A recent article in *Circulation* titled, “Myocardial Injury After Noncardiac Surgery and Its Association With Short-Term Mortality,” concludes that patients at risk for early death after noncardiac surgery are easily identified by routine postoperative troponin measurements and that the time interval between troponin elevation and death potentially allows physicians to modify prognosis.

The last author of this article, Wilton van Klei, MD, PhD, medical director, Division of Anaesthesiology, Intensive Care, and Emergency Medicine, and acting chair, Department of Anaesthesiology, University Medical Centre Utrecht, Utrecht, the Netherlands, comments, “Perioperative adverse cardiovascular events are the leading cause of morbidity and mortality after noncardiac surgery. Despite efforts to prevent their occurrence, the incidence of postoperative myocardial infarction is still high.”

Dr van Klei regards this article as among his most important and his proudest achievement because it has helped to “put the issue of postoperative myocardial damage and its relationship with mortality on the map.”

“We Found a Strong Association Between Postoperative Myocardial Injury and Death”

To test whether measuring cardiac troponin routinely after noncardiac surgery could help identify patients at risk of postoperative myocardial infarction, Dr van Klei and his team implemented routine troponin level monitoring on the first 3 days after surgery as part of standard postoperative care in patients ≥60 years of age undergoing intermediate- to high-risk surgery. Their observational, single-centre cohort study of 2232 patients estimated the incidence of myocardial injury after noncardiac surgery and its predictive value on the risk of death within 30 days with the use of data from routine postoperative monitoring of troponin. Postoperative myocardial injury diagnosed by troponin elevation was detected in 19% of the patients, and overall all-cause death within 30 days was 3%.

Dr van Klei says, “Although only a minority (<10%) of the patients had typical signs of myocardial ischaemia or electrocardiographic changes, we found a strong association between postoperative myocardial injury and death. Implementation of postoperative monitoring of troponin as a standard of care is feasible and may improve risk stratification and reclassification of patients at risk of early postoperative death.”

Dr van Klei’s work is funded through his department and grants. In 2011, he won the 2011 Clinical Scholar Research Award from the International Anaesthesia Research Society for his work titled, “Effect of Routine Postoperative Troponin Measurements on 1-Year Cardiac Events and Death.”

On other pages...

**Funding: German Cardiac Research Foundation** Antje Augstein, PhD, research fellow, Lab for Experimental and Molecular Cardiology, Dresden University of Technology, Dresden, Germany, received a grant to investigate SOX9 expression in the ischaemic area of infarcted mammalian heart.

**European Meetings Update, 13 to 31 October, 2013** Cardiovascular meetings taking place in Europe, September 13 to 31, 2013.
“Two of Our Articles Changed Preoperative Evaluation Practice in The Netherlands and Led to the Establishment of a ‘Preoperative Evaluation for Anaesthetic Nurses’ Education Programme”

Dr van Klei enjoys collaborations, and his work with colleagues, including Judith van Waes, MD, Hendrik Nathoe, MD, PhD, and clinical epidemiologist Professor Rick Grobbee, MD, PhD, has been among his most enjoyable. This has led to articles on the effects of preanaesthesia assessment and intraoperative haemodynamics on cardiovascular outcomes. 2–4

“It is inspiring to be at the front of a developing clinical and research area working with a group of people who all have the same goal,” comments Dr van Klei, who says that his most important articles investigate the implementation of preanaesthesia assessment clinics and optimising the staffing of these clinics.

He explains, “Two articles are particularly important, one in 2002 in *Anesthesia and Analgesia*5 and one in 2004 in *Anesthesia*,6 for which we developed a preoperative clinic and then showed that it led to fewer cancellations. It is better for people to come to our clinic before surgery so we have time to assess and educate them.”

However, the study also raised the question about whether it was necessary for all patients to be seen by anaesthesiologists, who were not only expensive but also a scarce resource in the Netherlands, or whether it was possible to train nurses to do the job.

These 2 articles changed practice in The Netherlands and led to the establishment of an education programme for nurses for this role. From 2007 to 2012, Dr van Klei was course director for the postgraduate course titled, “Preoperative Evaluation for Anaesthetic Nurses.” He says, “Every year between 20 and 25 nurses from the whole of The Netherlands are trained in preoperative assessment in Utrecht. This has changed clinical and anaesthesia practice before surgery in The Netherlands, so I think these articles are my most important from a perspective of impact.”

Dr van Klei’s research interests focus on improving postoperative care for high-risk patients, and involve collaborations with cardiologists, surgeons, clinical chemists, and epidemiologists within the University Medical Centre Utrecht’s Circulatory Health research programme. Focussing on atherosclerosis, heart failure, and stroke, Circulatory Health aims to create a state-of-the-art, internationally competitive, integrated research and patient care programme that stimulates translational, multidisciplinary research, innovative patient care, and excellent education and training to improve the prediction, prognosis, and prevention of vascular disease.

Dr van Klei explains that the added value of Circulatory Health lies in the cross-links created between scientists from the different participating research groups, as well as linkage of the research infrastructure (ie, patient cohorts, databases), all with a common research focus. The goal of this integrated programme for research and patient care is to reduce the cardiovascular disease burden both in The Netherlands and abroad.

6 Months’ Experience in Hospital at the Age of 7 Years Led to Dr Van Klei’s Medical Career

In 1977, at the age of 7 years, Dr van Klei spent 6 months in hospital with infection complications resulting from a problem with his oesophagus and diaphragm—an experience that inspired his medical career. He says, “I saw what it was like to not only be in hospital as a patient, but also to be a doctor.”

Dr van Klei studied at the University of Utrecht Medical School from 1990 to 1999, and then trained in epidemiology at The Netherlands Institute for Health Sciences in Rotterdam, The Netherlands, from 1999 to 2001. This was accompanied by training in anaesthesiology at University Medical Centre Utrecht from 1999 to 2006, which led to a PhD thesis on preoperative evaluation: risk management and implementation aspects. From 2006 to 2007, Dr van Klei worked at Ottawa Hospital, Ottawa, Canada, on a perioperative medicine fellowship, and from...
2009 to 2010, he worked at University Medical Centre Utrecht on a cardiothoracic anaesthesia fellowship. He is now medical director of the Division of Anaesthesiology, Intensive Care, and Emergency Medicine; acting chair of the Department of Anaesthesiology; and the Department’s principal investigator of the University Medical Centre Utrecht Circulatory Health research programme.

In recent years, Dr van Klei has been able to split his time equally between clinical work and research work, but at present, as interim chair of the Department of Anaesthesiology, he spends 1 day a week on clinical work, 1.5 days on research, and the rest on management.

One of Dr van Klei’s most enjoyable roles is mentoring PhD students. At present, he is supervising 5 PhD students on several clinical research projects focused on cardiovascular perioperative medicine. He says, “Most projects aim to unravel further the aetiology, detection, and treatment of asymptomatic myocardial injury after noncardiac surgery. These multidisciplinary and multicentre research projects are carried out in close collaboration with cardiologists, surgeons, clinical chemists, radiologists, and epidemiologists.”

Published articles written by others that have had the most impact on his work and the way he thinks describe the studies conducted by Professor Scott Beattie, MD, FRCPC, PhD, from the Department of Anesthesia and Pain Management at Toronto General Hospital, Toronto, Canada. Dr van Klei explains, “He [Professor Beattie] is a friend and working in the same areas as me, but he started earlier than I did. His way of thinking and approaching the problem of postoperative complications inspired me to go in this direction.”

From 2007 to 2010, Dr van Klei was chair of the Dutch Society of Anaesthesiology committee for the development of a national core dataset for preoperative evaluation.

“Anaesthesiologists Should Be Involved in Postoperative Care on General Wards”

Patients are still vulnerable after surgery in certain circumstances, and Dr van Klei believes there is an extended role...
for the anaesthesiologist to play in patient care, particularly postoperatively, because of their specific expertise.

He explains, “I am not a cardiologist, but an anaesthesiologist who has specialised in cardiac anaesthesia and perioperative medicine. During surgery, anaesthesiologists, and especially cardiac anaesthesiologists, are controlling the physiological functions that are normally maintained by the patient’s body, such as blood pressure and ventilation. This requires a combination of knowledge about (patho)physiology and pharmacology and surgical procedures, as well as communication skills to guide teamwork in the operating room.

“Perioperative medicine starts before surgery with the preanaesthesia assessment and currently often ends with the patient leaving the recovery room, except for a responsibility for postoperative pain management. However, in my opinion, anaesthesiologists should be involved not only in postoperative pain management, but also in providing postoperative care on general wards, monitoring vital functions and monitoring for complications likely to be related to surgical and anaesthesia care.

“I think as anaesthesiologists we should extend what we are doing in the operating room to the surgical floor postoperatively. Perioperative care for surgical patients, especially care outside the operating room, can be improved. I am working towards this by initiating research in those areas where evidence for optimal treatment is absent.”

In the future, Dr van Klei aims to develop ways in which anaesthesiologists can extend their role and responsibility from the operating room to the surgical floor postoperatively. “That is my future plan from both a clinical and a research perspective,” he says. He also plans to build on his recent work published in Circulation by further unravelling the aetiology and treatment of postoperative myocardial damage detected by troponin elevation.

References

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“In Terms of the Multiple Functions of the Transcription Factor Sox9 in Development and Its Influence on Cell Proliferation and Extracellular Matrix Deposition, Our Data Could Be Valuable for Identifying Signalling Pathways Influencing the Regenerative Potential of the Injured Heart”

Antje Augstein, PhD, research fellow, Lab for Experimental and Molecular Cardiology, Medical Faculty, Dresden University of Technology, Dresden, Germany, describes her research funded by a German Cardiac Research Foundation grant to Jennifer Taylor, BSc, MSc, MPhil.

Antje Augstein, PhD, research fellow, Lab for Experimental and Molecular Cardiology, Medical Faculty, Dresden University of Technology, Dresden, Germany, received a German Cardiac Research Foundation grant of €59,644 in 2012 over 2 years for her project titled, “SOX9 Expression in the Ischaemic Area of the Infarcted Mammalian Heart—Potential Mechanism of Regeneration?”

Dr Augstein is working on this basic research project in the Lab for Experimental and Molecular Cardiology headed by Professor Ruth H. Strasser, MD, PhD, chair of the Internal Medicine and Cardiology Clinic and medical director of the Heart Centre, University Hospital, Dresden University of Technology (see http://circ.ahajournals.org/content/123/8/f43). Dr Augstein’s coworkers are Dr Nadine Steinbronn, PhD student Anica Vergara, and technician Peggy Barthel.

The mammalian heart lacks the potential to regenerate efficiently after damage. Myocardial infarction is followed by substantial reorganisation of the infarcted tissue, which is characterised predominantly by adaptive mechanisms (remodelling) but scarcely by regeneration. In contrast to mammals, zebrafish efficiently repair damaged myocardium by producing new cardiomyocytes in the absence of scar formation. Understanding the key healing processes after myocardial infarction in zebrafish may result in identification of the barriers for efficient cardiac regeneration in mammals. In this context, the transcription factor Sox9a has been identified in the process of heart regeneration in zebrafish.

Mammalian Sox9 is widely expressed and plays an important role during the development of many organs. Mutations in the SOX9 gene cause campomelic dysplasia, a generalised disease of cartilage characterised by skeletal malformations associated with gonadal, heart, and brain abnormalities. Recently, Sox9 has been linked to diseases like fibrosis and cancer due to its function in extracellular matrix deposition and progenitor cell proliferation. These data raise the question about whether Sox9 is engaged in

Dr Augstein with her coworkers. From left to right: Dr Augstein, Dr Steinbronn, PhD student Anica Vergara, and technician Peggy Barthel. Photograph courtesy of Dr Augstein.
remodelling processes in the mammalian heart so in the long run may be involved in a regenerative response.

The Dresden group induced myocardial infarction in a wild-type C57BL/6 mouse by chronic ligation of the left anterior descending artery. The infarcted mouse heart showed extensive remodelling. The injury and its influence on cardiac function were monitored by echocardiography and pressure-volume catheterisation revealing a loss of cardiac function. They showed that SOX9 mRNA as well as Sox9 protein levels were significantly increased in the infarcted anterior wall compared with the nonaffected posterior wall and to sham operation. Immunohistochemical staining of the heart showed a clear nuclear localisation of Sox9 in cells resident in infarcted areas.

Based on these findings, the aim of the current project is to study the role of Sox9 in the process of remodelling of the injured mammalian heart. Dr Augstein and coworkers will therefore first characterise the Sox9 expression pattern in the infarcted heart and determine in which cell type(s) it is expressed. Second, conditional knockout mice will be created to specifically inhibit Sox9, focusing especially on cardiomyocytes. The subsequent analysis of the cardiac function coupled with gene expression analysis and immunohistochemical characterisation of the animals should give further hints about the role of Sox9.

Additionally, established cell culture models will be examined for Sox9 expression, and the regulation and functional consequences of its expression on proliferation and cell death will be differentiated. To translate these results to the human situation, a screening approach will be performed on an existing library of myocardial tissue from patients who have advanced heart failure. Dr Augstein says, “In terms of the multiple functions of the transcription factor Sox9 in development and its influence on cell proliferation and extracellular matrix deposition, our data could be valuable for identifying signalling pathways influencing the regenerative potential of the injured heart.”

The staff members in the Dresden research lab have long-term experience with rat and mouse surgery, especially cardiovascular operation techniques. Before this current study, Dr Augstein worked on basic regulation processes in the development of atherosclerosis.

References

Jennifer Taylor is a freelance medical journalist.