

# Circulation

JOURNAL OF THE AMERICAN HEART ASSOCIATION

## European Perspectives in Cardiology



### Music and the Heart



#### Luciano Bernardi, MD, a Cardiologist From Italy, Believes That Music Can Have a Beneficial Effect on the Cardiovascular System

**Dr Luciano Bernardi, associate professor at the Department of Internal Medicine, University of Pavia, Italy, feels convinced that music could serve as a useful tool in the management of cardiovascular disease. He discusses the evidence with Emma Baines, BSc.**

Listening to music, whether a Mozart concerto or the latest album from the top of the popular music charts, may not only help you to unwind at the end of a stressful day. It could also lower your blood pressure and improve your heart rate variability, according to Dr Luciano Bernardi, associate professor of internal medicine at the University of Pavia, Italy.

The idea that music has an effect on heart rate and blood pressure has existed for some time. In 1918, Hyde and Scalapino<sup>1</sup> reported that minor tones increased pulse rate and lowered blood pressure, whereas “stirring” music increased both blood pressure and heart rate. Dr Bernardi became interested in the effects of music on the heart as a result of his research on the ways that he could influence the rhythms of the autonomic nervous system to improve respiratory and cardiovascular function.

He explains, “We are interested in the effects of the autonomic nervous system on circulation and the heart. There are rhythms in the cardiovascular system and the autonomic nervous system that can send information to the blood vessels and the heart and affects these rhythms. But talking about rhythms involves the idea that external rhythms can influence internal ones.”

Initially, Dr Bernardi investigated the effects of research on how controlled breathing techniques such as those used in

yoga, meditation, and prayer could help regulate internal rhythms. “If, instead of breathing naturally, you superimpose a slow, steady rate of respiration on the body, you modulate the whole cardiovascular system,” he says.

In one study, he found that reciting either the rosary prayer or a yoga mantra enhanced heart rate variability and baroreflex sensitivity by slowing the breathing rate down to 6 breaths per minute.<sup>2</sup> In a more recent study, he has shown that breathing at this slow rate reduced blood pressure and enhanced baroreflex sensitivity in hypertensive patients.<sup>3</sup>

After several studies had shown that one could modulate internal rhythms through controlled breathing, Dr Bernardi became interested in whether other ways existed to modulate the rhythms of the autonomic nervous system. He says, “We wondered if perhaps other external stimuli could have an effect on the rhythms of the autonomic nervous system, and we decided to test the effects of different types of music.”

Dr Bernardi worked with Peter Sleight, MD, from the department of cardiovascular medicine, John Radcliffe Hospital, Oxford, United Kingdom, to test which aspects of music could produce changes in cardiovascular and respiratory variables.<sup>4</sup> They designed a study in which 24 healthy volunteers, half of whom had extensive musical training,

#### On other pages...

##### Spotlight: Evelyn Regar, MD, PhD

Dr Evelyn Regar is an interventional cardiologist at the Erasmus Medical Center, Rotterdam, the Netherlands. She talks about her career and her thoughts on training to become a cardiologist as a woman in the Netherlands.

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##### Long-Term Follow-up in Cardiac Surgery

Ron van Domburg, BSc, PhD, is responsible for collating the data on some of European cardiology’s longest follow-up studies and has spent nearly 30 years working as an epidemiologist in the Netherlands.

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**Figure.** Dr Bernardi has always benefited from playing and listening to different kinds of music, and has taken up playing the lute and other medieval instruments.

listened through headphones to 6 short tracks of music chosen for factors such as rhythm, syncopation, and speed while the researchers monitored their blood pressure, heart rate, breathing rate, cerebral artery flow velocity, and baroreflex.

The musical samples used in the study came from pieces by Beethoven, Vivaldi, the Red Hot Chili Peppers (a currently popular band), sitar music by Deborah Caudhuri, a dodecaphonic orchestral work, and techno music. These 6 samples of music played for 2 minutes each in a random order without pauses, and then repeated in a different random order for 4 minutes each. In addition, the sequence included a 2-minute period of silence.

Unlike earlier studies, this study found no effect of musical style or preference on any cardiovascular parameters. It showed that only 1 factor mediated the physiological effect of listening to music: tempo. Fast music, whether classical or techno, caused increases in blood pressure, heart rate, and breathing rate, and reduced baroreflex sensitivity. Slow music, on the other hand, whether classical music or reggae-style sitar music, caused a significant fall in heart rate and breathing frequency compared with the baseline.

Dr Bernardi says, “We discovered that controls and musicians all behaved the same way when listening to music. The faster the tempo, the faster the respiration, heart rate, blood pressure, and so on. When the music was slower, it had a slowing effect.”

They also observed an order effect. Slow-tempo music seemed to lower heart rate more when it followed a faster piece of music than if it came first. “Quicker music, whether it is Vivaldi or techno, has an arousing effect on the system which concentrates the attention. If you follow this with a

slower track, you reach a more profound level of relaxation,” Dr Bernardi says.

The most surprising observation had to do with the effect of the 2-minute silence in the middle of the music sequence. It had a greater impact in reducing heart rate and blood pressure than did the slowest-tempo music. “The silence had a totally different effect on heart rate and other parameters when it came after music than it did at baseline,” Dr Bernardi recalls. “Silence between music had the most profound relaxing effect. In fact, it acted as though it were music with a zero frequency.”

He explained this effect as similar to the relaxed state produced during transcendental meditation: “First, you have to concentrate hard, giving your attention to something. Then, when you release the attention, you become very relaxed,” he said. “Music may be able to achieve the same effect.” He said that this finding suggests that listening to music that alternates a quick tempo with slower passages or pauses could help induce relaxation as an alternative to meditation, and it could have a potential use in managing patients with cardiovascular disease.

“Our job at the moment is to find out the possibilities for using music to modulate the heart,” he says. “Really, more research needs to be done. But, if our finding is supported, then if you have high blood pressure I wouldn’t suggest listening to too much techno! Or, at least, you should follow it with more relaxing music.”

Dr Bernardi has himself always benefited from playing and listening to different kinds of music. He played rock music on the guitar and saxophone as a young man. More recently, he became interested in Renaissance and medieval music and has taken up playing the lute and other ancient instruments.

*Emma Baines is a freelance medical writer.*

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## Spotlight: Evelyn Regar, MD, PhD

### Racing Driver, Pilot, Engineer, or Doctor? In the End, Evelyn Regar, MD, PhD, Chose Medicine

**Dr Evelyn Regar practises as an interventional cardiologist at the Thoraxcenter, Erasmus Medical Center, Rotterdam, the Netherlands. She talks to Mark Nicholls about her mentors, her career, her hopes for the future, and her thoughts on training to become a cardiologist as a woman in the Netherlands.**



A natural curiosity about the mechanics of the heart would eventually persuade Evelyn Regar, MD, PhD, to pursue a career in cardiology. Born in Munich, she has several relatives who have an interest and aptitude for mechanical engineering. “I looked at the heart as the main organ and began to think it was pretty versatile with rhythm and a lot of mechanics involved on valvular, myocardial, and coronary artery levels. I found it an interesting organ,” she explains.

Dr Regar’s initial interest in medicine stems from her teenage years. She says, “I was intrigued by the complexity of the human being, physically and physiologically, though in between I did want to become a racing driver and then a pilot! But I turned back to medicine.” She did her preclinical studies at the University of Regensburg, Bavaria, Germany, for 2 years, before training at the Technical University of Munich, Germany, from 1990 to 1994. From there, she trained in internal medicine and cardiology at the University Hospital, Munich, where she remained until 1999.

Her choice of a subject for her thesis would shape the direction of her career. “When I was looking for a thesis for my doctorate degree, I had the opportunity to do research

with a group involved in coronary intervention,” says Dr Regar. “I became very enthusiastic about the possibilities of that, particularly being in the early 1990s, a time when stents and more treatments such as atherectomy and rotablator were becoming available and there was a great deal of innovation. It was an exciting time.”

For the past 8 years, Dr Regar, now 38 years of age, has worked at the Erasmus Medical Center in Rotterdam, where she now practises as an interventional cardiologist and has the post of clinical head of the catheter laboratory at the Thoraxcenter (Figure 1).

During her training and early career, she says she has benefited from the knowledge and expertise of a number of renowned clinicians and tutors, but she points to 3 in particular who inspired her.

With gratitude, she mentions Rudolph Blasini, MD, a professor from the Technical University of Munich, as the person who gave her the opportunity to do her doctorate thesis on intracoronary ultrasound. She also points to Harald Mudra, MD, a professor from the Ludwig Maximilians University, Munich, for introducing her to interventional cardiology. And, in more recent years, she has found a mentor and inspiration in Patrick Serruys, MD, PhD, professor of interventional cardiology at the Erasmus Medical Center (Figure 2). “He is a very inspiring person in terms of the huge knowledge that he has, his persistence and dedication, and his amazing capability to motivate people,” she says.

Areas of particular interest for Dr Regar include coronary imaging, the prevention of acute myocardial infarction, and treatment of coronary artery disease. She adds, “In interventional cardiology, I am also really intrigued by the potential of light-based technologies for coronary diagnosis, and I am looking forward to exciting developments in the next couple of years.” Dr Regar recently gave a presentation at the European Society of Cardiology meeting in September 2007 in Vienna, Austria, on bioabsorbable drug-eluting stents, and she has also edited a book on optical coherence tomography.

Dr Regar considers her natural curiosity a motivating force in her career. She explains, “I think that, as in all women, my main motivation is curiosity. I am curious, I want to understand the cause of disease, I want to improve outcomes. Also, working with patients, you realise that relatively simple procedures such as percutaneous coronary



**Figure 1.** Dr Regar became interested in interventional cardiology at an early stage and is now clinical head of a catheter laboratory.



Jan Tuin, Thoraxcenter

**Figure 2.** The Erasmus Medical Center, Rotterdam, where Dr Regar found a mentor and inspiration in Dr Patrick Serruys, professor of interventional cardiology at the institution.

intervention can improve the quality of life or even save lives. That makes it a very rewarding job.”

She has found combining her career as a cardiologist with her role as mother to her 1½-year-old daughter Vivienne manageable, yet challenging. When asked how she has found being a woman in cardiology, Dr Regar says, “We should not forget that men also have to work hard for their careers. But, as far as equality is concerned, that is something that differs very much within various parts of Europe.”

She continues: “The proportion of women in leading positions varies between 2% in Italy to 10% in Germany and 18% in Norway, despite an equal graduation rate of the sexes in their early careers. In Munich, I got the opportunity to gain a lot of knowledge. The Thoraxcenter in the Netherlands offers ideal conditions to follow up a career as a cardiologist and scientist. It was Dr Serruys who accepted me as the first woman for training in interventional cardiology in Rotterdam.”



Dr Patrick Serruys

Before that time, an impressively long list of national and international fellows had trained in interventional cardiology at the Thoraxcenter—all men. Dr Regar says, “I enjoy the privilege of working with a highly skilled, intelligent, and dedicated group of people at an

institute like the Thoraxcenter.”

She advises young people seeking to pursue a career in cardiology to hone their focus. “Cardiology offers so many possibilities; people find out what they really like and what they find satisfying and then pursue it,” she says.

On a personal level, Dr Regar aims to continue her research, very much focussed on trying to understand why apparently healthy people die from sudden myocardial infarction. “I also enjoy training young people,” she says. “For me, that is a way of giving back all the energy and patience that has been invested in me to somebody else. It is really satisfying to see how people develop and grow.”

As for the future in cardiology, she believes the field should focus on offering better treatment for

chronic heart failure and for the cardiovascular complications of diabetes mellitus. She also mentions electrophysiology as a rather young subspecialty holding the promise of novel treatment strategies for arrhythmias in the future. In interventional cardiology, Dr Regar believes that unravelling late stent thrombosis is an important short-term task. “We were able to do so in the past with brachytherapy, and our knowledge on drug-eluting stents is increasing by the day. Physicians and patients need to understand the risk and benefits of drug-eluting stent therapy—fear is not a good advisor.”

Dr Regar continues, “In the longer run, our tools to treat coronary artery disease will improve further, we will have dedicated devices to treat chronic total occlusions, and with magnetic navigation we have already today a technology in our hands that has the potential to fundamentally change our ways of working in the cath lab.”

Dr Regar explains further: “Noncoronary interventions such as percutaneous valve replacement will increase. It will be interesting to see how noninvasive imaging and development in drug therapy will change the entry of patients into catheter laboratories. However, invasive treatment will continue to be rather demanding on human, logistical, and financial resources. The increasing cost of health care that confronts most industrialised countries should drive our effort for innovative, cost-effective therapies.”

*Mark Nicholls is a freelance medical writer.*

# Long-Term Follow-up in Cardiac Surgery

## Ron van Domburg, BSc, PhD, is the Man Responsible for Collating the Data on Some of European Cardiology's Longest Follow-Up Studies

**Dr Ron van Domburg has spent nearly 30 years working as an epidemiologist at the Erasmus Medical Center in Rotterdam, the Netherlands. He talks to James Butcher, PhD, about his involvement in some of the longest follow-up studies ever done in cardiology, including a 30-year analysis of survival outcomes after coronary artery bypass grafts.**



In today's global research arena, it seems unusual for a successful academic to have worked at only 1 institution throughout a 27-year career. But that is exactly what Dr Ron van Domburg, an epidemiologist who has participated in one of the longest follow-up cardiology studies ever undertaken, has done. "The climate here is very good—we have the freedom to do what we want," explains Dr van Domburg, who joined the Erasmus Medical Center in Rotterdam in 1980 and has worked there ever since. "In the Netherlands, we don't have a culture that we go abroad. Only very few people from medicine go abroad to do research. It is more or less the other way around. Because of Patrick Serruys, MD, PhD, professor of interventional cardiology, people are attracted to come here and work with him."

Dr van Domburg's primary role involves providing statistical and epidemiological advice to cardiovascular clinicians, especially on coronary artery bypass grafts (CABG) and percutaneous coronary interventions.

"My specialism is follow-up after CABG and percutaneous coronary interventions," he says. "I was involved in the first percutaneous coronary interventions and the first CABG surgical procedures, and since then I have been involved in all the follow-up studies every 5 or 6 years."

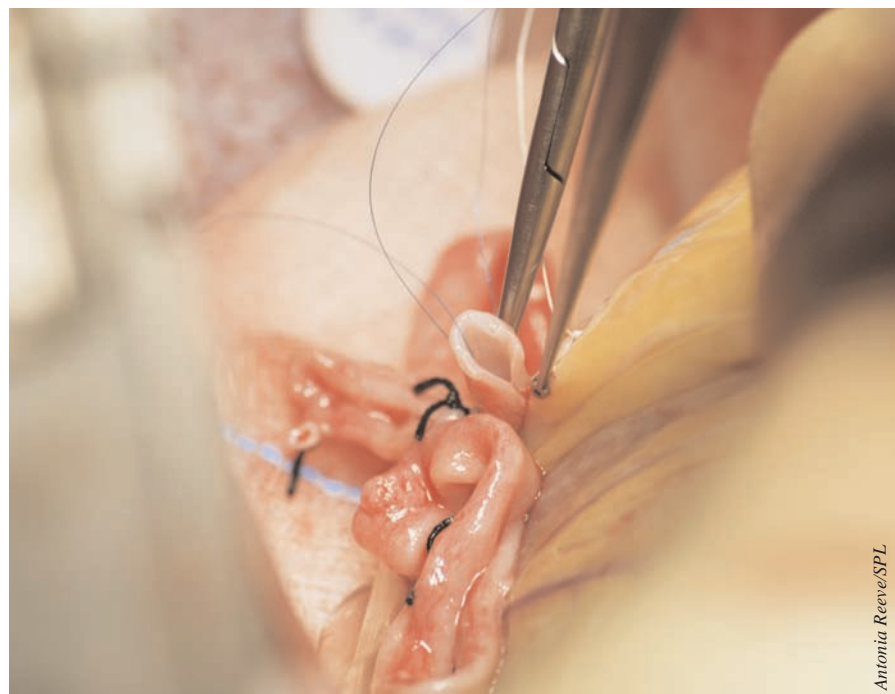
Indeed, Dr van Domburg presented data at the European Society of Cardiology's annual meeting in Vienna, Austria, in September 2007, on the outcome of 1041 patients who underwent a first isolated venous CABG procedure between 1971 and 1980.

Remarkably, he and his colleagues have managed to collect data on 98% of the patients, with a mean follow-up of 30 years, by reviewing hospital records for cardiac events and by contacting general practitioners. Because patients had a mean age at baseline of 53 years, most of them died during the 30 years that followed, providing accurate data

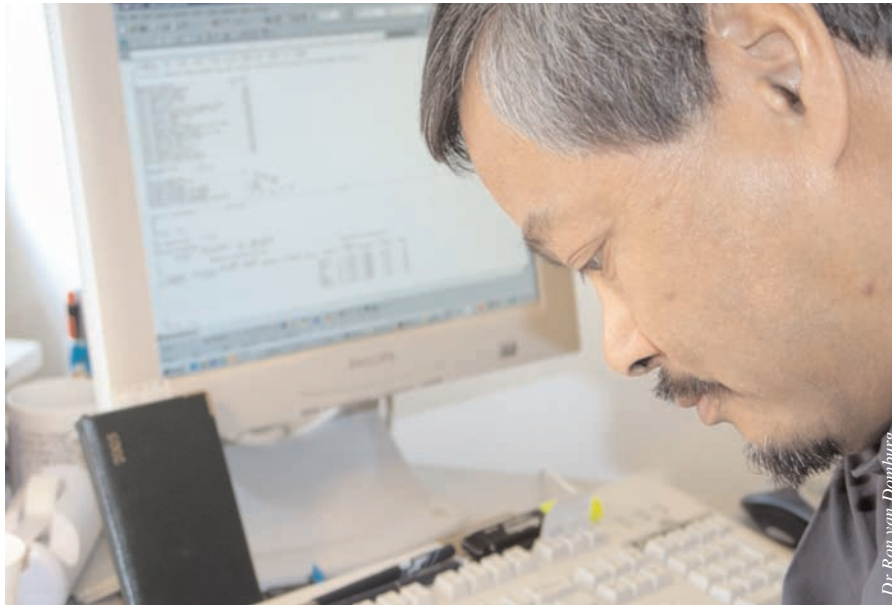
on the life expectancy of patients treated in the hospital with CABG. "The main finding is that although mortality is higher in people after CABG than in the normal population in the first 15 years after the index operation, survival rates decreased more slowly in the CABG group thereafter and eventually converged to the normal population," explains Dr van Domburg.

Dr van Domburg graduated in mathematical statistics from Delft University, Delft, the Netherlands, in 1980, at the age of 29. For his first job, he worked as a statistician/scientific system manager at the departments of epidemiology and clinical and experimental information processing at the Erasmus Medical Center.

"When I started, no databases existed on which we could perform data analyses, so during the first years I developed computer programs in order to collect the data," he recalls. "I developed a software program to generate patient discharge letters at the coronary care unit, the medium care unit,



**Figure 1.** Coronary artery bypass graft: Dr van Domburg has been involved in the follow-up of these operations almost since the first procedures were carried out in Rotterdam.



Dr Ron van Domburg

**Figure 2.** Between 1984 and 1987, Dr van Domburg developed a database management system—a software program called CLINT—that preceded programs such as Dbase and Access. The program included tools such as a dictionary generator, data entry, clinical trial tools, and data analysis.

catheterisation laboratory, cardiothoracic surgery departments, and outpatient clinic,” he says. He also designed a dedicated database to collect the baseline characteristics and other clinical relevant data.

Between 1984 and 1987, he developed a database management system—a software program called CLINT—that preceded programs such as Dbase and Access. “The program included tools such as generating a dictionary, data entry, edit queries, clinical trial tools, and data analysis—including extensive syntax rules,” says Dr van Domburg. “The software is still used and is working throughout the hospital network.”

Since then, his work has moved from information and communications technology towards clinical epidemiology; he defended his PhD thesis, entitled *Long-Term Survival and Predictors of Mortality in Coronary Heart Disease*, in 1998. Since then, he has served as an author on approximately 300 publications, including a 2007 paper in *The Lancet* entitled “Early and Late Coronary Stent Thrombosis Of Sirolimus-Eluting and Paclitaxel-Eluting Stents in Routine Clinical Practice: Data From a Large Two-Institutional Cohort Study.”<sup>1</sup>

“We have a lot of interest at the moment in drug-eluting stents, and I am involved in the longest and greatest study that used drug-eluting stents in all patients,” Dr van Domburg says. “We have a consecutive cohort since 2002 that includes about 8000 patients with drug-eluting stents in which we did angioplasty. It is very exciting because we are doing the follow-up of them and writing a lot of papers.” In total, Dr van Domburg estimates that the research group of Dr Patrick Serruys, to which he belongs, has published around 80 papers on drug-eluting stents in high-impact journals.

But research represents only 1 aspect of Dr van Domburg’s busy academic life, which also includes a heavy teaching load. “I always have about 10 students and 10 to 20 fellows

around, and most of the time I am helping them. It might be with the design of studies or the analysis of studies, advising them on what kind of statistical analysis should be performed.”

Dr van Domburg explains that he especially enjoys working with the research fellows who come from all over the world to work at the Erasmus Medical Center. “Mostly, they have a deadline because they are working here for only 2 years, and then they have to be finished for their thesis, so there is a drive to work hard, and mostly they go home only to sleep, and they work 14 or 15 hours a day. It is a pleasure to work with those kinds of guys,” he says.

Dr van Domburg also supervises the medical students who have to do a 6-month scientific study in which they collect data and then write up a thesis. “Mostly, I tell them to collect data for their successors, and they can write about data collected by their predecessors. In this way, they can write up a study during the 6 months. I guide them to do that properly, and that takes a lot of time,” he says.

“By the end, they know if they like clinical research and if they are able to do it. About half of them tend to like clinical research by the end of the 6 months, and the other half say ‘Okay, it was nice, but no more, thanks,’” he concludes wistfully.

*James Butcher is a freelance medical journalist.*

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## European Perspectives

*Circulation*. 2007;116:F139-F144

doi: 10.1161/CIRCULATIONAHA.107.187676

*Circulation* is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231

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Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the  
World Wide Web at:

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