JORGE FELIX SAUCEDO, MD, MBA: a conversation with the editor on optimizing antiplatelet and antithrombotic therapy in patients having percutaneous coronary intervention for acute coronary syndromes

Jorge Felix Saucedo, MD, MBA, and William Clifford Roberts, MD

Figure. Jorge Felix Saucedo, MD, MBA.

William Clifford Roberts, MD (hereafter, Roberts): *Dr. Saucedo (Figure), I appreciate your coming to Baylor University Medical Center at Dallas to give a cardiology conference (on 5 October 2011) and particularly for the opportunity to talk to you about some of your work. Before focusing on antiplatelet and antithrombotic agents and percutaneous coronary intervention in acute coronary syndromes, could you briefly summarize your early life and describe your parents, siblings, and how you got to Oklahoma City?*

Jorge Felix Saucedo, MD, MBA (hereafter, Saucedo): It is a pleasure and honor to be here in Dallas in this wonderful medical center. Although her parents were from Lebanon, my

mother was born in Mexico City, and my father immigrated to Mexico City from Spain at the age of 17 in 1947. He was a self-made man. Although not well educated, he worked hard, had a good work ethic, and consequently did quite well in Mexico. He died at the age of 66 from idiopathic pulmonary fibrosis. My mother, a wonderful lady, died at age 77 of lymphoma. Both were Catholics. We were raised as Catholics with strong conservative values.

I have a brother and two sisters. My older brother, Fernando, lives in Mexico. Initially, he was in the dress and textile industry, but 5 years ago he franchised four International House of Pancakes. My older sister, Rebecca, age 51, has Down syndrome. She works full-time at a McDonald's in Mexico, cleaning tables. She can read. She is somewhat independent even though she lives with my younger sister, Myriam, a housewife, with her son in Mexico City.

I went to Catholic primary and secondary school and entered medical school right out of high school—the National Autonomous University of Mexico in Mexico City. I went to medical school for 6 years. The fifth year of my medical school was like an internship in the USA. I had a 1-year clinical rotation in Houston, spending a few months at Methodist and Hermann Hospitals and at some other hospitals in the area. That was an important year for me. It was the first year I had lived independently, and it was the year that I met the person who became my wife. Karyn was born in Austin and raised in Houston. She was studying nursing and we were living next door to each other in the same dorm (Favrott Hall) in the middle of the Texas Medical Center. After that 1 year of training in Houston, I returned to Mexico to finish medical school (the sixth year) doing research in the pathology department at the best hospital in Mexico, the National Institute of Nutrition, and arguably one of the best hospitals in Latin America for internal medicine.

Roberts: *How old were you then?*

Saucedo: I finished medical school at age 22, and the night before I was to interview for residency I was still trying to decide if I wanted to be a surgeon or an internist. I had interviews for both programs. I finally decided on internal medicine. I like to diagnose. I did my internal medicine training at the National Institute of Nutrition. The training was tremendous. I was very happy there. I worked over 110 hours per week in the wards. We only had a few hours to rest on Saturday evenings and Sunday

afternoons and began at 5:00 AM on Monday through Saturday. I was often called in the middle of the night for my 22 patients. Those years in internal medicine were crucial in my formation and were some of the most fulfilling years of my career. I lived in the hospital taking care of patients day and night.

Roberts: *When was that?*

Saucedo: From 1989 to 1992. I knew I wanted to be a cardiologist, and the best place in Mexico was the National Institute of Cardiology in Mexico City. It was founded 60 years ago as the first heart institute in the world by Dr. Chavez. I did 3 years of cardiology training there. I wanted to become an interventional cardiologist, and to accomplish that goal meant coming to the USA for training. I got accepted to do interventional training at the Mayo Clinic and at the University of Michigan Ann Arbor. I decided to go to Michigan. I trained there for 2 years with Eric Bates, Mauro Moscucci, Steve Werns, and David Muller. After the first year, I started getting a little antsy to go to another place that offered the next level of complex interventions and clinical trials. I wrote Martin Leon at the Washington Hospital Center, Washington, DC, interviewed with him, and was accepted. I spent 1.5 years of formal training at the University of Michigan and then 1 year at the Washington Hospital Center.

Roberts: *What year did you finish your training?*

Saucedo: June 1996. David Talley, chief of cardiology of the University of Arkansas for Medical Sciences, approached me at an American Heart Association meeting about 3 months before I was planning to return to Mexico. He offered me the directorship of the catheterization lab at the Veterans Administration Hospital and at the University Hospital in Little Rock, Arkansas. I accepted and stayed almost 5 years (1997 until 2001). I ran a busy research organization after Dr. Talley left. We had 15 to 20 research personnel doing a large number of clinical trials. In April 2002 I moved to the University of Oklahoma because of more opportunities, and I have been there since (9+ years).

Roberts: *Do you still do percutaneous interventions?*

Saucedo: I am the director of the cath lab. I spend 3 days a week in the cath lab and about 1.5 to 2 days a week in the clinic seeing patients. I am the medical director of the cath lab and the vice chief for the Division of Cardiology. Dwight Reynolds, the chief, is a device expert (defibrillators, pacemakers, etc.). Four years ago he was the president of the Heart Rhythm Society. I have a rather small research operation. About 80% of my time is devoted to seeing inpatients and working in the cath lab.

Roberts: *You have done a lot of different research involving the cath lab in the past 15 years. What are the investigative accomplishments that you are most proud of?*

Saucedo: In Little Rock I led a large organization that allowed us to have a strong presence as trialists in the US. While in Little Rock with Robert Letterman, we published a report using angiogenesis for patients with claudication. We injected fibroblast growth factor directly into the common femoral arteries and showed it to be superior to placebo, permitting patients to walk longer with less pain. In collaboration with Dr. Eidt, we were the first group to perform an endovascular repair of an abdominal aortic aneurysm. Also, we were first in the state of Arkansas to have access to some of the newest stents, cath lab

devices, antiplatelet drugs, and endografts. I also had a small platelet lab and did light transmission aggregometry, a technique I had learned at the University of Michigan working with Dr. Lucchesi of the Department of Pharmacology. In Little Rock I continued with light transmission aggregometry, looking at platelet function, and published a couple of papers on this subject. I started to work with the antiplatelet agent abciximab, an intravenous glycoprotein 2b/3a antagonist.

Roberts: *What has happened to fibroblast growth factor?*

Saucedo: The problem with most angiogenesis trials is that most have a very strong placebo effect. Follow-up studies have not been as positive as initial studies. We are doing a few trials on patients with claudication and also those with critical limb ischemia. We hope at some point that there will be a drug, injected intramuscularly, intravenously, or interarterially, that will help produce collaterals to improve outcomes.

Roberts: *I presume that you are now in the midst of trials on antiplatelet and antithrombotic agents? Which drugs are going to win?*

Saucedo: For about 14 years we only had two oral antiplatelet agents, other than aspirin, that were approved by the Food and Drug Administration: *ticlopidine* and *clopidogrel*. We used clopidogrel as the preferred second oral antiplatelet agent available after aspirin. Two years ago, *prasugrel* was approved in the US, mainly on the basis of data from the TRITON and TIMI 38 trials. This study showed that in both ST-elevation and non-ST-elevation patients having coronary angioplasty, prasugrel was associated with about a 20% relative risk reduction of death, myocardial infarction, and stroke. There was more bleeding with prasugrel than with clopidogrel. That is one of my passions: getting to that “sweet spot” where there is a perfect balance between reducing myocardial ischemic complications without increasing bleeding risk. Prasugrel is metabolized easier than clopidogrel. The active metabolite of both drugs is similar, but because of the easier metabolism of prasugrel, it is a more active drug. Prasugrel inhibits platelets more rapidly and more intensely than clopidogrel. There is also less variability of its antiplatelet effect compared with clopidogrel.

The newest oral antiplatelet agent approved in the US is *ticagrelor*. This drug is not a thienopyridine like prasugrel and clopidogrel. It acts on the same receptor within the platelet, which is P2Y₁₂, also known as the ADP receptor. This drug was tested in the PLATO trial and compared with clopidogrel. Compared with clopidogrel, ticagrelor reduced myocardial ischemic events, including death, when given to patients presenting with acute coronary syndromes. There is another receptor in the platelets called the “thrombin” receptor or the proteinase-activated receptor (PAR-1), which is activated through thrombin. Investigational drugs such as *vorapaxar* block the effect of thrombin, thus preventing the platelet from being activated by thrombin. The major clinical trial, TRACER, published in November 2011 in the *New England Journal of Medicine* showed a minimal efficacy improvement but a significant increased risk of bleeding complications, including intracranial hemorrhage.

Roberts: *Which antiplatelet agent are you using now?*

Saucedo: Prasugrel. In patients with a history of stroke, old age, and those with low body weight, prasugrel should be avoided or used in low doses. Patients <60 kg are given 5 mg rather than 10 mg. Patients >75 years of age bleed more than younger patients, but they benefit from prasugrel as long as they are at high risk for ischemic events, such as those with diabetes mellitus or a history of myocardial infarction. It is my drug of choice for all patients with ST-elevated myocardial infarction and for those with diabetes mellitus.

Roberts: *With clopidogrel coming off patent, how will the difference in cost affect your choice of antiplatelet agent?*

Saucedo: It is going to have a profound impact in the market. For the patient with complex coronary anatomy requiring multiple stents and for patients with diabetes, I will still continue to make the case for using the more potent antiplatelet agent, namely prasugrel, because it is metabolized easier, is more bioavailable, and inhibits platelets more potently.

Roberts: *Are you keeping patients either on clopidogrel or prasugrel longer than 1 year after percutaneous coronary intervention?*

Saucedo: Yes, I am doing that routinely despite lack of data. The DAPT study—a 30,000+ patient trial sponsored both by the National Institutes of Health and pharmaceutical companies—hopefully will provide that missing data. In this study, after 1 year of dual antiplatelet therapy, patients are randomized to either placebo (aspirin alone) or dual antiplatelet therapy (prasugrel or clopidogrel) in a blinded fashion for another 18 months.

Roberts: *Routinely how much aspirin are you giving?*

Saucedo: Either 81 or 162 mg daily, depending on which other drugs I use.

Roberts: *Is there any reason to use 162 mg over 81?*

Saucedo: No. A dose of 324 mg is probably too much. Whether 162 or 81 is better is unclear. In Europe they use 100 mg as their standard dose.

Roberts: *Do you take aspirin yourself?*

Saucedo: No. I probably need to start taking a statin but I haven't yet.

Roberts: *What are your cholesterol numbers?*

Saucedo: My low-density lipoprotein (LDL) cholesterol is around 145 and my high-density lipoprotein (HDL) cholesterol is about 80 mg/dL.

Roberts: *Are you positive the HDL is protective?*

Saucedo: By the guidelines I do not have any risk factors, and the guidelines suggest lipid-lowering drug therapy if the LDL cholesterol needs to be <160 mg/dL. We are talking about risk reduction. By the Framingham risk score I have a 2% risk of

a major cardiovascular event in the next 10 years. I have a 98% chance in the next 10 years that I will not have an event, and taking a statin would reduce that to 99%, but there is a cost to it. The cost of saving a life in my case probably would be more than what we deem reasonable, probably more than \$50,000 a year. If the statins were a magic pill with absolutely no side effects or cost, every human being should be on them. Nevertheless, I think I will be taking statins in the near future.

Roberts: *The guidelines, in my view, hinder cardiovascular health. It's very difficult in my view to be very enthusiastic about lowering cholesterol in your patients if you are not enthusiastic about lowering it in yourself. I believe we should switch gears and forget about "decreasing risk" and switch to "preventing plaques." If your LDL cholesterol is 145 you are forming plaques right now.*

Saucedo: You make a good point about preventing plaque.

Roberts: *You are 47. What are your goals now?*

Saucedo: I have been a cath lab director for the last 14 years, and I publish close to 10 papers a year. I teach. What is the next challenge? I am not sure I have an answer at this point. Oklahoma has been very good to me. The last year has been a difficult year for our division. We've been below budget and feeling pressure from the administration. I love what I am doing and my family is very happy in our current situation, but I still have potential that hasn't been tapped yet.

Roberts: *What is your daily schedule?*

Saucedo: I get up between 4:45 and 5:15 AM and work out at a gym for an hour. I usually arrive at work at 7:30 AM for a conference and leave about 5:30 to 6:00 PM.

Roberts: *What time do you go to bed?*

Saucedo: 10:00 PM.

Roberts: *Do you have children?*

Saucedo: Yes, two boys, aged 16 and 14.

Roberts: *Do you do much professional work at night?*

Saucedo: Some. I also try to spend time with the family.

Roberts: *What about weekends?*

Saucedo: I'm fully dedicated to the family. If I'm not on call, I exercise 2 hours on Saturday, go to the movies, go swimming, watch the kids' soccer and basketball games, go to church, and have friends over.

Roberts: *How much time do you take off a year?*

Saucedo: About 4 weeks.

Roberts: *How many trips do you take a year?*

Saucedo: About 20. It has been a pleasure and an honor to spend this time with you.

Roberts: *Thank you.*