Acute Stroke Research: Being Part of a Game-Changer with Dr. Dar Dowlatshahi, Scientific Director of the Ottawa Stroke Program

Faizan Khan, BSc[1,2], Marc-Olivier Deguise, BSc[1,2]

[1]Faculty of Medicine, University of Ottawa
[2]Ottawa Hospital Research Institute

ABSTRACT

Dr. Dar Dowlatshahi, MD/PhD, is a stroke neurologist, an assistant professor at the University of Ottawa, and a neuroscientist at the Ottawa Hospital Research Institute (OHRI). As the Scientific Director of the Ottawa Stroke Program, he is conducting cutting-edge research in the area of acute stroke, with a special interest in intracerebral hemorrhage (ICH). He was part of the recent ESCAPE trial, a national groundbreaking study that has redefined the scope of stroke therapy around the world. We had the incredible opportunity of speaking with Dr. Dowlatshahi about his exciting career as a clinician-scientist, as he educated us about the unique features of stroke, informed us of the recent advancements in his research, and provided advice for interested students and trainees who want to pursue a career in academic medicine.

RÉSUMÉ

Dr. Dar Dowlatshahi, MD/PhD, est un neurologue spécialisé en AVC, professeur adjoint à l'Université d'Ottawa, et un neuroscientifique à l'Institut de recherche en santé d'Ottawa (IRSO). Comme directeur scientifique du Programme d'AVC à Ottawa, il mène des recherches de pointe dans le domaine de l'AVC aigu, avec un intérêt particulier dans l'hémorragie intracérébrale (HIC). Il a fait partie de l'essai récent « ESCAPE », une étude révolutionnaire nationale qui a redéfini le cadre de la thérapie de l'AVC autour du monde. Nous avons eu l'incroyable opportunité de parler avec le Dr. Dowlatshahi à propos de sa carrière passionnante comme clinicien-chercheur. Il nous informa ainsi sur les caractéristiques uniques de l'AVC, des récents progrès dans ses recherches, et nous a fourni des conseils pour les étudiants et stagiaires voulant poursuivre une carrière en médecine académique.

TELL US A BIT ABOUT YOURSELF AND HOW YOU GOT TO WHERE YOU ARE RIGHT NOW.

I am a stroke neurologist at The Ottawa Hospital, and an Assistant Professor in the Departments of Medicine and Epidemiology & Community Medicine at the University of Ottawa. I am also the Scientific Director of the Ottawa Stroke Program, which means I run most of the clinical research concerning stroke. I was always interested in asking questions, particularly in grey areas of medicine and science in general, and that very naturally lead to a path of a clinician-scientist training; to ultimately try to ask questions that arise during my practice and generate the very data that, in later instances, I will use to treat my patients.

Keywords: Acute stroke; Intracerebral hemorrhage; Clinician-scientist

TELL US ABOUT YOUR EDUCATIONAL/CAREER PATH. HOW DID YOUR RESEARCH/CLINICAL INTERESTS DEVELOP TO WHERE THEY ARE NOW?

I started as a grade C level student in university. I got interested in psychiatric diseases and wondered why people acquire these diseases and what causes them. I met a very prominent researcher in that area who offered me to join on and do some advanced studies/research with him. At that point, I decided to pursue a Master's degree in that area. I absolutely loved the research I was doing and decided that I wanted to be a medical researcher. Thus, I started a PhD degree in neuroscience. During my PhD, I was captivated by clinical medicine because it provided better context for the disease I was studying. I got particularly inter-

ested in the areas of high acuity care, emergency care, and intensive care settings. Simultaneously, when you find something you like, your grades go up. Grades reflect interest. I suddenly became a high enough academic candidate for medical school. I was not trying to be a doctor; that was not my intention. My supervisor was a clinician-scientist who was a great role model. I just thought that I could conduct research more effectively if I had a clinical training and understood the disease from outside the lab. Thus, I applied to medicine, got lucky and got in. I decided not to quit my research because the desire to ask questions, particularly about disease causing phenomenon and its reversal, was always something I pursued and it was the primary reason I applied to medicine. Accordingly, I decided to combine the two degrees (MD/PhD).

During the medical program, I was exposed to neurology. I continued having a strong interest in neuroscience, and stroke involved fast and important decision-making; the high acuity area of neurology I was looking for. During my residency, I had an excellent mentor, Dr. Antoine Hakim, a very famous stroke researcher, who offered to support my first research project. My first year was a tremendous success with a couple of publications. Towards the end of residency, I met my other mentor, Dr. Andrew Demchuk, a brilliant stroke neurologist who asked me to join his research team in Calgary. At that time, I started ICH research since it had been mainly overlooked. It was a strong clinical/research year for me and job offers started coming in. I chose to come back to Ottawa as it was the perfect fit. They wanted to start a program and they wanted to give me all the opportunities to build it. I accepted the challenge. It ultimately grew into the Ottawa Stroke Program.

WHAT IS UNIQUE ABOUT STROKE AND ITS MANAGEMENT?

Stroke is the only neurological condition that gets better with time; thus, the natural history of stroke is towards improvement. On the other hand, stroke is a sudden onset [condition] that can cause lifetime disability for many patients that may never get back to their own initial functional state. Most people don't realize that death is [the] number two fear of your average Canadian. Disability is number one. Stroke is the primary cause of disability and becomes the primary fear of most people. I prefer to practise in the area of acute stroke and the unique thing about doing acute stroke research/therapy is that you literally have seconds to minutes to act. Every minute is 1.9 million brain cells lost. You have to act efficiently and precisely when you see a patient. A person's likelihood of being disabled for life, their number one fear, is on the line and only your choices and actions can actually allow avoiding this eventuality.

TELL US ABOUT YOUR PAST AND CURRENT STROKE RESEARCH PROJECTS.

There are three main areas of research in stroke: prevention, acute treatment, and recovery. Currently, we have over twenty projects at the Ottawa Stroke Program. In the prevention field, we are looking for new possible and modifiable risk factors for stroke, such as smoking cessation as well as targeting pre-diabetes. We are also investigating effects of stroke in the susceptible population that could lead to dementia and depression as well as the overlaps with other conditions.

As mentioned earlier, my personal work is often in the area of acute medicine. I spend some of my [time devoted to] research developing new diagnostic neuroimaging standards for identification of acute thrombus in the neck vessels that we often miss. More specifically, we are modifying our computerized tomography (CT) angiogram technology to be able to identify the thrombus more easily. Additionally, I have a strong research interest in intracerebral hemorrhage (ICH), [a condition in which] about a third of the patients that present are still bleeding in the brain, yet you can't see it. It is crucial for us to identify the bleeding in these patients because they require a different type of therapy. We developed a CT angiogram technique to image the ongoing bleeding in the brain. Consequently, we can target the therapies towards those patients that are affected by ongoing bleeding and not the ones who have already stopped bleeding.

We just made a major breakthrough in January as a large international collaboration to introduce a therapy called mechanical thrombectomy; removing blood clots from the brain. This study, called the ESCAPE trial [1, 2], has changed the way we treat stroke all across the world. This procedure has significantly reduced the death and disability rate from major strokes.

We have also started in stroke recovery research for the first time this year. We are using iPads to treat stroke patients who are in the hospital. We hypothesize that you can speed up recovery by providing the patient the tools to rehabilitate early (i.e., within two days) after stroke. Generally, about fifty percent of Canadians don't get into rehabilitation within two weeks. This project, called iRecover, allows patients to improve in various areas including speech, cognition, and occupation, using an iPad in their own time.

IN WHAT WAYS HAS THE MANAGEMENT OF STROKE CHANGED SINCE THE START OF YOUR CLINICAL/RESEARCH PRACTICE?

During medical school, back in 2001, I encountered a patient who had a stroke halfway through an interventional procedure, as a result of a complication. Unfortunately, the doctors had nothing to offer. At that time, there were no stroke doctors at this major

institution. The patient was completely disabled, ended up in a nursing home and almost certainly passed away from it. Later, I started pulling out all the data to realize that tissue plasminogen activator (tPA), a new clot-busting medication, not only worked, it very well could have saved that lady's life. But neurologists at the time did not believe in its effectiveness. Additionally, we now know that [a] mechanical thrombectomy procedure could have been used. In fact, we could have completely reversed her deficit, on that table, within minutes. However, we had no idea that it was feasible because those studies hadn't been done yet. Today, a patient with an intra-procedural stroke stays on that table and neurointerventionalists are quickly able to reverse the stroke with the same tools that were previously being used. These patients now walk off that table like nothing ever happened. It is a completely different world.

WHAT RESEARCH DO YOU THINK IS NEEDED IN ACUTE STROKE?

The biggest challenge is treating ICH. This forms one fifth of strokes and it accounts for most of the stroke-disabled patients. Moreover, forty percent of ICH survivors will die within the first two days. Thus, it is a very lethal and disabling type of stroke and there is no real effective therapy. In our recent studies, we have shown that blood pressure reduction could help. We are also working towards other therapies such as hemostatic approaches and neuroimaging techniques. Although we still work on all other areas in stroke research, including recovery, my major goal would be to treat patients with ICH; a type of stroke we cannot efficaciously treat yet.

WHAT IS A TYPICAL WEEK FOR YOU? TELL US ABOUT YOUR MULTIPLE ROLES IN THE ACADEMIC SETTING.

As a clinician-scientist, every day is different. I have my pure clinical days, where one day I'll run a stroke prevention clinic: I'll see patient after patient, review their risk factors, establish if they [have] had a transient ischemic attack (TIA) or an actual stroke, and work on preventing the next one. On another day, I'll be in the neurovascular unit treating the medical complications associated with acute strokes and trying to figure out why they had a stroke. This is a few of all the things I do during my clinical days. Then, there are my pure research days, where I'll run the Ottawa Stroke Program. I essentially set the directions of the research. I also have to secure funding for the program; therefore, I apply for grants, pitch in ideas, and raise awareness in order to move the science forward. I also have my own personal research days where I write my manuscripts and publish them. I have my education days where I give lectures to undergraduate medical students, residents as well as family physicians and neurologists. Lastly, I have a role for advocacy and knowledge translation, which means working on practice guidelines. With a team, I review and update all the guidelines routinely.

It forms kind of a cycle [Figure 1]. The interesting thing with being a clinician-scientist and an academic neurologist is that you get to see the entire loop. The loop starts with the research. The research then gets published and goes to guidelines committee. When it gets used for the guidelines, you then sit on the guideline committee where you incorporate others' research as part of the guidelines. This is knowledge translation. From there, you naturally take on the educational role and inform people on these guidelines and on the research leading to them. Next, you use the recommended treatment on your patient. While seeing the patient in the emergency room, you hit a grey area where you feel puzzled about the next step to take. This is your next research project and you go back to the beginning of the cycle. In a given week, I literally do all of that.

HAVING YOURSELF COMPLETED THE COMBINED MD/PHD PROGRAM, WHAT WOULD BE YOUR BEST ADVICE TO CURRENT AND INCOMING MD/PHD STUDENTS AND THOSE INTERESTED IN PURSUING A SIMILAR EDUCATIONAL PATH?

I think that there is no formal program that will make you what you want to be. The most important drivers are yourself, how flexible you are, and how you react to the external environment. It is crucial to understand that, sometimes, things will go badly and, other times, you will come across unexpected opportunities. Ultimately, you want to look at the horizon, and say that's where I want to be. You don't want to speculate on how long it is going to take for you to get there and start counting the years. In contemplating whether you should pursue [an education in] an MD/PhD program, an MD program, or a PhD program, look at the horizon, see where you want to be, and then look at what opportunity presents to you. Pick what seems to be the best fit for you at the moment. It might not be the program you wanted in the first place but this will gradually get you to where you want to be. Then, once this opportunity is over, think about what could bring

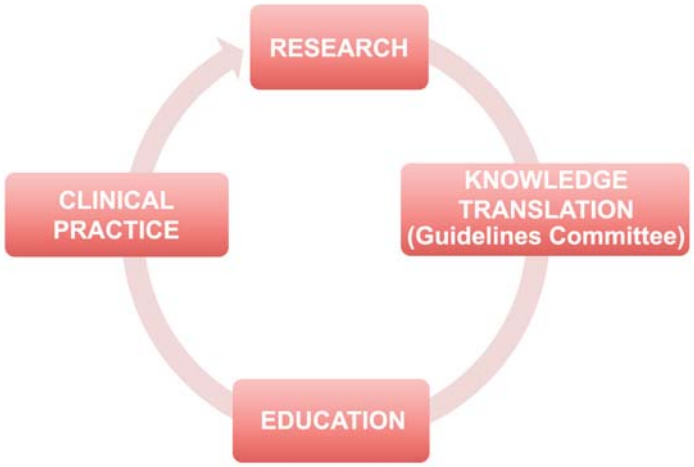

Figure 1. Progression of the various roles of a clinician-scientist.

you one step closer to your ultimate goal. The last thing you want to do is give up. Persistence and an overall sense of direction are critical, but flexibility and looking for unexpected opportunities are equally as essential.

ACKNOWLEDGEMENTS

The authors would like to thank Dr. Dar Dowlatshahi, MD/PhD, for kindly taking the time to answer all of their questions and for approving the final version of this article. For further information about Dr. Dowlatshahi and his research projects, please visit the Ottawa Stroke Program website at http://ottawastrokeprogram.com.

REFERENCES

1. Goyal M, Demchuk AM, Menon BK, et al. Randomized assessment of rapid endovascular treatment of ischemic stroke. N Eng J Med. 2015;372(11):1019-30.
2. Demchuk AM, Goyal M, Menon BK, et al. Endovascular treatment for Small Core and Anterior circulation Proximal occlusion with Emphasis on minimizing CT to recanalization times (ESCAPE) trial: methodology. Int J Stroke. 2015;10(3):429-38