versus interventional therapy in myocardial infarction, optimal medical therapy for SCAD, best interventional strategies (when needed), and management of the post-SCAD chest pain syndrome, including the development of customized cardiac rehabilitation programs (2,6,15-20).

During the past decade, much progress has been made in understanding SCAD, but there is much work to be done because myriad unanswered questions remain. As seen in the work of Tweet et al., patients who have survived SCAD are highly motivated to participate in clinical research (2,3). Unfortunately, this enthusiasm still has few outlets. A recent query of clinicaltrials.gov using the term “spontaneous coronary artery dissection” identified only 9 observational or interventional studies that enrolled patients with SCAD, 2 of which are described in the current study. I hope the field has now achieved adequate momentum, and that we will soon see an exponential proliferation of clinical and translational research studies to further understand the pathogenesis of SCAD, to identify mechanisms for primary and secondary prevention, and to determine the best treatment approach. The zebra has been spotted and has been well cataloged, the time is now to study its stripes.

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