MENTORS IN ORTHOPEDICS

ROB NELISSEN

https://doi.org/10.71165/2105-j9ce

SUMMARY

Professor Rob Nelissen's trajectory reflects a rigorous commitment to data-driven surgical precision. From early research on artificial hearts in Utah to chairing the Department of Orthopaedics at Leiden University, his focus remains on objective outcomes. As a founder of the Dutch Arthroplasty Register, he transitioned from clinical practice to establishing European quality standards. His current research explores novel solutions like induction heating for infections, advocating for a holistic, evidence-based approach that prioritizes patient safety and international collaboration.

Rob Nelissen is a professor in Orthopaedics and chairman of the Department of Orthopaedics at Leiden University Medical Center. He was president of the European and Netherlands Rheumatoid Arthritis Surgical Society and recently president of the Netherlands Orthopaedic Association. He is cofounder of the Dutch Arthroplasty Register and currently chairman of the Network of Orthopaedic Registries of Europe. But do not be fooled by all these pompous titles - he is a lively mind, curious and original. Get to know an orthopedist from the 3rd millennium.

So, you're working in a very big university hospital !

> Well, it's not the biggest hospital in the Netherlands, but Leiden is certainly the oldest university. It dates back to 1575. The city of Leiden actually got the university when the Dutch liberated Leiden after a two-year siege by the Spanish, during the 80-year war, 1568 to 1648. So we are the eldest, and as we're "modest" too, we think we are the most important university in the country or even Europe.

Did you do your medical studies there?

> Yes. Actually. I was born in the south next to Maastricht. My first choice for university was Leiden. In the Netherlands we had 6-7 years of medical school including rotating internships for 18 months. So, 3 months general surgery, 3 months internal medical, 6 weeks of ENT, 2 weeks eyes, etc. When I was a medical student, I did some research, it was about clubfeet if I remember correctly. As a medical student I got the opportunity to go to the United States and to work during the first artificial heart transplant. It was co-invented by Willem Kolff who also invented the artificial kidney in 1948 in the Netherlands, then went to Salt Lake City. Anyway, as a student I did some research on anesthesiological and physiological challenges during this artificial heart transplant in Salt Lake City.

Was that when you started your residency in orthopaedics ?

> Not really. Because when you finish your medical school including your internship you still have to apply for a residency spot. During my 7 months of research in Salt Lake City with the first artificial heart transplant, I also worked with the chief thoracic surgeon whose great-grandfather was from the Netherlands and he knew the professor in thoracic and heart surgery in Leiden. So I

had a spot for heart surgery, but I liked Orthopaedics much more. Unfortunately there were no jobs available and since I also had a spot for a PhD position in the anaesthesiology department, I started the PhD trajectory. Luckily for me, a residency spot in Orthopaedics eventually opened up.

So you did eventually manage to do what you truly wanted ...

Correct. In the Netherlands, the residency program during my time was two years general surgery and four years orthopaedics. But after general surgery I stopped the clinical part of my residency for a while and started a PhD position focussed on orthopaedic epidemiology. Finally I also finished my training in Orthopaedics, which is always a combination of university and teaching private hospitals. We were trained in all fields of orthopaedic surgery. At the end of my training, I received a grant for a total joint fellowship at UCLA, California and Toledo, Ohio.

Who were the big names in Netherlands during your residency?

For joint replacement we had Piet Rozing and we had Antonie Taminiau for bone tumors. Piet was the chairman in Leiden. He stayed at the Hospital for Special Surgery in New York for two years and when he came back in 1978, he performed one of the first total knees in the Netherlands. He also developed his own wrist implant in the 80s and 90s and a short stem shoulder prosthesis, while others still used long stems. In those days you could still design your own implant as an investigator-driven idea. During my training in Leiden, back in the 90s I learned to use this short stem shoulder implant, which - 25 years later - is now standard care in shoulder surgery.

You did a lot of basic research before starting with the knife...

Yes, I like evidence based on data, thus statistics and epidemiology are essential for this. The co-supervisor of my PhD was Ronald Brand, a biostatistician. One of my papers in the American JBJS '92 was on the value of survivorship analyses. How to interpret them in orthopaedics - how big data can be interpreted, and misinterpreted! Sometimes it's about “gigo”: garbage in, garbage out. Even when you have good data, you can reach the wrong conclusions when using wrong methodology or wrong data interpretation.

Could you give an example?

For instance, you have a knee implant with a 10-years mean survival of 95%, indicating that at 10-year follow-up you have only a mean of 5% revision. That's an excellent implant. And for some other knee you get only 85% survival at 10 years and the first reaction might be: “Hey 95% survival is much better than 85% survival”. However, the studied population might be different. For the population with 95% survival, the mean age at the first operation is 70 years while the one which has only 85% survival, the mean age is 55 years. Thus, there is a very simple explanation for the difference: a confounder which effects the outcome “survival” of the implant). But you can also have a lot of rheumatoid arthritis patients, bigger deformities which mean more soft tissue releases, thus if you compare those with an osteoarthritic population, the results will be worse. So, just stating a number of 95% versus 85% is “gigo” - garbage in, garbage out - since variables which have a direct effect on outcome results were not taken into account. The interesting thing is that clinicians know this, but do not always know how to use the exact methodology to account for it.

What is your field in surgery?

In my department we are doing orthopaedics and traumatology. Since Rehabilitation and Physiotherapy are also part of our department, there are ample opportunities for collaboration. In

the Netherlands trauma surgery is done by orthopaedic surgeons and also general surgeons, most with a training in trauma. At my Orthopaedics department in Leiden, we are the largest bone tumor and soft-tissue center in the Netherlands. About 40% of all bone and soft tissue tumors of the country are treated in my department in Leiden. We have three consultant surgeons who do this. Personally, my interest is brachial plexus and nerve injuries and complex revision surgery; these complex revisions include prosthetic joint infections. So, the topics of the department are bone and soft tissue tumors, brachial plexus injuries, complex revision surgery with focus on infections, pediatric orthopaedics and complex trauma.

What brought you to the arthroplasty registry?

Actually it goes back to the 90's - during my PhD I was interested in objective measures and methodology for arthroplasty outcome. My PhD thesis co-supervisor, Ronald Brand, had developed national and European registries for bone marrow transplants and caesarean sections. Not all Orthopaedics, but these registries had positive feedback on clinical practice. Thus I knew we needed this in the Netherlands as well and got involved. For that matter I received the biannual prestige Anna Orthopaedic Research prize in 1996. Secondly RSA is the gold standard for measuring 3D micromotion of implants. The engineers from Leiden developed an automatic RSA technique. This Roentgen Stereophotogrammetric Analysis using a stereo image can measure up to 0.01mm of migration and 0.1 degrees of rotation of implants within the bone... When you have an imaging technique like RSA for micromotion measurements, the other thing you need is a registry with real-world data of your implants to check how they perform. At that time, mid 90's, the registry wasn't working well. When I became president of the Netherlands Rheumatoid Arthritis Surgical Society in the mid-90s, we started again with a registry with "rheuma" surgeons but this also had low completeness. Around 2000, we received a small grant, along with support from Ronald Brand and we restarted the registry with seven regional hospitals around Leiden. We called it RODA which means Regional Orthopaedic Data Analysis.

You convinced them?

Yes, by giving them an online, easy-to-use feedback tool for their arthroplasty patients. I convinced them that the data could improve the results of their patients. They tried it and they liked it. The latter was important, to create momentum towards the Netherlands Orthopaedic Association for a restart of the national Registry, the LROI. Since a national registry, with at those times 55,000 hips and knees a year in 102 hospitals could not be run by volunteers alone, like Ronald Brand, professor in statistics and myself, more funding was necessary. The board of the Netherlands Orthopaedic Association organised this with the National Insurance authorities.

Was there any financial encouragement for the surgeons?

The main incentive to surgeons was the real-time online feedback on their patient characteristics, their implants in comparison to the rest of the Netherlands overall. Furthermore, the Dutch Arthroplasty, LROI, provided support to surgeons, like free barcode scanners, free support with data analysis and annual reports on quality indicators. I remember when they asked me to run the national registry in 2005, during the General Assembly of the NOV, the Netherlands Orthopaedic Association, some guys from NOV said that they could do it cheaper, kind of "going Dutch", but they forgot to take into account essential people: data managers, epidemiologists etc. These are essential to have valid data and correct evaluations, since data can be misinterpreted and even misused. But of course, since Leiden orthopaedics and statistics was a dominant factor

in the beginning, there was some jealousy. This was resolved by having 4 other members not from Leiden on the board. This was also essential : stressing the fact, that the LROI is for all members of the NOV.

How is the registry working now?

An essential part is the fact we have an excellent professional LROI, Dutch Arthroplasty bureau: manager, epidemiologists etc... and a scientific advisory board with orthopaedic surgeons, researchers, statisticians, epidemiologists and a governing board. Data input by orthopaedic surgeons works on a voluntary basis. With this model we have 100% coverage of all hospitals and 99% completeness of all knee, hip and shoulder implants. Elbow, ankle, wrist, finger are slightly less. This is excellent considering we are about 850 orthopaedic surgeons. Members can log in real-time and see their data, also PROM data, with respect to the national level, reports can made automatically for external review or personal use or patient information. At an European level, EFORT also became involved; one of the standing committees is NORE, the Network of Orthopaedic Registries of Europe, of which I am the chairman. Orthopaedic registries, although not yet done in all countries, are still at the front edge of quality assessment compared to other medical specialities.

How did you get involved in EFORT?

Actually, my first encounter with the European platform was during my residency, with the COCOMAC, "Comité des Sociétés d'Orthopédie du Marché Commun", fellowship in Vienna ; a great experience to see the diversity of European practices. Years later, the board of the Netherlands Orthopaedic Association selected me to be the national delegate at the EFORT around 2001. Years before I was also involved in EFORT because I was president of the European Rheumatoid Arthritis Surgical Society. That year I organised the EFORT fellowship in the Netherlands around 2002. So, I have been involved with the EFORT for quite a while. But the true reason is that I feel I am somehow more European than Dutch. When I was in the USA, I was always talking about Europe and I think that we have much to offer : great culture, great food and freedom of speech. I like the diversity of Europe. It is nice.

Was it your idea to build a European registry?

Actually, there was already the European Arthroplasty Registry, EAR, run by Prof Böhler, president and Gerold Labek, both from Austria. EAR was a separate entity, but since EFORT wanted to have the knowledge from registries presented to all EFORT participants, EFORT started NORE: Network of Orthopaedic Registries of Europe. An all-inclusive platform for all arthroplasty and other orthopaedic registries. They asked me to run this, because I was also involved in the EAR.

What exactly does NORE do?

With NORE the main goal is to educate orthopaedic and trauma surgeons on the value of real-world data from registries for their clinical practice. This has been done now for the last 6 years. Secondary goals are to reach an agreement between european registries to have minimal datasets and variables and to give advice to emerging registries. Last year we also organised meetings with EU regulators, MedTech, ODEP on the quality of medical devices. So, in the near future we might give an implant Quality certification, like EFORT-approved. The goal is to have excellent, safe

products for our patients. Another option could be to give warnings if more complications are present for one type of implant.

How do you see the future of EFORT?

If you remember, in the former century, meetings of speciality societies were mainly in Europe, but no real general orthopaedic meeting existed. These more general orthopaedic meetings could compile all the keynote information of the speciality societies, but in a more condensed form. So an umbrella organisation like EFORT can also address topics not covered by speciality societies, but that are nevertheless important to all orthopaedic and trauma surgeons. At present, the advantages of EFORT as an umbrella organisation are evident. As such EFORT can have an important voice in Europe by being present in European Commission discussion groups or the European Parliament. Our current EFORT president, Per Kjaersgaard-Andersen just addressed the EU parliament on medical devices. Of course, we all know surgeons are very individual but together we are stronger. We can easily speak to those within our own speciality and share our knowledge, but we also have to be able to do this with the outside non-orthopaedic world. With the appropriate ethics, they cannot bypass us. We know what the best is for our patients, not politicians, but we need each other to optimise healthcare for our patients. As such EFORT has a big task in education. In my opinion the EFORT congresses are better than the AAOS, since EFORT congresses and discussions have more diversity in the presentations, debates resulting in more innovative approaches to problems. This is probably due to rich European diversity - although we know there isn't one solution, we should strive for evidence-based health-care. Of course hip surgeons or shoulder surgeons will always attend the European Hip Society congress and ESSSE/SECEC congress but there are also a lot of general orthopaedic surgeons with a super speciality. They are very happy to have the whole field of orthopaedic surgery, traumatology and basic science. in one congress. In my opinion, it's better to have a generalist with a subspeciality than only super specialists. It's still better to have a holistic approach to our patients since reductionism might lose the patient out-of-sight. So two tasks of EFORT: education for the general orthopaedic surgeon with input from the specialist societies and an umbrella organisation in professional, ethical and political aspects.

What were your main scientific works?

The main research themes are about prediction of clinical outcome and optimising clinical outcome in arthroplasty patients, for instance : using implant migration RSA measurements, value added healthcare etc... For that mattter large observational cohorts are established. The themes are mainly on outcome prediction of arthroplasty and infected joint prostheses. Next to this, our neuromechanics lab is used for upper extremity research. One of the spinoffs of brachial plexus surgery, is that in large rotator cuff ruptures, our first step is still to do a latissimus dorsi or teres major transfer and not a reverse prosthesis. Our group has written several articles on this using shoulder lab data, as well as on the non-effectiveness of acromioplasty. Comparing acromioplasty surgery with bursectomy in a prospective study, we found no statistically significant differences between the two treatments. The severity of symptoms had a greater influence on the clinical outcome than the type of treatment. Most of the time, primary subacromial impingement syndrome is largely an intrinsic degenerative condition causing kinematic disturbances rather than an extrinsic mechanical disorder. In other words, an acromioplasty can be considered placebo surgery in the majority of patients. The correct name is

> subacromial pain syndrome or SAPS, explaining the central theme of pain, but also the difficulty to grasp its cause, which is more complex.

One of your papers was about heating infected implants!

> Correct. I always have lots of crazy ideas. This one came when a lady with a shoulder prosthesis had an MRI for her brain. After the MRI she complained that her shoulder was warm.... This was caused by induction heating and I thought that it might be a solution to treat bacterial implant infection without antibiotics. Bart Pijls and I started an in vitro study using a disassembled induction cooking plate and non-porous titanium cylinders exposed to five different mico-organisms. We studied the effect of the level of temperature and heating duration. The results were good. Non-contact induction heating of metallic implants appears feasible and is effective in vitro to limit survival of various bacterial species and yeast, including spore-forming bacteria. First we used increased temperature, but then we found that 55 degrees is also sufficient when you add a very low dose of Vancomycin, the bacterial cell membrane becomes permeable at those temperatures. We got a small grant of 150,000 euros for our studies, currrently we are applying for big grant with an international consortium... hopefully for millions.

Other bright ideas?

> What about gene therapy and hip prosthesis loosening? Revision surgery for loose implants in elderly patients with comorbodity has a high rate of mortality or morbidity. My idea to avoid open surgery in those cases was to destroy, by gene therapy, the periprosthetic tissue and then inject cement percutaneously to stabilise the prosthesis. The cells of the interface tissue are synovial-like cells, like fibroblast. The purpose of gene therapy is to sensitise the interface cells to a prodrug which will act as a poison to them. The first step is to modify the program of the cells by using an adenoviral vector, harmless to humans. This adenovirus will carry a gene which is built into the normal gene of the cells. Then the modified cells are exposed to a prodrug and their metabolism results in apoptosis or cell death. The "in vitro" study showed that the interface cells can be killed with this method. The next step was a phase II study on 12 clinical cases on very old patients, ASA 3 with loosened hipprostheses. Percutaneous injection of cement around the prosthesis was used, once the interface tissue was destroyed. The average age was 92 and 3/4s of those patients could walk again. The next step would be a phase 3 randomised study but we need serious funding for this research.

What do you do when you're not working ?

> I have a wife and two daughters, both are in medical school; the eldest, Anne 22 years, in Amsterdam, the youngest, Sophie 20 years, in Utrecht. I used to play squash and field hockey, a very popular sport in the Netherlands, but I stopped because I'm not as young as I was. Now my sport is tennis, using my bicycle to work, like eveybody in these Low Lands.