Cardiovascular Medicine

285 Marc Russo, Maurizio Taramasso, Andrea Guidotti, et al.
The evolution of surgical valves

Triathlon – triple challenge to athletes and doctors

300 Eliane Schwegler, Marta Bachmann, Nazmi Krasniqi, Urs Eriksson
Pericarditis in a Swiss regional hospital

305 Benedikt Altermatt, Beat Schäer
Publication rate and impact factor of abstracts presented at SSC congresses 2011 to 2014
Review article

Marc Russo, Maurizio Taramasso, Andrea Guidotti, Alberto Pozzoli, Fabian Nietlispach, Ludwig K. von Segesser, Francesco Maisano

The evolution of surgical valves
Lessons can be learned from the history of heart valve prostheses.

Original articles


Triathlon – triple challenge to athletes and doctors
The assessment of endurance athlete with possible AMI is very challenging because application of the classical diagnostic tools requires specific knowledge regarding the cardiovascular phenotype of the endurance athlete in general and during a competitive event.

Eliane Schwegler, Marta Bachmann, Nazmi Krasniqi, Urs Eriksson

Pericarditis in a Swiss regional hospital
Chest pain and ECG changes are the most common clinical findings in the emergency department and outcome is generally favourable with low recurrence rates.
Publication rate and impact factor of abstracts presented at SSC congresses 2011 to 2014

Abstracts presented during the congresses had a high chance of being published, usually in papers with a good IF. This reflects the good quality of research in cardiology in Switzerland.

Case report

Valerian Valiton, Nicolas Brugger, Denis Graf, Stéphane Cook, Diego Arroyo

Double trouble – a case of atrial fibrillation and pulmonary embolism

Right atrial appendage thrombus is a rare complication of atrial fibrillation that can also lead to cardioembolic pulmonary embolism.

News

Research Prize of the Swiss Heart Foundation 2018

The Swiss Heart Foundation awards an annual prize for outstanding publications on scientific research in the field of prevention, diagnosis and/or treatment of cardiovascular diseases.
Lessons can be learned from the history of heart valve prostheses

The evolution of surgical valves


* University Heart Center, Universitätsklinik Zürich, University of Zurich, Switzerland; b Cardio-Vascular Research Department of Surgery and Anesthesiology, CHUV, Lausanne, Switzerland

Summary

The treatment of heart valve diseases started in 1914 with closed heart procedures. In 1952, the first valvular heart prosthesis was implanted in the heterotopic position. In almost one century, cardiovascular surgery has progressively evolved in several steps that represented correct answers to upcoming clinical challenges. In this review we retrace the history of heart valve prostheses, from the first steps to the present. Several key concepts as “operative mortality”; “durability”; “thromboembolic events”; “less-invasiveness” guide our long journey and help us to explain the mechanisms of this evolution.

Key words: mechanical heart valves; biological heart valves; transcatheter heart valve implantation; valve durability; less invasiveness

Introduction

On 7 September 1896, a 22-year-old man was stabbed in the heart and collapsed. Two days later Dr Ludwig Rehn, from Frankfurt, performed the first reported heart surgery operation, suturing the wound in the heart through a left thoracotomy approach [1]. Since that time, many changes have occurred and cardiovascular surgery has evolved exponentially since its beginning in 1953 when, John Gibbon performed the first closure of an atrial septal defect with use of a heart-lung machine. But the history of surgical valve treatment starts even earlier. Before the availability of the heart-lung machine, valve surgery was performed via a closed approach, on the beating heart. The first “closed heart procedure” was performed in 1914 when Theodor Tuffier treated an aortic valve stenosis by digitally opening the valve through the aortic wall [2]. In 1923, Elliot Carr Cutler, in conjunction with his cardiology colleague, Samuel Levine, performed a closed transventricular mitral commissurotomy. Digital commissurotomy was introduced in 1948 by Bailey in Philadelphia and Harken in Boston and for many years was the treatment of choice for patients with mitral valve stenosis. The first valve prosthesis was a “sutureless valve”: Charles Hufnagel [3], in 1952, implanted an heterotopic valvular heart prosthesis in the descending aorta of a patient with aortic valve regurgitation. This represented the first step in a long journey that lasted more than 50 years and is not finished yet. It is inspiring that most modern-generation surgical valves have some features already researched in the early days of surgical evolution, such as sutureless implantation, plastic leaflets and the beating heart approach. Heart valve innovation has been one of the most important factors influencing the evolution of cardiovascular medicine. Denton Cooley often said “Apply, Simplify, Modify”. This philosophy inspired generations of cardiac physicians and describes well what happened in the evolution of heart valve prostheses. Continuous and passionate research into new materials, technologies and techniques to overcome the infinite challenges of replacing a natural structure with an artificial implant. Heart valve innovation is also a good example of teamwork, between physicians and engineers. Albert Starr, a surgeon from Colombia University and Lowell Edwards, an engineer close to retirement, met in 1957 and created the first commercial mechanical valve prosthesis with a long history of successful implants: the Starr-Edwards balloon cage prosthesis. A multidisciplinary team composed of a cardiac surgeon, Dr Nicoloff, an industrial engineer, Dr Posis, and an entrepreneur, Manuel Villafana, together developed, in 1976, the first bileaflet prosthesis [4]. The early days of prosthetic valve development provided much information that is still of value today. What can we learn from the good, the bad and the ugly experiences of the pioneers of valve innovation?

Abbreviation list:

SVD = structural valve deterioration
EOA = effective orifice area
PPM = patient-prosthesis mismatch
TAVI = transcatheter aortic valve implantation
THV = transcatheter heart valve
TMVI = transcatheter mitral valve implantation
We would like to give an overview of the history and evolution of heart valves, focusing not only on the technical features of each prosthesis, but also on the trends and mechanisms that influenced this continuous development. We have divided the paper in sections that each describe the evolution of a subtype of heart valve, from mechanical and biological surgical prostheses to the transcatheter valves, and explain the reasons that determined the emergence of the “next-step valve”. With this purpose, we are not going to mention all the devices, but take example of the major ones to understand the trend of evolution.

First steps in heart valve surgery

The evolution of heart valves began in the late 1940s, when, Charles Hufnagel designed a methacrylate chamber containing a methacrylate ball that was implanted in the descending aorta of a patient with aortic regurgitation. More that 200 patients were treated after 1952 [5]. The opportunity to work with an open heart permitted Dwight Harken, in 1960, for the first time to implant, in an annular position, a “double-caged ball” prosthesis called the Harken-Soroff [6, 7]. In the same year, Nina Braunwald started her experience with mitral valve replacement using a flexible polyurethane mitral prosthesis with attached Teflon chordeae tendineae [8] and Albert Starr performed the first mitral valve replacement with the Starr-Edwards ball-valve. This valve was inspired by an old bottle stopper and was developed as a ball valve with a single methacrylate cage and a Silastic ball inside, as occluder. The first results of this procedure were published in 1961 in an enthusiastic and innovative manuscript, which is still inspirational today. A careful reading of the original paper of Albert Starr and Lowell Edwards reveals challenges and questions that are still valid today, and that affected the evolution of the last generation of surgical valves, endovascular implantable transcatheter valves [9]. The authors were confronted with the (still) difficult choice between the more physiological option of valve repair and the more reproducible and reliable option of valve replacement.

A high operative mortality represented the first limiting factor, mostly related to the complexity of operation and perioperative care. A lower profile valve that enabled easier and faster implantation appeared to be mandatory from the first. This was one of the first steps in the evolution of heart valve design: Starr modified the Harken valve by removing the second cage to simplify implantation. The issue of durability was raised as long ago as 1961. The Starr-Edwards valve was tested in vitro and, according to the results, a durability of 40 years would have been expected. Recently this hypothesis was confirmed [10].

The haemodynamic performance of the heart prostheses should be as close as possible to the native “perfect” valve, with low resistance to the forward flow and allowing only trivial regurgitant backflow once the occluder closes [11]. Paravalvular leakage and the risk of endocarditis were immediately detected: they were the indications for reoperation in the two surviving patients of Harken’s initial series. Valve noise was recognised as an important problem and was solved early, for instance by replacing the methacrylate ball in the Hufnagel prosthesis with a nylon one coated with a silicone rubber. Initial preclinical studies with mechanical valves showed the high level of anticoagulation needed to avoid valve occlusion and an elevated risk of thromboembolic events was also described. All these aspects were already clear in the first decades of heart valve surgery and they have steadily guided the evolution of heart valve prostheses. These “old concepts” will be the “key words” adopted in this review, to explain the prostheses’ evolution.

Mechanical heart valves: past, present and future

The poor haemodynamic performances of the “ball-cage” valves indicated a need for the development of a second generation of mechanical prostheses. In fact, the central ball occluder caused lateralisation of forward flow and therefore high turbulence; moreover, the high profile and the large sewing ring produced a restricted effective orifice area (EOA), and limited efficacy in the mitral position, with the risk of outflow tract obstruction [11, 12].

The need for the central flow, reproducing a more physiological pattern, led, at the end of the 1960s, to the development of tilting-disk prostheses. The Björk-Shiley valve was the first tilting-disc prosthesis to be widely implanted: it was designed with a central disk held in place by two struts [13]. The open valve had two orifices, with the turbulent flow limited to the area near to the occluder. The flow resistance was related to the disc design and to the degree of the opening angle, and for this reason the disc was progressively modified into a convexo-concave shape that could slide about 2 mm during its movement, increasing the EOA. These minor engineering modifications, with the aim to achieve a better haemodynamic profile, led unexpectedly to a higher incidence of leaflet blockade and embolisation due to the excessive “leverage-loading” on the outflow strut [13]. This brought about the end of production of this prosthesis. The history of the Björk-
Shiley is a paradigmatic example of how delicate the evolution of mechanical heart valves was. Hoping to improve haemodynamics, Kalke and Lillehei developed the first prototype of a rigid bileaflet valve, but very limited clinical use was reported. In 1977, the St. Jude Medical (SJM) bileaflet prosthesis was introduced and implanted by Nicoloff and associates [14]. This design produces three flow areas through the valve orifice, with a more uniform and laminar central flow. Better haemodynamics was associated with less blood stagnation and the lower profile allowed easier implantation. Recently, the valve has been redesigned as the SJM Regent valve. The sewing ring and the external profile were modified to further increase the effective orifice area, especially in the smaller aortic prostheses [15].

After more than 50 years of evolution, mechanical valve replacement represents an optimal treatment for patients with heart valve disease. Mortality decreased progressively and no differences in term of prognosis have been described when comparing mechanical with biological valves [16–17]. Figure 1 shows the evolution of mechanical heart valve prostheses.

But what can we expect in the current era from this old tool? Could innovation in valvular heart therapies alter the role of mechanical valves? Could mechanical valves benefit from new anticoagulation strategies? Studies in animals showed that dabigatran was effective in preventing valve thrombosis and was associated with reduced mortality after mitral valve surgery. These encouraging data have not yet translated into human practice [18]. New materials could be less thrombogenic and patient selection could be redefined accordingly, but there is not yet sufficient evidence to change the standard anticoagulation management. As a matter of fact, today most patients prefer to receive a tissue valve, to avoid anticoagulation, and the age threshold is continually reduced in guidelines, ranging between 60 and 65 years.

Reducing anticoagulation-related events: the advent of biological valves

The evolution of biological tissue valves is a mix of biochemistry, mechanical engineering and biology. A tissue valve provides some clear advantages in terms of biocompatibility, with concerns related to its durability.

The history of tissue valves originated from evidence of the haemodynamic and biological advantages of cadaveric homografts, first implanted in the aortic position by Donald Ross in 1962 [19]. His effort was largely based on the premise that “our entire physical makeup and body structures represent the end result of millions of years of evolutionary development” [20], and the assumption that no prosthetic valve can replicate such perfection.

Since homograft cadaveric valves were difficult to collect and preserve, the next step was to use xenografts – valves collected from animals. The first generation of biological valves was substantially consisted of porcine valves, the valves most similar to human ones. Several new issues were debated. How can these xenografts be preserved and how made immunologically inactive? What is the haemodynamics of non-human valves and their durability after implantation?

Tissue valve engineering began with the use of formalin to sterilise and fix the fresh xenograft tissue. This technique was complicated by collagen breakdown, with risk of early cusp calcification and occurrence of fibrosis with a big shortfall in expected valve durability. Remembering the origin, Carpentier wrote some years later: “It became obvious that the future of tissue valves would depend upon the development of methods of preparation capable of preventing inflammatory cell reaction, and penetration into the tissue” [21]. Therefore, he suggested the use of glutaraldehyde for the chemical treatment of porcine valves [22]. Creating cross-links in collagen molecules, this treatment protected the leaflets from denaturation and made the tissue immunological inactive due to antigen modification. Anticalcification treatment changed the history of tissue valves, increasing the expected durability. Moreover, in 1966 Carpentier began to mount the

Figure 1: Mechanical heart valve evolution. From Hufnagel heart valve to the current bileaflet prostheses.
whole porcine valve into a stent, obtaining a proper three dimensional space relationship between the leaflets and simplifying the implantation technique. From the haemodynamic standpoint, a central flow was achieved but further analyses revealed an important pressure drop attributed to several factors, such as the restriction of leaflet opening caused by the stent, the stiffness of the fixed geometry imposed by the pig’s anatomy and the presence of artificial commissures. The roles played by haemodynamic factors, mechanical stress and biological response in structural valve failure led to a growing interest in alternative strategies and new materials to improve outcomes [12].

Increasing the durability and improving haemodynamics: from porcine to pericardial

As postulated by Carpentier, an understanding of the chemical properties of biological tissue led to continuous and intensive research into the creation of a bioprosthesis that would provide longer freedom from structural deterioration. Bovine pericardium was identified as a promising alternative tissue source for producing artificial leaflets, because of its histological and physical characteristics in terms of thickness, pliability, abundance and wide availability [23]. In 1971, Ionescu in Leeds started the production and implantation of pericardial heart valves. The concept was to create a completely “man-made” prosthesis, to optimise the anatomical configuration and avoid the fixed geometry of an animal valve. Bovine pericardium treated with glutaraldehyde was mounted on Delrin flexible stent, in order to achieve a synchronous opening of the three leaflets (Ionescu-Shiley valve). In vitro haemodynamic studies showed more symmetrical opening than with the porcine ones. Despite the first enthusiasm, after 5 years of follow-up the first cases of structural valve deterioration (SVD) were detected. Analysis of the explanted valves revealed that the leaflets were torn by movements within the stent. The mode of failure was very unfortunate, and led to sudden severe aortic regurgitation, occasionally fatal. The technique of suturing the pericardium onto the stent was modified, such that it was sewn in the outermost part, in order to reduce impingement. Moreover, different types of stent were introduced; these were more flexible and thinner, with stress reduction in the commissural site, and allowed supra-anular implantation so that larger prostheses could be used [23].

To improve durability, after 1980 most prostheses were developed by treating the leaflets with zero- or low-pressure fixation. The goal of these methods was to maintain a more normal morphology of the leaflets. Several antimineralisation methods were invented by different companies to obtain durable leaflets, and characterised the continuous evolution of biological valves [6].

Figure 2 summarises schematically biological prostheses for the mitral and aortic positions.

Patient-prosthesis mismatch: how to manage it by use of different prostheses

Firstly reported by Rahimtoola in 1978, patient-prosthesis mismatch (PPM) represents an important issue in current practice [24]. Patients with valves with an EOA too small for their body size develop PPM and are at higher risk of postoperative mortality, reduced mass regression and limited functional benefit. The negative impact of PPM on patient prognosis after aortic valve replacement has been reported in several studies showing an increased risk of mortality and SVD [25]. As previously mentioned, a totally supra-anular valve implantation technique was proposed: the third generation of bioprosthesis (St. Jude Trifecta, Sorin Mitroflow, Carpentier-Edwards Perimount Magna) were designed to achieve a larger EOA through modification of the stent architecture, but here surgical technique plays a major role. Surgeons should be aware of the consequences of implantation of a valve too small for the patient, and avoid it.

Figure 2: Biological heart valves evolution. In the first line mitral prostheses, porcine (Carpentier Edwards Porcine) and pericardial (Hancock II and Epic). In the second line 3rd generation of aortic prostheses.
Various alternative solutions have been suggested to overcome the issue of PPM. Stentless valves were introduced by Tirone David in 1988. They are xenograft, both porcine and pericardial, without any stent or sewing cuff, and represent the extreme of the continuous reduction in valvular stent dimensions. Providing a large valve orifice and improved haemodynamics, they could theoretically induce a greater reduction of ventricular mass and avoid PPM. These promising results are balanced by a more difficult and time-consuming implantation, which requires specific skills in aortic root surgery. Initial experience with stentless prostheses revealed a high rate of perioperative aortic regurgitation due to a discrepancy between the valve annulus and the native sino-tubular junction. Complete root replacement was thus encouraged and new prostheses were developed, such as the complete porcine root (fig. 3). The great enthusiasm for these valves culminated in the late 1990s, and faded because no superiority over stented valves was detected in long-term studies [26]. The stentless technology made a big contribution to the next wave of valve technology evolution. Both sutureless and transcatheter valves were designed on the foundation of stentless bioprostheses, and furthermore, several new antimineralisation strategies and the use of equine pericardium (3F aortic bioprosthesis) were developed during the evolution of stentless valves.

A route to less invasiveness: the role of sutureless aortic valves

During the 1990s, minimally invasive cardiac surgery was rapidly developing [27]. This concept brings at least two benefits: a reduction in surgical access in order to minimise surgical trauma and wound complication and a reduction in cross-clamp and cardiopulmonary bypass time. Moreover, several datasets showed that the prevalence of frail patients with heart valve disease, and aortic stenosis in particular, was progressively increasing [28]. Three valves were introduced: the Livanova Perceval S, the Edwards Intuity and the Enable 3F (fig. 3). The aim was to reduce surgical time by avoiding the use of sutures to fix the valve to the annulus as a result of a new stent configuration, which can expand and thus anchor the valve in the right position [29]. The stent characteristics depend on the properties of nitinol, which has memory of shape and becomes flexible according to the temperature. Although several studies showed optimal results with sutureless valve implantation instead of an increased risk of complete atrioventricular block and residual paravalvular leaks, the use of 3F has been discontinued owing to late valve migration. Haemodynamic features were comparable to those of stentless prostheses, but long-term durability is still unknown [30]. Although sutureless aortic valves were initially intended for intermediate-high risk patients, the rapid development of transcatheter valve technologies profoundly affected the course of their evolution. Their current role is still to be clarified, but several conditions, such as small aortic root, multiple valve surgery, or use as a facilitating tool in minimal invasive aortic valve surgery could represent fields of application.

The last step of the evolution: transcatheter valve procedures bring surgery back to the time of “closed-heart” procedures

Transcatheter valve interventions are the most advanced development in cardiac surgery and were initially introduced as the ideal solution to the new epidemiological scenario of a large number of untreated elderly and high-risk patients with aortic stenosis. Transcatheter valves take advantage of decades of valve evolution to deliver surgical grade interventions involving miniaturised instruments (catheter-based devices) by an endovascular approach, without the need of cardiopulmonary bypass and cardioplegia [31]. Percutaneous mitral valve commissurotomy was the first surgical treatment converted into a transcatheter...
procedure. Its development is a model in the field. Initially, balloon valvuloplasty was restricted to high-risk and inoperable patients; more recently, balloon valvuloplasty became the gold standard treatment for all comers, and surgery is performed only in patients with anatomical contraindications to transcatheater treatment. The first implantation of a transcatheter valve into a human was performed in 2000, when Bonhoeffer implanted a pulmonary transcatheter valve [32]. Two years later, this approach was translated to the aortic position by Cribier, with worldwide clinical resonance [33].

When read together, the first report of mechanical heart valve implantation by Starr [9] and the Cribier’s first transcatheter aortic valve implantation (TAVI) report [33] have many similarities. Just as Starr treated end-stage patients, so TAVI was introduced as a “last resort” solution. The same enthusiasm and the same passion of a cardiac surgeon in 1960 and a cardiologist about 40 years later characterise the two papers. This parallel demonstrates how the evolution represents a continuous cycle of different solutions to treatment of the same pathology, with continuously new technologies. Each step is a fundamental contribution to knowledge and fosters further developments. Many problems in this process can be avoided by reading and digesting the history of previous mistakes.

The development of percutaneous heart valves brought together the evolution of bio-valves, stents and delivery catheter design. In order to permit endovascular releasing, the prosthesis should be crimped, with a decrease in dimensions of more than three folds without any damage to the leaflet. Two types of stents were developed: the stainless steel balloon-expandable stent and the self-expanding nitinol ones (fig. 4).

Since the beginning of this technology several issues have been identified as potential limiting factors: paravalvular leakage, a high rate of vascular complications, risk of neurological events and complete atrioventricular block.

The Cribier-Edwards (previously PVT) balloon-expandable valve (Edwards Lifesciences) was the first transcatheter aortic prosthesis (2002). It consisted initially of equine pericardium and a stainless-steel frame. In order to improve sealing, a polyethylene terephthalate fabric skirt was introduced; this modification represented the first Edwards SAPIEN model (2006) [34]. Owing to the high profile of the delivery system, several patients were treated via a transapical approach. The SAPIEN XT (2009) valve was then designed with a lower-profile tubular cobalt-chromium stent that made it possible to downsize it to reduce peripheral access complications and increase the use of the transfemoral approach. The last development of the SAPIEN valve is the SAPIEN 3 (2013), in which an additional outer skirt was added to increase sealing and an expandable 14/16 F sheet was designed to minimise femoral invasiveness. All the valves were treated with an anticalcification process involving glutaraldehyde fixation and phospholipid extraction, and a new “mild-heat” treatment that removes unstable glutaraldehyde molecules was introduced.

The prototype of self-expandable valves is represented by the Medtronic Corevalve (2005). This consists of pericardial leaflets mounted on a nitinol frame. The first-generation leaflets were made of bovine pericardium, but a switch to porcine pericardium, with the use of a more flared outflow design, allowed the development of a lower profile device. The evolution of the Corevalve resulted in the EVOLUT R. Several improvements made this device repositionable, resheathable and recapturable, and the height and diameter of the delivery system were reduced. Recently the Evolut PRO device was approved by the US Food and Drug Administration. New features include an outer wrap that adds surface area contact between the valve and the native aortic annulus to improve valve sealing.

Innovation profoundly changed the clinical use of TAVI. In contrast to the early stages, when its use was limited to high risk and inoperable patients, intermediate-risk patients are currently treated since recent data showed that TAVI is a non-inferior, and sometime superior, alternative to surgery in the short term. The design of TAVI valves gives them optimal haemo-

![Figure 4: Transcatheter aortic valve implantation devices currently in use.](image-url)
dynamic results [35], which might support the clinical superiority, particularly in patients at risk of PPM. The transcatheter approach is also used in the treatment of atrioventricular valve diseases, most of all in repair procedures. Recently, transcatheter mitral valve implantation (TMVI) became an option for patients with degenerated bioprosthesis or with recurrence of mitral regurgitation after ring annuloplasty. Although TMVI presents a number of challenges as a result of the native anatomy, its feasibility in high-risk patients with functional and degenerative valve disease has been recently reported [36].

Several devices (fig. 5) have been introduced, but the procedure is still technically demanding and the patient’s anatomy is still a controversial issue for feasibility. Risk of left ventricular outflow tract obstruction, optimal fixation to the native mitral annulus and access nowadays represent the greatest challenges in TMVI procedures [37]. Whether to repair or replace the mitral valve was for a long time a matter of debate in the surgical context. Similarly, we could expect that, once a reliable replacement device becomes available, most operators would abandon repair. However, with time and experience, valve repair could come back as an option to limit the drawbacks of a permanent implant in the mitral position (Starr and Edwards said the same in the 1960s, a prediction which turned out to be true today for surgery).

How the “new” valves are changing the “old” valves

“Valve-in-valve” procedures have been recently introduced and rapidly became the treatment of choice, in order to avoid surgical reoperation, for patients who experienced the limited durability of bioprostheses. The anatomical characteristics and the size of the previously implanted valve represent the major limiting factors for the implantation of a TAVI valve in valve. This new therapeutic scenario created a new need for bioprosthesis design to provide a more efficient “re-valving” procedure in the future and provide patients and surgeons an ad-hoc platform from which to expand indications for tissue valves in the aortic position, and possibly also in the mitral position, to a population younger than 60 years of age.

The INSPIRIS valve (Edwards Lifescience) was developed as a new class of surgical valves. The Cobalt-chromium stent has an area of possible expansion that gives the valve the capability to be enlarged in the case of a future valve-in-valve procedure. Moreover, the bovine pericardial tissue is transformed by means of a novel integrity preservation technology that eliminates free aldehyde molecules while protecting and preserving the tissue [38]. The COMMENCE Trial to evaluate the results of this promising technology, also in mitral and pulmonary positions, is ongoing.

Beyond the present: tissue-engineered heart valves

All the devices described exhibit a lack in remodelling and growth capability. This concept has led to the development of innovative valve substitutes called regenerative valves or tissue-engineered valves (TEHVs). This novel approach is based on various tissue engineering technologies that provide an alternative crimpable valve replacement device thought to be a definitive solution, also for younger and paediatric patients [39].

A TEHV would be a living organ, capable of responding and growing like the native valve. The immune response plays a special role in regulating remodelling after implantation. This technology aims to become the most advanced means to improve valve durability [40].

Experience with TEHVs is still preclinical and, even if transcatheter implantation is successfully performed in animal models, the way the device could interact with a calcified annulus must be clarified, before it can be translated into clinical practice [39, 40].

Figure 5: Transcatheter mitral valve implantation prostheses.
What can we expect from new-era prostheses and new-era physicians?

The long process of evolution of heart valves demonstrates how innovation induces changes in practice and contributes to better patient treatment. Different subcategories of patient and new challenges have been overcome during almost one century of cardiovascular interventions. And the story is not finished yet (fig. 6).

The latest evolution of transcatheter therapies has induced a revolution in clinical practice, moving the view from “operator-related” to “patient-related”. The concept of “heart team” was introduced in order to define which patient could benefit from a particular treatment. Cardiac surgeons, cardiologists, anaesthesiologists, imaging physicians and dedicated nurses, started to work in cooperation to build a new environment of cardiovascular medicine, focused on patient-centred care. Creating new competences and new evidence nowadays represents the main goal of our profession. In this ever evolving landscape, looking back into history will pave the way to the future.

Figure 6: Evolutionary steps in heart valve technology. Images courtesy of Prof. von Segesser [4].

Disclosure statement
F. Nietlispach is a consultant for Abbott and Edwards Lifesciences.
F. Maisano is consultant surgeon for Abbott, Medtronic and St. Jude.
The other authors have no conflict of interest to declare.

References
The full list of references is included in the online version of the article at www.cardiovasmed.ch.
Challenges of evaluating endurance athletes with symptoms of possible AMI during or after a race

Triathlon – triple challenge to athletes and doctors

Rainer König*, Hans Rickli*, Pierre-Alexandre Krayenbühl†, Ahmed Ouda‡, Christian M. Schmied‡, Micha T. Maeder*

* Department of Cardiology, Kantonsspital St Gallen, Switzerland; † Department of Internal Medicine, Spital Uznach, Switzerland; ‡ Department of Cardiac Surgery, University Hospital Zürich, Switzerland; Department of Cardiology, University Hospital Zürich, Switzerland

Summary

Acute myocardial infarction (AMI) in endurance athletes such as triathletes is rare but not impossible. However, the assessment of endurance athlete with possible AMI is very challenging because application of the classical diagnostic tools, i.e., history, electrocardiogram and cardiac troponin testing is different from their use in “normal” AMI patients and requires specific knowledge regarding the cardiovascular phenotype of the endurance athlete in general and during a competitive event. To illustrate this, we report on three different subjects referred with similar presentations but very different underlying problems on a single day during one single triathlon event.

Key words: acute myocardial infarction; exercise; endurance; cardiac troponin; electrocardiogram

Introduction

Triathlon, i.e., swimming, cycling and running over moderately long to ultra-long distances in a row, is one of the most demanding endurance sports disciplines as it requires a both highly trained and very versatile athlete. It does not come as a surprise that athletes completing a long distance triathlon (3.8 km swimming, 180 km cycling, 42.195 km running) are referred to as “ironmen” and “ironwomen”. Although heart disease is very rare in such endurance athletes, and regular exercise reduces the lifetime risk of acute myocardial infarction (AMI), it is well known that there are athletes with previously unknown significant cardiac disease that may manifest for the first time, and potentially in a fatal manner, during a sports competition [1–3]. In particular, AMI has been reported during endurance sport events such as marathon running [4]. However, the assessment of the endurance athlete with possible AMI is very challenging because application of the classical diagnostic tools, i.e., history, electrocardiogram (ECG) and cardiac troponin (cTn) testing is different from their use in the “normal” AMI patients and requires specific knowledge regarding the cardiovascular phenotype of the endurance athlete in general, and during and early after a competitive event. Intense endurance training over years leads to adaptations of the cardiovascular system including remodelling of the left ventricle and right ventricle [5] and the atria (“athlete’s heart”) with associated changes of the ECG [6], which makes ECG interpretation challenging. In addition, prolonged and intense exercise has been repeatedly shown to be associated with an acute rise of circulating cTn [7]. Thus, cTn testing to exclude or diagnose AMI may be challenging or even impossible in the setting of an endurance exercise competition. To illustrate the problem of the assessment of these athletes in the emergency setting, we report on three different subjects referred with similar presentations but very different underlying problems on a single day during one triathlon event.

Case series

On a Sunday in June 2017, a middle-distance triathlon (1.9 km swimming, 70 km cycling, and 21.1 km running) took place in eastern Switzerland. Among 2036 athletes taking part in the race, 1940 were able to finish within 7.5 hours. The 2017 race was notable because of the hottest temperatures in the history of this particular triathlon event (>30°C) [8]. We herein report on three athletes who were referred to our cardiology service by the local hospital or ambulance teams because of suspected AMI.

Case 1

A 47-year-old experienced male Caucasian triathlete (>10 triathlons) with possible mild dyslipidaemia (total cholesterol 4.9 mmol/l, low-density lipoprotein cholesterol not measured) but no other cardiovascular risk factors had to give up the race during the cycling course because of acute chest pain, which had started during swimming and which was ongoing and prevented the patient from faster cycling. He was assessed by the local medical team and because of ongoing chest pain an ECG was performed, which showed widespread ST segment elevation (fig. 1). The patient was
transferred immediately from the field directly to our catheter laboratory by helicopter. He had been given aspirin, ticagrelor and heparin by the emergency physician. Coronary angiography revealed a left dominant coronary circulation with plaque rupture and thrombus formation in the distal left main and thrombotic occlusion of the distal left anterior descending artery (fig. 2). Cardiac troponin I at that time was 223 ng/l (cut-off <30 ng/l). An intra-aortic balloon pump was placed, and owing to the presence of a complex left main lesion in a left-domination circulation with a significant risk of further embolisation during a percutaneous intervention, as well as the very large diameter of the left main, the patient was transferred for emergency bypass surgery. The in-hospital course after surgery was uneventful, and the patient was discharged one week later.

Case 2

A 46-year-old Caucasian man without cardiovascular risk factors (low-density lipoprotein cholesterol 1.6 mmol/l) was referred because he experienced chest pain...
discomfort starting during the cycling course. He had been exercising on a regular basis for years, but had not specifically trained for this race. He was able to complete the entire race but had to reduce speed and to walk slowly several times during the final half-marathon. On admission he had no chest pain but felt unwell. The ECG showed significant ST segment elevation in the precordial leads (fig. 3) and T wave inversions in leads II, III and aVF; cTn was above the cut-off for AMI (cardiac troponin I 245 ng/l; cut off <30 ng/l). The patient was initially treated in the local hospital and was then urgently transferred to our emergency department by helicopter. An echocardiogram revealed a structurally normal heart with overall normal left ventricular ejection fraction but possible mild anterolateral hypokinesia. Coronary angiography revealed mild atherosclerosis, but no stenosis or occlusion of a coronary artery. The patient then remembered that he had been told in the past that his ECG was abnormal. All three ECGs during the hospital course of 24 hours looked the same, i.e., there were no dynamic ECG changes. The patient’s symptoms resolved within two hours after rehydration. The ECG was interpreted as a normal variant, the cTn rise was attributed to the triathlon race per se, and the patient’s symptoms were attributed to exhaustion and dehydration in the context of suboptimal training status and extreme weather conditions.

Case 3

A 37-year-old Caucasian woman experienced sudden onset of shortness of breath and chest discomfort during swimming. She was unable to complete the swimming course because of these symptoms, and she was subsequently admitted to the local hospital with a peripheral oxygen saturation of 88%. Chest x-ray revealed mild pulmonary oedema (fig. 4), the ECG was abnormal (fig. 5), and cTn was above the local threshold for the diagnosis of AMI. The patient was given furosemide, aspirin, ticagrelor and heparin, and she was transferred to our cardiology department by helicopter. On admission, she had no symptoms, but there was a further rise in cTn (cardiac troponin I 244 ng/l; cut-off <30 ng/l). An echocardiogram revealed left ventricular hypertrophy most prominent at the apex, but normal left ventricular ejection fraction and regional wall motion (fig. 6), and normal diastolic left ventricular function with no evidence of an increased left ventricular filling pressure (ratio of peak early [E] to atrial mitral

Figure 3: 12-lead ECG showing incomplete right bundle-branch block, ST segment elevation in leads V1–5, and negative T waves in II, III and aVF. There is an elevated J point by 0.1 mV in leads V2–4 (borderline V5), and associated terminal T wave inversions in V3–5.
inflow velocities 1.6, peak early mitral annular velocity [e'] averaged from the septal and lateral annulus 8 cm/s, E/e' 10). Computed tomography coronary angiography excluded coronary artery disease, but still showed mild pulmonary oedema. Eighteen hours later, there was a fall in cardiac troponin I to 114 ng/l. On further questioning it turned out that a cardiomyopathy had been known for years, but that the patient had missed regular follow-up appointments and had stopped beta-blocker therapy. An apical form of hypertrophic cardiomyopathy was diagnosed. However, for the acute symptoms during the race, we considered swimming-induced pulmonary oedema the most likely diagnosis. A follow-up visit was organised, and future participation in competitive sports events was discouraged.

Discussion

Our series of three triathletes taking part in exactly the same competition on exactly the same day all presenting with a similar combination of symptoms and findings – chest discomfort and acute exercise intolerance, abnormal ECG, and abnormal cTn – but very dif-
different underlying cardiac status highlights the difficulties in the acute assessment of these athletes during and after a race if the conventional noninvasive diagnostic tools usually applied for the evaluation of possible AMI are used. The diagnosis of AMI is primarily based on symptoms, ECG and cTn [9, 10]. However, although physicians are generally familiar with the interpretation of history, ECG and cTn findings in “normal” patients admitted to the emergency department, special knowledge and considerations are required when using these tools in endurance athletes after a race. Here, we briefly discuss these aspects.

In the setting of a triathlon competition, symptoms may be difficult to interpret since some sort of chest discomfort, shortness of breath and exhaustion is not uncommon in such a race where athletes go to, or sometime beyond, their limits, particularly if there are extreme additional external factors (e.g., extreme temperature and/or humidity). General exhaustion, dehydration, gastrointestinal problems, hypothermia, heat stroke and muscular problems are common phenomena, which are far more common than AMI in the triathlon setting but which may be hard to differentiate clinically in the acute setting. All three patients had symptoms leading to medical contact. First of all, the fact that an athlete asks for professional medical advice and support is an alarming sign itself, since these athletes typically know their body well, have longstanding experience in interpreting symptoms and a strong will to suppress those during the race, and will well recognise if anything is happening that they are not familiar with. Thus, the problem has to be taken seriously, although the differential diagnosis is broad, and only a small minority of such patients will end up having AMI [1]. Notably, the probability of any coronary artery disease in endurance athletes is not extremely low [11, 12]. Among 152 master marathon runners >50 years, nearly 50% of men have been shown to have coronary plaques, and this prevalence was higher than in age-matched sedentary men. Interestingly, plaque composition was different in athletes and sedentary men, with more calcified plaques in athletes and more mixed plaques in sedentary men [12], which may explain the relatively low incidence of plaque rupture and AMI in these athletes. In recent years, the participation in demanding endurance exercise competitions such as marathon running has become very popular among middle-aged subjects [3], and these subjects may have cardiovascular risk factors and silent coronary artery disease. The vast majority of sports-related sudden cardiac deaths occurs in athletes older than 35–40 years [13] and, in contrast to young patients, sports-related cardiac events in this age group are mostly related to coronary artery disease rather than cardiomyopathies [14]. Our first patient had plaque rupture and extensive thrombus formation in the left main in a left-dominant coronary system, and thus timely and correct diagnosis was crucial.

The ECG is the primary tool for risk stratification in patients with possible AMI [10]. Patients with ST segment elevation must immediately undergo cardiac catheterisation to establish reperfusion, whereas in those without ST segment elevation, a secondary risk stratification is based on serial cTn measurements and other clinical factors [10]. Physicians involved in the management of patients with possible AMI are usually well trained in the interpretation of the ECG. However, although the typical AMI patient is a non-athlete older than 40–50 years, younger patients and particularly athletes often show abnormal ECGs even when there is no underlying coronary artery disease [6, 15]. The differentiation of the athlete’s ECG from a pathological ECG is difficult, and has been subject of numerous papers and a recent expert consensus statement [6]. Whereas most often ECGs in athletes are performed in the context of screening for a clinically silent cardiomyopathy, i.e., in an outpatient setting where there is time to think about the need of further examinations, in particular an echocardiogram [6], the setting of possible AMI is less common but requires a quick decision. Some degree of ST segment elevation and J point elevation, particularly in the precordial leads in men <40 years, is normal [15], and most often previous ECGs will

---

**Figure 6:** Transthoracic echocardiography, apical four-chamber view, showing left ventricular hypertrophy predominantly at the apex. A: end-diastolic still frame, B: end-systolic still frame.
AMI, including acute heart failure, myocarditis, paroxysmal tachycardia, stress cardiomyopathy and sepsis [10]. Several studies have shown that long-distance endurance exercise such as the triathlon or marathon leads to an increase in cTn above cut-offs for the exclusion of AMI in the majority of participants [19, 20] (summarised in [7]). The extent of cTn elevation in this context is modest, and cTn typically returns to baseline within 72 hours [20], which is in contrast to most patients with AMI. The exact mechanisms underlying this cTn release are unknown and may include true cardiomyocyte necrosis or increased membrane permeability with cTn leakage [7], as discussed for patients with sepsis-associated cTn release [21]. There is no evidence that this cTn release is associated with adverse long-term consequences [7]. Thus, measurement of cTn immediately after a triathlon most often will not be helpful for the exclusion or inclusion of a diagnosis of AMI, and it must be realised that cTn may be above the cut-off for the exclusion of AMI up to two days after the triathlon. Still, significantly elevated cTn after/during triathlon in an athlete with symptoms of a possible acute or chronic cardiac disease must not be attributed to the effect of triathlon alone without further thinking and consideration of additional diagnostic steps. In the first patient, cTn did not influence decision making, as in every “normal” patient presenting with suggestive ST segment elevation myocardial infarction. In the second patient, symptoms and ECG led to the decision to perform echocardiography and coronary angiography, and only after that, could cTn be attributed to intense long-distance exercise with high probability. In the third patient, the presence of pulmonary oedema was the intriguing finding. Cardiac decompression due to cardiomyopathy and associated cTn release would have been another option. This seems unlikely, however, in a patient who had been asymptomatic and had had very good exercise capacity for years. More likely, elevated cTn was a reflection of structural heart disease exposed to additional stress. Given that the patient gave up the race already after swimming (less than one hour), cTn increase was unlikely to have been caused by exercise alone. The patient’s symptoms were most likely related to swimming-induced pulmonary oedema, a known pathology in swimmers and triathletes [22]. The pathophysiology of swimming-induced pulmonary oedema is still incompletely understood. Both hydrostatic (increased pulmonary pressure) and non-hydrostatic (increased permeability) factors seem to play a role. Interestingly, left ventricular hypertrophy has been suggested as a predisposing factor [22]. In the present third patient there was no evidence of increased left ventricular filling pressure at the time of the echocardiogram. How-
ever, the patient may not have been euvoilaemic after the race and without a meal (probably rather hypovolaemic) at that time, and we had not assessed her during exercise. Notably, in subjects with hypertrophic cardiomyopathy, participation in competitive sports events is generally not recommended, based on expert consensus [23]. In conclusion, our series of three triathletes participating in the same race on the same day and presenting to the same hospital and team highlights the challenges and special considerations when evaluating endurance athletes with symptoms of possible AMI during or after a triathlon race.

Disclosure statement
No financial support and no other potential conflict of interest relevant to this article was reported.

References
A retrospective analysis of “real-world” data on pericarditis patients

Pericarditis in a Swiss regional hospital

Eliane Schwegler, Marta Bachmann, Nazmi Krasniqi, Urs Eriksson

Background: Pericarditis is a probably underestimated differential diagnosis of acute chest pain. Pericarditis outcome is favourable, but no real-world data for Swiss hospitals are available as yet. Therefore, a retrospective single-centre analysis on a prospective cohort of patients with pericarditis was conducted in a regional hospital with specialised tertiary care in Switzerland.

Methods: Between January 2011 and December 2016, a total of 44 patients with pericarditis were prospectively registered at the emergency department of the GZO Zurich Regional Health Centre and followed up for 7–79 months. Based on this database, a retrospective analysis was performed. Analysis included presumed aetiology, symptoms at enrolment, ECG changes, echocardiographic and laboratory findings, comorbidities, therapy, recurrence rate and complications.

Results: Of the 44 registered patients, 33 had a first episode of pericarditis and 11 were classified as recurrences. Male to female ratio was 5.7:1 for patients below 45 years, and 1.2:1 above the age of 45. In 35 cases pericarditis was classified as idiopathic and in 9 cases it was due to postcardiomyopathy injury syndrome (Dressler syndrome). Nearly two thirds of patients reported either influenza-like symptoms or infections 2–4 weeks prior to the hospitalisation. Thirty-nine patients (89%) presented with chest pain; 36 (82%) patients showed ECG changes and 31 (71%) had a pericardial effusion. Pleural effusions were detected in 30% of the cases (13 patients). A pericardial friction rub was reported in 6 patients (14%) only. Ninety-one percent of patients had elevated C-reactive protein levels at enrolment; 36 (82%) patients showed ECG changes and 31 (71%) had a pericardial effusion. Pleural effusions were detected in 30% of the cases (13 patients). A pericardial friction rub was reported in 6 patients (14%) only. Ninety-one percent of patients had elevated C-reactive protein levels at enrolment. Troponin elevations were reported for 23 patients (52%). Five patients (11%) were treated with aspirin, and 31 patients (70%) received another NSAID. Colchicine was administered to 33 patients (75%) corticosteroids to 8 patients (18%) and mycophenolate to 2 patients (5%). On follow-up, 30 patients with a first diagnosis of pericarditis and 8 patients with a recurrence remained free from further recurrences. Three recurrences affected patients with a first episode of pericarditis and three further recurrences were observed in patients who were enrolled after pericarditis recurrence.

Conclusions: In patients with pericarditis, males predominate, but the male to female ratio shifts towards a higher proportion of women in patients above 45 years of age. Chest pain and ECG changes are the most common clinical findings in the emergency department and outcome is generally favourable with low recurrence rates.

Key words: pericarditis; myopericarditis; age; gender; treatment; recurrence

Introduction

Pericarditis is a probably underestimated differential diagnosis of acute chest pain. It accounts for 5% of all chest pain emergency referrals [1]. Approximately 80% of pericarditis cases are either idiopathic or postviral [1, 2]. Accordingly, many patients report respiratory or intestinal infections several weeks before disease onset [2, 3]. In addition, postcardiac injury syndrome (PCIS), which comprises postinterventional, postsurgery and posttraumatic pericarditis, accounts for a relevant number of cases [2, 4]. PCIS most likely reflects autoimmune responses against cardiac and pericardial self-antigens released during heart injury [4]. PCIS typically appears after a latent period of a few weeks [5]. Men have a higher risk of developing an acute episode of pericarditis than women [6].

Acute pericarditis is defined by the following criteria: chest pain, pericardial friction rub, pericardial effusion or typical electrocardiogram (ECG) changes [2, 5, 7]. Two of these four criteria are required for diagnosis [2, 5, 7, 8]. Patients commonly show elevation of C-reactive protein (CRP) levels and other markers of inflammation [5, 7, 9]. Several studies suggested that increased CRP levels are required for a pericarditis diagnosis [2, 9, 10]. Troponin elevations are also common in pericarditis and reflect myocardial involvement, as well as damage to cardiomyocytes extending from the root of the pulmonary artery to the pericardium [2, 5].

The 2015 European Society for Cardiology (ESC) Guidelines recommendation for first-line treatment of acute pericarditis consists of aspirin or nonsteroidal anti-inflammatory drugs (NSAIDs) combined with colchicine [5]. Colchicine prevents recurrences and expedites...
healing [8, 11, 12]. Corticosteroids are rather discouraged in idiopathic or viral pericarditis because of a higher recurrence risk [12]. Nevertheless, corticosteroids are still required in pericarditis associated with systemic autoimmune disease or in patients refractory to NSAIDs, aspirin and colchicine [7, 12]. Postviral and idiopathic pericarditis are usually self-limiting and have, despite a remarkable risk of recurrences, an excellent prognosis [7]. Predictors of poorer outcome are major risk factors such as fever >38°C, a subacute disease course, cardiac tamponade, pericardial effusions larger than 20 mm and failure to respond to NSAIDs or aspirin [13]. Complications of pericarditis are cardiac tamponade, constriction and recurrences [13]. The most frequent complication is recurrence [7].

Methods

Study design and setting
A retrospective analysis of a prospectively generated database of patients with the diagnosis pericarditis was performed. All patients with an acute, incessant (“persistent pericarditis or with a symptom free interval of less than 6 weeks”), chronic (>3 months) or recurrent (“defined by a first episode, a symptom free interval of 4–6 weeks or longer and detection of subsequent recurrent pericarditis”) pericarditis who were admitted to the emergency department of the GZO Zurich Regional Health Centre between January 2011 and December 2016 were registered and followed up [5]. All patients were evaluated and treated according to in house standard operating procedure guidelines. The retrospective analysis was approved by the Ethics Committee and informed consent was obtained from all patients.

Study population and diagnostic criteria
Pericarditis was diagnosed with two of the following four criteria as reported in the ESC Guidelines 2015, based on several key papers [2, 5, 7]: pericardial chest pain, pericardial friction rub, pericardial effusion and electrocardiogram changes. Typical ECG changes were defined as widespread concave ST elevations in all areas, and/or PR depressions in leads I–III, aVF, V1–V6 or PR elevation in avR. Pericardial effusion was detected with echocardiography or computed tomography (CT).

Patients with an ejection fraction <45% at enrolment were excluded. Patients with an elevation of myocardial injury markers were included as myocardial injury markers, if they fulfilled diagnostic criteria for pericarditis and showed wall motion abnormalities in echocardiography [7]. One enrolled patient refused consent to evaluate his data.

Follow-up
Two to four weeks after diagnosis and initiation of therapy, as well as after 3, 6 and 12 months, a clinical visit including routine laboratory test and ECG was carried out. Echocardiography was performed at enrolment and after 12 months in all uncomplicated cases, or at the discretion of the attending physician in charge of the patient. Magnetic resonance imaging or CT scans were ordered if indicated.

Study parameters
Study parameters included demography (age, gender, residence, aetiology), first episode or recurrence at enrolment, diagnostic criteria and symptoms at presentation, presence or absence of flu-like symptoms or infections 2–4 weeks prior hospitalisation, comorbidities (coronary heart disease, cancer history, renal disease, hypothyroidism, autoimmune disease), major risk factors (fever >38°C, failure to respond to NSAIDs within 7 days, subacute course, large effusion >20 mm, cardiac tamponade), minor risk factors (myopericarditis, immunosuppression, trauma, oral anticoagulant therapy), pleural effusion, classification of pericardial effusion (mild <10 mm, moderate 10–20 mm, large >20 mm), previous cardiac surgery or cardiac interventional procedure, PCIS, number of cardiovascular risk factors (family history, hypertension, dyslipidaemia, diabetes, smoking), drugs, outcome (death, constrictive pericarditis, tamponade, recurrence on follow-up), ejection fraction, diastolic dysfunction, clinical findings (blood pressure, heart rate, body core temperature), laboratory findings (creatinine, electrolytes, troponin I and T levels, liver enzymes, CRP-levels, haemoglobin, leucocytes, thyroid hormones, antinuclear antibodies, anti-DNA-antibodies, rheumatoid factor, serum electrophoresis, urine analysis) as well as therapy (NSAIDs without aspirin, aspirin, colchicine, corticosteroids, mycophenolate, intravenous immunoglobulin [IVIG], interleukin-1 receptor antagonists, azathioprine).

Statistical analysis
Data from 44 patients were available. In PivotTables, the sum and percentages of the study parameters mentioned above were computed and compared between
men and women, idiopathic/viral pericarditis versus PCIS and the group of patients with a first episode versus those enrolled with a recurrence of pericarditis. Fisher’s exact test was performed on categorical data. A p-value <0.05 was considered significant.

Results

Patient characteristics and comorbidities

The study cohort consisted of 44 patients aged 15 to 84 years (mean age 44.45 years). There were more male (n = 28, 64%) than female (n = 16, 36%) patients. Interestingly, almost all patients younger than 45 years were male (male to female ratio 5.7:1). In contrast, the gender distribution was nearly balanced in the patients aged >45 years (male to female 1.2:1) (fig. 1). The difference in male to female ratios between patients <45 versus patients >45 were significant (p = 0.011). All patients were Swiss residents and all except five were of Caucasian origin. Cardiovascular risk factors were present in 29 patients (smoking in 17, hypertension in 14, diabetes in 9, dyslipidaemia in 13, family history for coronary arterial disease in 10). Coronary heart disease affected nine patients (21%, four women, five men). Eleven patients had undergone cardiac surgery or a cardiac interventional procedure during the year prior to the pericarditis diagnosis. Eight patients were immunosuppressed on admission and four received anticoagulant therapy. Hypothyroidism, history of cancer, renal or pre-existing autoimmune diseases were rare (table 1). On the basis of elevated cardiac enzymes, myopericarditis was diagnosed in 23 (52%) of patients. Pericarditis was considered idiopathic in 35 patients and autoimmune in 9 cases. All of these nine patients fulfilled PCIS criteria. Patients with PCIS had a previous cardiac interventional procedure or cardiac surgery and suffered more frequently from coronary heart disease. All PCIS patients had one or more cardiovascular risk factors.

Diagnostic criteria, and clinical, laboratory and echocardiographic findings

Of the total cohort, 39 patients (89%) had chest pain on admission, 36 (82%) showed ECG changes and in 31 (71%) pericardial effusions were detected. Pericardial effusions were classified as mild (n = 22, 50%), moderate (n = 5, 11%) or large (n = 4, 9%). Pericardial friction rub occurred less frequently (n = 6, 14%). In three cases only, all four diagnostic criteria were met. Eighteen patients showed three, and 23 only two diagnostic criteria. In addition, further clinical findings were noted: fever (n = 4, 9%), tachycardia (n = 8, 18%) and hypertension (n = 9, 20%).

In six patients a reduced ejection fraction of <55% and in seven diastolic dysfunction was detected. In addition, pleural effusions were found in 30% of cases (n = 13). Pleural effusions were more common in patients with PCIS; however ECG changes, chest pain and elevated CRP levels occurred more frequently in patients with idiopathic pericarditis. Twenty-six of the cases with idiopathic pericarditis and one patient with PCIS reported either influenza-like symptoms or infections 2–4 weeks prior to the hospitalisation. CRP levels >5 mg/l were present in 40 patients (91%). Troponin-T elevations >0.014 µg/l were detected in 23 cases (52%) (table 2). All patients with a troponin increase also had CRP elevations. Leukocytosis was present in 55% (n = 24) and lymphopenia in 30% (n = 13) of patients.

Table 1: Comorbidities.

<table>
<thead>
<tr>
<th>Comorbidity</th>
<th>Number of patients (n = 44)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiovascular risk factors</td>
<td>29 (66%)</td>
</tr>
<tr>
<td>Family history</td>
<td>10 (23%)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>14 (32%)</td>
</tr>
<tr>
<td>Dyslipidaemia</td>
<td>13 (30%)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>9 (21%)</td>
</tr>
<tr>
<td>Smoking</td>
<td>17 (39%)</td>
</tr>
<tr>
<td>Coronary heart disease</td>
<td>9 (21%)</td>
</tr>
<tr>
<td>Hypothyroidism</td>
<td>3 (7%)</td>
</tr>
<tr>
<td>Renal disease</td>
<td>7 (16%)</td>
</tr>
<tr>
<td>Pre-existing autoimmune disease</td>
<td>4 (9%)</td>
</tr>
<tr>
<td>History of cancer</td>
<td>5 (11%)</td>
</tr>
<tr>
<td>Influenza-like symptoms / infection</td>
<td>27 (61%)</td>
</tr>
<tr>
<td>Alcohol</td>
<td>13 (30%)</td>
</tr>
</tbody>
</table>

Figure 1: Age distribution in patients with pericarditis; p = 0.011 male to female in patients <45 years vs patients >45 years.
combined with colchicine (n = 33, 75%). Out of these patients, two were additionally treated with corticosteroids and another two with corticosteroids/mycophenolate. Furthermore, seven patients obtained solely anti-inflammatory and one patient solely corticosteroid therapy. Corticosteroids and colchicine were combined in three patients.

Outcomes
In 35 cases pericarditis was considered idiopathic (80%) and in 9 patients due to PCIS (20%). Of the 44 registered patients, 33 (75%) were enrolled due to a first pericarditis episode, whereas 11 cases (25%) were enrolled owing to a recurrence of pericarditis. Out of the 11 patients with recurrent pericarditis, 6 (14%, 3 enrolled after the first episode and 3 enrolled after a recurrence) experienced another recurrence on follow-up. Thirty-eight patients (86%, n = 30 with a first episode, n = 8 of those with a recurrence) remained healthy. There was no death, cardiac tamponade, constrictive pericarditis or a new cancer diagnosis on follow-up (table 3).

Discussion
Major findings
The present study provides real-world data on patients with pericarditis referred to a regional hospital in the greater Zurich area in Switzerland.

Table 2: Diagnostic criteria of pericarditis.

<table>
<thead>
<tr>
<th>Diagnostic criteria</th>
<th>Number of patients (n = 44)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chest pain</td>
<td>39 (89%)</td>
</tr>
<tr>
<td>ECG changes</td>
<td>36 (82%)</td>
</tr>
<tr>
<td>Pericardial friction rub</td>
<td>6 (14%)</td>
</tr>
<tr>
<td>Pericardial effusion</td>
<td>31 (71%)</td>
</tr>
<tr>
<td>CRP &gt;5 mg/l</td>
<td>40 (91%)</td>
</tr>
<tr>
<td>hsTroponin &gt;0.014 µg/l</td>
<td>23 (52%)</td>
</tr>
</tbody>
</table>

Table 3: Outcomes of pericarditis.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Number of patients (n = 44)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recurrences in all patients enrolled</td>
<td>6 (14%)</td>
</tr>
<tr>
<td>Recurrences in patients enrolled after a first episode</td>
<td>3 (9%)</td>
</tr>
<tr>
<td>Tamponade</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Constrictive pericarditis</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Cancer diagnosis on follow-up</td>
<td>0 (0%)</td>
</tr>
</tbody>
</table>

Gender differences
Pleural effusions were significantly more common in women (n = 9, 56%) than men (n = 4, 14%; p = 0.0058). Likewise, pericardial effusions were present in all female and in more than half of male patients (57%) (fig. 2). Smoking was the most common cardiovascular risk factor in men. On the other hand, hypertension, diabetes and dyslipidaemia were more frequently found in female patients. These differences, however, were not statistically relevant. Almost every man and nearly two thirds of the women showed typical ECG changes. Elevation of troponin I and T was more frequent in men than women, but not significant for the numbers of patients in our study (fig. 3). CRP levels were balanced in both genders and no other relevant differences in laboratory findings were evident.

Therapy
NSAIDs without aspirin were prescribed for 31 (70%) patients, aspirin was given to 5 (11%) and a combination of NSAIDs and aspirin to 4 patients (9%). NSAIDs were prescribed most frequently, followed by colchicine (n = 36, 82%), corticosteroids (n = 8, 18%) and mycophenolate (n = 2, 5%). Most patients received aspirin or NSAIDs combined with colchicine (n = 33, 75%). Out of these patients, two were additionally treated with corticosteroids and another two with corticosteroids/mycophenolate. Furthermore, seven patients obtained solely anti-inflammatory and one patient solely corticosteroid therapy. Corticosteroids and colchicine were combined in three patients.

Outcomes
In 35 cases pericarditis was considered idiopathic (80%) and in 9 patients due to PCIS (20%). Of the 44 registered patients, 33 (75%) were enrolled due to a first pericarditis episode, whereas 11 cases (25%) were enrolled owing to a recurrence of pericarditis. Out of the 11 patients with recurrent pericarditis, 6 (14%, 3 enrolled after the first episode and 3 enrolled after a recurrence) experienced another recurrence on follow-up. Thirty-eight patients (86%, n = 30 with a first episode, n = 8 of those with a recurrence) remained healthy. There was no death, cardiac tamponade, constrictive pericarditis or a new cancer diagnosis on follow-up (table 3).

Discussion
Major findings
The present study provides real-world data on patients with pericarditis referred to a regional hospital in the greater Zurich area in Switzerland.
The study population, 33 cases with a first episode and 11 cases with a recurrence of pericarditis, included patients from adolescence to elderly (mean age 44.45 years).

Men, who made up 64% of the study population, were more often affected by pericarditis than women. This is in line with data from previous studies [6, 8]. Our observation that male predominance was much more pronounced in patients younger than 45 years has not been described before. Nevertheless, these data are hypothesis-generating only because of the small numbers of patients in our study. It would be interesting to replicate these findings from larger databases in Switzerland or to analyse the gender difference in data registries of already published cohorts.

The present study showed that idiopathic pericarditis is the most common aetiology of pericardial inflammation in Switzerland [1, 2, 7]. Idiopathic pericarditis is most commonly presumed to be viral [14]. Viral infections are supposed to trigger immune-mediated inflammation [6, 14]. In the present study this hypothesis was supported by the fact that nearly two thirds of the study cohort reported either influenza-like symptoms or infections prior to the hospitalisation.

PCIS after a previous cardiac interventional procedure or cardiac surgery accounted for a remarkable number of cases in the present study. Nevertheless, given the high numbers of post-cardiac surgery patients entering our hospital, we would have expected much more cases of PCIS. The exact incidence rates of PCIS, however, have not been established yet [4]. Nevertheless, an incidence between 10 and 40% for post-pericardiectomy patients has been reported in the literature [4]. We believe that many post-pericardiectomy patients were missed because they were discharged before PCIS onset and PCIS was only mild in most of them.

Myocardial inflammation is common in patients with pericarditis and was observed in half of our patients [3]. Moreover, we found high rates of pleural effusions. The high rate of pleural effusion, although only nine patients presented as PCIS, was conspicuous and probably reflected our institutional policy to perform ultrasound evaluation of the pleural space routinely together with echocardiography. Troponin elevation, and pericardial and pleural effusions were frequent, but particularly obvious in women. Gender-dependent differences in troponin elevation, pericardial and pleural effusions had also not been described before. Compared with the literature, chest pain (89%) and pericardial friction rub (84%) were equally frequent, but ECG changes (82%) and pericardial effusions (71%) were more frequent in our cohort [5]. Almost all of our patients (91%) showed increased CRP levels, which is higher than the 78% in a recent study [15]. Normal CRP values on admission can result from previous anti-inflammatory treatment or, more likely, early referral [15].

Overall, 75% of patients were treated according to the 2015 ESC guidelines with aspirin or NSAIDs combined with colchicine. Reasons for non-administration of colchicine were sparse data on the effect of colchicine in children and adolescents, and renal dysfunction in some patients. Nevertheless, our hospital reached high guideline adherence.

Our data showed that 86% of all included patients with an acute or a first recurrent pericarditis episode completely recovered without further recurrences. However, 14% of the total study population, 9% of patients enrolled after the first episode and 27% of patients enrolled after a recurrence of pericarditis, suffered from at least one further episode of recurrence within the follow-up period. Previous studies indicated a recurrence rate of up to 15–30% after a first episode of pericarditis and up to 50% if a first recurrence were treated without colchicine [8, 12]. The COPE trial showed a recurrence rate of 10.7%, which is comparable to the recurrence rate of 9% in our study [12]. Our low recurrence rate and therefore the good prognosis of patients with pericarditis is most likely due to application of colchicine, as well as an adequate guideline.

**Limitations and expansion capability**

Data were obtained from a single hospital centre on 44 patients only. These low numbers affect the power of the statistical analyses. Moreover, the retrospective study design and the fact that diagnosis was made by different physicians, who were not in the study team, might imply potential biases.

**Conclusions**

Pericarditis, which is a relevant differential diagnosis of acute chest pain, mainly affects men younger than 45 years. At an age above 45, the disease occurrence is balanced between both sexes. Owing to an adequate guideline and consequent application of colchicine, the recurrence rate is low and outcome is favourable.

**Disclosure statement**

No financial support and no other potential conflict of interest relevant to this article was reported.

**References**

The full list of references is included in the online version of the article at www.cardiovascmed.ch
Publication rate and impact factor of abstracts presented at SSC congresses 2011 to 2014

Benedikt Altermatt, Beat Schaer
Department of Cardiology, University Hospital Basel, Switzerland

Summary

BACKGROUND: The annual congress of the Swiss Societies of Cardiology and Cardiac Surgery is the most important national platform for Swiss researchers in these specialities. Every year there are a high number of oral presentations and posters. However, more important is their publication in international journals. We determined publication rates, impact factors (IFs) and their temporal trends in seven cardiological domains.

METHODS: The abstract booklets of the congresses 2011–2014 were downloaded and all talks and posters presented during the meeting extracted. In PubMed we assessed whether each of these papers was published, the journal and its IF in the respective publication year. We excluded case reports, papers published >6 months before the congress and abstracts presenting national data from multicentre studies (unless the first/last author of the paper was from Switzerland). The percentage of published papers and their mean/median IF were calculated overall and per year separately for each domain. We also compared major Swiss hospitals regarding their individual publication rates.

RESULTS: A total of 715 abstracts were included, of which 52% were published as of February 2017. The lowest average publication rate in a domain was 36% and the highest 69%, with mean IFs between 2.5 and 7.8. The lowest average publication rate in one of the major hospitals was 16% and the highest 70%.

CONCLUSIONS: Abstracts presented during the congresses had a high chance of being published, usually in papers with a good IF. This reflects the good quality of research in cardiology in Switzerland.

Key words: abstracts; publication; impact factor; Swiss Society of Cardiology
searched for via PubMed and if they had been published, we documented the journal and the publication year. All studies that were not found in the first round were searched for again in spring 2016 and finally in February 2017; if they had been published, they were added as described above. The abstracts were initially screened for with the submitted title, then if untraceable with relevant keywords and in a third attempt with the first and/or last author name. The IF of the year in which each paper was published was recorded. As the IFs of 2016 were not released at the time of final analysis, the IF of the previous year was used, but this concerned only isolated papers. The impact factors of the journals were taken from the website http://admin-apps.webofknowledge.com. If they were not available there, they were searched for on the journal homepage. Journals for which the IF could not be determined were rated with an IF of 0.

Excluded were seven papers published more than 6 months before the corresponding SSC congress (we doubt that it was correct to submit them as abstracts to the SSC congress, according to congress rules), case reports, and all abstracts presenting national data from a multicentre study (unless the first, last or corresponding author of the published paper was from a Swiss hospital). Published and unpublished studies were then assigned to the corresponding hospital, according to the abstract booklet and the first, last or corresponding author of the paper. In some cases when more than one hospital was involved in the publication, the hospital of the last or corresponding author was chosen. For interhospital comparison we present separate data for the seven hospitals with the most successfully submitted abstracts. The remaining hospitals that submitted at least one abstract are also shown, but results have to be interpreted with caution because of mostly very small numbers of accepted abstracts. For calculation of the delay between presentation at the congress and publication, we allowed for a certain simplification. It would not be possible to determine the exact date of publication and so we set it to December of the year of publication.

Statistics
We used the statistic program acula statistics calculator to determine means, medians and interquartile ranges in the different categories. A Cox regression analysis was performed to investigate whether there was a higher likelihood of publication of abstracts presented in earlier congresses. The temporal trend of the publication rates was calculated with the two-sided Cochran-Armitage Trend Test and the use of SAS Version 9.4 (SAS Institute, Cary, NC). Regardless of distribution (normal or skewed), we always present mean and median values with either the standard deviation (SD) and 95% confidence interval or the IQR (interquartile range), as to avoid confusion among the many tables and congress years that are shown.

Results
A total of 900 abstracts were accepted in the years 2011 to 2014. Of those, 185 were excluded in accordance with the criteria described in the methods section. Of the remaining studies, 369 (51.6%) had been published as of February 2017 (see fig. 1). Most abstracts were submitted in the domains of “cardiac surgery” and “CAD” with 124 and 123 abstracts, respectively, the lowest number (76 abstracts) in “epidemiology”. The highest publication rates were seen in “heart failure” (70%) and in “biology” (65%), with the lowest in surgery (36%). The highest mean IF was recorded in “biology” at 7.8 and “heart failure” at 6.2, with the lowest in “cardiac surgery” at 2.5. The highest median IF was recorded in “biology” at 5.9 and “heart failure” at 4.2, with the lowest in “cardiac surgery” at 1.3. Looking at temporal trends, we generally noticed a slight decrease in publication rates from 54% in 2011 to 47% in 2014 and stable median IFs. In the different domains, “biology” showed a slight increase in publication rate with rather stable IFs. “Devices” exhibited a stable publication rate and increasing IFs. “Heart failure” had a stable publication rate and a decline in IFs. Of note is the exceptional high mean IF in 2012 due to one NEJM, one Circulation, and three European Heart Journal papers. “CAD” had a decrease in publication rates, but IFs remained stable. “Epidemiology” and “imaging” had undulating publication rates and stable IFs, and finally “cardiac surgery” an increase in publication rates and stable IFs. The domains “heart failure”, “CAD”, and “imaging” showed a borderline decrease in numbers of accepted papers (p-values for trend 0.06, 0.08 and 0.08, respectively). More details

Figure 1: Number of abstracts submitted included and published.
are shown in the tables 1–7. Table 8 shows the percentage of accepted posters and oral presentations. Table 9 depicts publication rates of the different hospital groups. The mean delay between the congress and publication date was 20 months for the 2011 congress, 23 for the 2012 congress, 21 months for the 2013 congress, and 17 months for the 2014 congress. Cox regression showed no higher likelihood of publication of abstracts presented at earlier congresses (p-value 0.983).

**Discussion**

The main finding of our analysis was the overall high quality of cardiology research in Switzerland, based on a high publication rate with good IFs of abstracts accepted for the congresses. There are, however, differences with regard to the domain of research and the performance of the individual hospitals. Results might encourage researchers in domains and/or hospitals with poorer results to further strengthen their efforts to get their work accepted in high ranking journals.

To the best of our knowledge, such a study has never been undertaken in Switzerland before; at least none has been published. The policy on accepting abstracts for national congresses in nearby countries such as Germany or France might be completely different and cannot be compared. Our results simply reflect the situation in Switzerland and should be seen as this.

On a European level, abstracts presented to the ESC congress 2006 have been evaluated regarding publication, IF and citation index [1]. A random selection of 10% of all abstracts submitted (n = 1002) was assessed 4.5 years after the congress. In that year, the acceptance rate was 38%, 18% accepted as oral presentations. Factors favouring acceptance were a prospective design and a higher number of patients in the study. Our study was not able to investigate these aspects, as we have no data on rejected abstracts of the congresses. Regarding full-text publication, only 38% of all accepted studies (with no difference between posters and oral presentations) were finally also published, as opposed to 52% in our study. This positive finding could be due to the fact that Swiss researches have more zeal “to take the last mile” compared with their colleagues submitting to the ESC congress, even though the ESC congress is by far larger and more renowned. At ESC level, there was only a small difference among the domains (range 24–31%) as opposed to our study (range 31–65%). Factors that favoured publication at ESC level were the academic setting of the place of research and basic research. This can also be seen in Switzerland where “biology” had the second-highest publication rate and the highest mean and median IF, and the publication rate of university hospitals exceeded that of other hospitals.
### Table 5: Results in the domain of epidemiology, risk factors, rehabilitation, and thromboembolic disease.

<table>
<thead>
<tr>
<th>Year</th>
<th>Submitted</th>
<th>Excluded</th>
<th>Published (%)</th>
<th>Mean IF</th>
<th>SD</th>
<th>95% CI</th>
<th>Median IF</th>
<th>IQR</th>
</tr>
</thead>
<tbody>
<tr>
<td>2011</td>
<td>24</td>
<td>3</td>
<td>9 (43)</td>
<td>4.7</td>
<td>3.4</td>
<td>2.1–7.4</td>
<td>3.8</td>
<td>5.4</td>
</tr>
<tr>
<td>2012</td>
<td>17</td>
<td>3</td>
<td>9 (64)</td>
<td>4.7</td>
<td>4.5</td>
<td>1.2–8.1</td>
<td>4.9</td>
<td>(1.9–7.3)</td>
</tr>
<tr>
<td>2013</td>
<td>16</td>
<td>8</td>
<td>5 (63)</td>
<td>3.3</td>
<td>1.0</td>
<td>2.0–4.5</td>
<td>2.9</td>
<td>(1.5–6.3)</td>
</tr>
<tr>
<td>2014</td>
<td>19</td>
<td>1</td>
<td>8 (44)</td>
<td>3.9</td>
<td>1.5</td>
<td>2.6–5.1</td>
<td>3.9</td>
<td>(2.4–4.3)</td>
</tr>
<tr>
<td>Overall</td>
<td>76</td>
<td>15</td>
<td>31 (51)</td>
<td>4.2</td>
<td>3.1</td>
<td>3.1–5.4</td>
<td>3.8</td>
<td>(2.2–6.2)</td>
</tr>
</tbody>
</table>

### Table 6: Results in the domain of cardiac imaging, and congenital and paediatric cardiology.

<table>
<thead>
<tr>
<th>Year</th>
<th>Submitted</th>
<th>Excluded</th>
<th>Published (%)</th>
<th>Mean IF</th>
<th>SD</th>
<th>95% CI</th>
<th>Median IF</th>
<th>IQR</th>
</tr>
</thead>
<tbody>
<tr>
<td>2011</td>
<td>35</td>
<td>2</td>
<td>19 (58)</td>
<td>4.3</td>
<td>2.2</td>
<td>3.2–5.4</td>
<td>4.3</td>
<td>2.7</td>
</tr>
<tr>
<td>2012</td>
<td>32</td>
<td>3</td>
<td>13 (45)</td>
<td>3.2</td>
<td>1.8</td>
<td>2.1–4.2</td>
<td>3.9</td>
<td>(3.3–5.9)</td>
</tr>
<tr>
<td>2013</td>
<td>25</td>
<td>3</td>
<td>10 (46)</td>
<td>4.5</td>
<td>2.3</td>
<td>2.8–6.1</td>
<td>4.4</td>
<td>(1.3–4.6)</td>
</tr>
<tr>
<td>2014</td>
<td>15</td>
<td>1</td>
<td>4 (27)</td>
<td>4.0</td>
<td>1.0</td>
<td>1.0–9.0</td>
<td>4.4</td>
<td>(2.8–5.6)</td>
</tr>
<tr>
<td>Overall</td>
<td>107</td>
<td>9</td>
<td>47 (45)</td>
<td>4.4</td>
<td>2.2</td>
<td>3.3–4.6</td>
<td>4.1</td>
<td>(0.8–6.8)</td>
</tr>
</tbody>
</table>

### Table 7: Results in the domain of cardiac surgery.

<table>
<thead>
<tr>
<th>Year</th>
<th>Submitted</th>
<th>Excluded</th>
<th>Published (%)</th>
<th>Mean IF</th>
<th>SD</th>
<th>95% CI</th>
<th>Median IF</th>
<th>IQR</th>
</tr>
</thead>
<tbody>
<tr>
<td>2011</td>
<td>35</td>
<td>2</td>
<td>12 (36)</td>
<td>3.9</td>
<td>5.2</td>
<td>0.6–7.2</td>
<td>2.8</td>
<td>3.5</td>
</tr>
<tr>
<td>2012</td>
<td>30</td>
<td>1</td>
<td>8 (28)</td>
<td>2.3</td>
<td>2.0</td>
<td>0.7–4.0</td>
<td>1.1</td>
<td>(0–3.5)</td>
</tr>
<tr>
<td>2013</td>
<td>28</td>
<td>1</td>
<td>11 (41)</td>
<td>1.7</td>
<td>1.3</td>
<td>0.8–2.5</td>
<td>1.1</td>
<td>(1–3.8)</td>
</tr>
<tr>
<td>2014</td>
<td>31</td>
<td>1</td>
<td>12 (40)</td>
<td>2.1</td>
<td>1.3</td>
<td>1.2–2.9</td>
<td>2.4</td>
<td>(2.2–5.6)</td>
</tr>
<tr>
<td>Overall</td>
<td>124</td>
<td>5</td>
<td>43 (36)</td>
<td>2.5</td>
<td>3.1</td>
<td>1.6–3.5</td>
<td>1.3</td>
<td>(0.8–6.8)</td>
</tr>
</tbody>
</table>

### Table 8: Published posters and oral presentations in the different domains (years 2011 to 2014 together).

<table>
<thead>
<tr>
<th>Domain</th>
<th>Posters</th>
<th>Oral presentations</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiovascular biology</td>
<td>31/46 (67%)</td>
<td>22/35 (63%)</td>
<td>0.81</td>
</tr>
<tr>
<td>Pacemaker/defibrillator and electrophysiology</td>
<td>23/58 (40%)</td>
<td>23/58 (40%)</td>
<td>0.01</td>
</tr>
<tr>
<td>Cardiac failure, cardiomyopathy, transplant</td>
<td>22/41 (54%)</td>
<td>33/38 (87%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>38/69 (55%)</td>
<td>27/48 (56%)</td>
<td>1</td>
</tr>
<tr>
<td>Epidemiology, risk factors</td>
<td>20/40 (50%)</td>
<td>11/21 (52%)</td>
<td>1</td>
</tr>
<tr>
<td>Cardiac imaging, congenital and paediatric cardiology</td>
<td>23/57 (40%)</td>
<td>23/41 (56%)</td>
<td>0.15</td>
</tr>
<tr>
<td>Cardiac surgery</td>
<td>27/80 (34%)</td>
<td>16/39 (41%)</td>
<td>0.54</td>
</tr>
<tr>
<td>Overall</td>
<td>184/391 (47%)</td>
<td>159/263 (61%)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
Table 9: Results of the seven hospitals with the most successfully submitted abstracts, followed by "all others".

<table>
<thead>
<tr>
<th>Hospital</th>
<th>Included</th>
<th>Published</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>University Hospital Geneva</td>
<td>64</td>
<td>45</td>
<td>70</td>
</tr>
<tr>
<td>University Hospital Basel</td>
<td>97</td>
<td>63</td>
<td>65</td>
</tr>
<tr>
<td>University Hospital Zurich</td>
<td>119</td>
<td>68</td>
<td>57</td>
</tr>
<tr>
<td>University Hospital Berne</td>
<td>156</td>
<td>84</td>
<td>54</td>
</tr>
<tr>
<td>Cardiocentro Lugano</td>
<td>32</td>
<td>12</td>
<td>38</td>
</tr>
<tr>
<td>University Hospital Lausanne</td>
<td>60</td>
<td>22</td>
<td>37</td>
</tr>
<tr>
<td>Stadtspital Triemli Zurich</td>
<td>32</td>
<td>5</td>
<td>16</td>
</tr>
<tr>
<td>Hôpital de Morges</td>
<td>2</td>
<td>2</td>
<td>100</td>
</tr>
<tr>
<td>Hôpital de la Tour</td>
<td>4</td>
<td>3</td>
<td>75</td>
</tr>
<tr>
<td>Kantonsspital St. Gallen</td>
<td>17</td>
<td>11</td>
<td>65</td>
</tr>
<tr>
<td>Kantonsspital Luzern</td>
<td>13</td>
<td>8</td>
<td>62</td>
</tr>
<tr>
<td>Hôpital Fribourgeois</td>
<td>17</td>
<td>8</td>
<td>47</td>
</tr>
<tr>
<td>Children Hospital Zurich</td>
<td>16</td>
<td>7</td>
<td>44</td>
</tr>
<tr>
<td>Kantonsspital Olten</td>
<td>3</td>
<td>1</td>
<td>33</td>
</tr>
<tr>
<td>Ospedale Regionale di Bellinzona e Valli</td>
<td>9</td>
<td>3</td>
<td>33</td>
</tr>
<tr>
<td>Children Hospital Geneva</td>
<td>2</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Hôpital du Jura, Delémont</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Kantonsspital Aarau</td>
<td>2</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Kantonsspital Chur</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Overall</td>
<td>87</td>
<td>43</td>
<td>49</td>
</tr>
</tbody>
</table>

An analysis of the different years did not show a lower overall publication rate in the year 2014, which could be expected because of the shorter time frame in which the abstract could have been published. Generally, the vast majority of abstracts are published in the year of the congress, or within the following two years. As shown with the domain of “heart failure” in the year 2012, a few very high-ranked papers can heighten the mean IF of a specific year, so the median value must also be considered.

Limitations
We are aware that results regarding IFs strongly depend on the IFs of the journals in a specific domain. This mainly applies to research work that is not at such an extremely high level as to be submitted to a top journal. However, overall publication rates are not affected by this limitation. Our last PubMed access was February 2017 and some papers may still be published after that date. This, however, applies to all domains. Papers in journals without an IF and/or that are not PubMed listed (e.g., this very journal) were excluded but may still have their merits. However, in the huge field of often dubious online journals it is very difficult to separate the wheat from the chaff. As we were not able to identify abstracts that were rejected, we could not analyse them regarding possible publication. Finally, the period of 4 years provides only a momentary snapshot, and results might be different in other time frames or longer observation periods.

Acknowledgement
The authors thank Kris Denhaeryst for his help to calculate the temporal trends and Mrs Rehana Huber, MD, for language editing.

Disclosure statement
No financial support and no other potential conflict of interest relevant to this article was reported.

Reference
Right atrial appendage thrombus and pulmonary embolism due to the insufficient anticoagulation

Double trouble – a case of atrial fibrillation and pulmonary embolism

Valerian Valiton, Nicolas Brugger, Denis Graf, Stéphane Cook, Diego Arroyo

* Department of Cardiology, University and Hospital Fribourg, Switzerland; b Department of Cardiology, Bern University Hospital, Switzerland

Case report

A 71-year-old male with permanent atrial fibrillation and recently diagnosed stage IIA colorectal adenocarcinoma was admitted to the hospital electively for colorectal surgery. His usual treatment included acenocoumarol, verapamil, and oxazepam. There were no symptoms related to atrial fibrillation (European Heart Rhythm Association score I), the ventricular rate was well controlled with verapamil, and the patient had never undergone cardioversion nor catheter ablation. He was scheduled for subtotal colectomy with ileo-colostomy. The anticoagulation regimen was switched to therapeutic enoxaparin 60 mg subcutaneously twice daily during the perioperative period. The immediate postoperative period was uneventful but the patient developed *Proteus vulgaris* abdominal sepsis on day 13. An exploratory laparotomy showed peritonitis without any perforation or anastomotic leak. He fully recovered with extensive peritoneal lavage and a course of intravenous antibiotic therapy. During the abdominal sepsis workup, a thoracic and abdominal computed tomography angiography was performed, which showed an incidental hypodense lesion of 17×30 mm attached to the upper lateral portion of the right atrium, as well as a right segmental posterior and lateral basal pulmonary embolism (fig. 1). The patient was asymptomatic from the pulmonary embolism.

**Figure 1:** Thoracic computed tomography with contrast; (A) white arrow point to right segmental pulmonary embolus; (B) white arrow points at thrombus in the right atrium.

Summary

Atrial fibrillation is a cause of left atrial thrombus leading to cardioembolic stroke, which can be effectively prevented with oral anticoagulation. Right atrial appendage thrombus is a rare complication of atrial fibrillation that can also lead to cardioembolic pulmonary embolism. We present the case of a 71-year-old male with atrial fibrillation, thrombus in the right atrial appendage and pulmonary embolism.

Key words: right atrial appendage; thrombus; atrial fibrillation; pulmonary embolism
During the perioperative period, the patient was insufficiently anticoagulated with enoxaparin 60 mg subcutaneously twice daily, with an anti-Xa activity between 0.18 and 0.22 UAXA/ml (target: 0.5–1.0 UAXA/ml). The workup was completed with transthoracic echocardiography, which revealed a moderately dilated, hypertrophic left ventricle with preserved systolic function, bi-atrial dilatation, moderate mitral regurgitation and an nonspecific thickening of the right atrium (fig. 2). Transoesophageal echocardiography (TEE) with 3D reconstruction confirmed a right atrial appendage mass which was suspected to be a thrombus (figs 3A and 4A). The left atrium and left atrial appendage were thrombus free. The enoxaparin dose was increased to 80 mg subcutaneously twice daily as the previous dose was below the effective therapeutic range. The suspected thrombus and pulmonary embolism were considered to be due to the insufficiently anticoagulated atrial fibrillation, and decision was made to resume acenocoumarol with

Figure 2: Transthoracic echocardiography parasternal short-axis view: white arrow point to thrombus in the right atrium.

Figure 3: 2-Dimension transoesophageal echocardiography, mid-oesophageal 40° view; (A) white arrow points at thrombus at time of presentation; (B) 3 months later after anticoagulation.

Figure 4: 3-Dimensional transoesophageal echocardiography; (A) white arrow points at thrombus in right atrial appendage; (B) 3 months later after anticoagulation.
target INRs of 2–3. The right atrial appendage mass had disappeared at 3-month follow-up (figs 3B and 4B).

Discussion

Whereas the pathophysiology of left atrial appendage thrombus and its role in cardioembolic strokes is well defined and studied, data on right atrial appendage thrombus are scarce [1]. This could be explained, in part, by the less severe consequences of a small thrombus in the lung circulation compared to that of a cardioembolic stroke. The prevalence of right atrial appendage thrombus in atrial fibrillation patients varies in the literature from 0.7 to 5.8% [2–4]. In a large study, Cresti et al. showed that among 805 patients with atrial fibrillation or flutter who underwent TEE-guided cardioversion, the incidence of right atrial thrombus was 0.75% (6 of 805 patients) compared with 10.3% (83 of 805 patients) for the left atrial appendage [4].

In atrial fibrillation patients, the right and left atrial appendages are larger and the emptying velocities lower compared with those in sinus rhythm [2]. The morphology and the inner structure of the right atrium seem to be less favourable for thrombus formation because of a better blood flow compared with the left atrium [5]. The smaller amount of pectinate muscle in the right atrium and its dendritic structure may contribute to a decreased blood stagnation compared with the left atrium.

The location, risk-factors and the fact that the right atrial appendage mass disappeared under effective anticoagulation, point towards right atrial appendage thrombus rather than any other cause. Several different factors, such as cancer, the perioperative period and the subtherapeutic anticoagulation, in addition to atrial fibrillation may have contributed to right atrial appendage thrombus formation and pulmonary embolism.

The relationship between pulmonary embolism and atrial fibrillation is complex and bi-causal. The increased right ventricular afterload seen in some pulmonary embolism patients could trigger atrial fibrillation. On the other hand, as was more likely the case here, atrial fibrillation can lead to right atrial appendage thrombus formation and pulmonary embolism. Some patient characteristics are simply shared factors such as advanced age, heart failure, obesity and inflammatory states [6]. Free-floating large right atrial thrombi generally have a poor prognosis, with reported mortalities of up to 17% [7]. Depending on patient characteristics and specific contraindications, treatment options include thrombolysis, and surgical or percutaneous mechanical embolectomy.

This case highlights the possibility of right atrial appendage thrombus in atrial fibrillation and its implication in cardioembolic pulmonary embolism. The right atrial appendage should be screened for thrombus, particularly if TEE is performed in the workup of a patient with a suspected cardioembolic event or for any reason in a patient with atrial fibrillation.

Disclosure statement
No financial support and no other potential conflict of interest relevant to this article was reported.

References
Research Prize of the Swiss Heart Foundation 2018

The Swiss Heart Foundation awards an annual prize of Swiss Francs 20,000 for one or several outstanding publications / accepted manuscripts on scientific research in the field of prevention, diagnosis and/or treatment of cardiovascular diseases. Swiss researchers or research teams working in Switzerland or abroad and foreign researchers working in Switzerland are entitled to participate. The age limit is 45 years at the time of application. Previous prize winners are not eligible for the prize. In addition, scientific publications that have already been awarded or elected for another prize are not eligible. The prize winner will be chosen by the Research Committee of the Swiss Heart Foundation.

Applications should be submitted by 31 December 2017 (date of postmark) by post (one copy) as well as by email with:
- one signed accompanying letter
- the publication(s) / accepted manuscript(s) to be considered
- list of references
- brief curriculum vitae (max. 1 page)

For further information and detailed rules, see www.swissheart.ch/forschungspreis

Correspondence:
Swiss Heart Foundation
Research Committee
Dufourstrasse 30
P.O.Box 368
CH-3000 Bern 14
E-Mail: research[at]swissheart.ch