Current trends in dual antiplatelet therapy: a 2017 update

Rapidly changing world of cardiac surgery

The Annual Scientific Congress of the Swiss Society of Cardiology in Baden, Switzerland, June 7–9, 2017

Atrial standstill

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Current trends in dual antiplatelet therapy: a 2017 update

Luigi Biasco, Giulia Montrasio, Marco Moccetti, Giovanni Pedrazzini
Fondazione Cardiocentro Ticino, Division of Cardiology, Lugano, Switzerland

Introduction
Platelet inhibition represents the cornerstone of cardiovascular therapy, owing to the central role of platelets in the genesis of acute ischaemic events. Dual antiplatelet therapy (DAPT) addresses two main pathways of platelet activation: inhibition of cyclo-oxygenase-mediated thromboxane A2 formation by aspirin; and inhibition of the ADP-activated surface receptor P2Y12 by means of a family of drugs including cangrelor, clopidogrel, prasugrel, ticagrelor and ticlopidine (fig. 1).

Historical background
The hypothesis of an auxiliary effect of clopidogrel on top of aspirin in reducing cardiovascular ischaemic events rose from the well-established knowledge that platelet adhesion and activation occur through many different molecular mechanisms [4, 5]. After the introduction of bare metal stents (BMSs) in the early 1990s, aspirin was combined with an additional anti-thrombotic drug, initially ticlopidine, later clopidogrel, to prevent stent thrombosis during the first 4 weeks after stent implantation [6].

The first data in the BMS era, showing a clinical advantage of extended (>1 month) combination therapy with clopidogrel and aspirin in non ST-segment elevation ACS, came in 2001 from the CURE trial (Clopidogrel in Unstable Angina to prevent Recurrent Events), where the prolonged combined treatment led to an absolute reduction of 2.1% in risk for the composite endpoint, with a benefit maintained over time, particularly in the subgroup of patients undergoing percutaneous revascularisation [7, 8]. A similar trend was observed in 2003 in the CREDO trial, which showed an absolute 3% and a relative 27% risk reduction in the cumulative...
Available drugs

A summary of currently used P2Y₁₂ inhibitors is available in table 1.

Clopidogrel

Clopidogrel (300–600 mg loading dose and 75 mg/day maintenance dose) is an oral thienopyridine derivative. Its active metabolite blocks platelet P2Y₁₂ receptors irreversibly, thereby preventing the binding of adenosine diphosphate (ADP) and thus counteracting ADP-dependent activation of GpIIb-IIIa, the major platelet receptor for fibrinogen. As an inactive prodrug, clopidogrel requires a two-step oxidation by the hepatic cytochrome P450 system (specifically by CYP2C19) to generate an active metabolite. This two-step conversion results in a slower onset of action than those of prasugrel and ticagrelor. Furthermore, substantial interindividual variability in the antiplatelet response to this drug has been documented: several different alleles of CYP2C19 have been related to reduced or increased enzymatic activity of the cytochrome and variable clinical efficacy of clopidogrel.

Prasugrel

Prasugrel (60 mg loading dose and 10 mg/day maintenance dose) is an orally inactive prodrug, also derived from thienopyridine, which irreversibly binds and thus inhibits P2Y₁₂ receptors on platelets. Prasugrel requires conversion to an active metabolite through a one-step cytochrome P450-dependant reaction, ensuring a faster onset of action and a more predictable clinical effect than with clopidogrel. According to the TRITON-TIMI 38 post-hoc analysis data, prasugrel is contraindicated in patients with prior stroke (or transient ischaemic attack), or in patients older than 75

Table 1: Details of available P2Y₁₂ inhibitors.

<table>
<thead>
<tr>
<th>Drug class — antiplatelet mechanism</th>
<th>Oral administration</th>
<th>Intravenous administration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thienopyridine P2Y₁₂ inhibitor</td>
<td>Clopidogrel</td>
<td>Prasugrel</td>
</tr>
<tr>
<td>Thienopyridine P2Y₁₂ inhibitor</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thienopyridine P2Y₁₂ inhibitor</td>
<td></td>
<td>Cangrelor ATP analogue</td>
</tr>
<tr>
<td>Loading/maintenance dose</td>
<td>300–600 mg / 75 mg once daily 60 mg / 10 mg once daily</td>
<td>180 mg / 90 mg twice daily</td>
</tr>
<tr>
<td>Reversibility</td>
<td>Irreversible</td>
<td>Reversible</td>
</tr>
<tr>
<td>Bio-activation</td>
<td>prodrug, variable cytochrome P450 metabolism</td>
<td>prodrug, predictable cytochrome P450 metabolism</td>
</tr>
<tr>
<td>Onset of action</td>
<td>2–6 hours</td>
<td>30 min.</td>
</tr>
<tr>
<td>Duration of action</td>
<td>3–10 days</td>
<td>7–10 days</td>
</tr>
<tr>
<td>Withdrawal before surgery</td>
<td>5 days</td>
<td>7 days</td>
</tr>
<tr>
<td>Cost</td>
<td>740 CHF/year</td>
<td>1135 CHF/year</td>
</tr>
</tbody>
</table>
years or with low body weight (<60 kg) [2, 3, 14]. The role of a reduced 5-mg dose of prasugrel in these subsets of patients is currently under investigation.

**Ticagrelor**

Ticagrelor (180 mg loading dose and 90 mg twice a day maintenance dose) is an oral P2Y\(_{12}\) receptor antagonist belonging to the chemical class of cyclopenyltriazolopyrimidines [16]. It acts through a double antiplatelet mechanism, inhibiting both P2Y\(_{12}\) receptors and adenosine reuptake via the equilibrative nucleoside transporter 1 (ENT1). Unlike clopidogrel and prasugrel, ticagrelor binds reversibly to the P2Y\(_{12}\) receptor, leading to a faster offset of action with more rapid recovery of platelet function (5 days). Furthermore, ticagrelor is an orally active drug requiring no metabolic activation, which provides a much faster onset of action and more reliable inhibition than clopidogrel. Adverse effects, potentially linked to its inhibition of ENT1, include dose-related episodes of dyspnoea and bradycardia. To date, the only head-to-head comparison data between ticagrelor and prasugrel come from the recent, but greatly underpowered, Prague 18 trial, which did not show any difference between the two potent anti-thrombotic drugs in term of predefined endpoints at 7 and 30 days in 1250 “real world” patients with ST-segment elevation myocardial infarction (STEMI) treated with primary PCI [17].

**Cangrelor**

Cangrelor (30 mg/kg bolus and 4 mg/kg/min infusion) is an intravenous adenosine triphosphate analogue that binds directly and reversibly to the P2Y\(_{12}\) receptor, without requiring metabolic activation. It produces reversible and highly effective platelet inhibition, with an almost immediate onset after administration of the intravenous bolus. It has a short plasma half-life (3–6 min), thus allowing restoration of platelet function within 1–2 hours after infusion discontinuation. The CHAMPION-PHoenix trial, comparing cangrelor with clopidogrel in an all-comers population with stable coronary heart disease and acute coronary syndromes [18], failed to demonstrate any convincing and cost-effective advantages of the parenteral drug. Thus, current use of cangrelor is limited to a bridge to surgery in patients with a high bleeding risk, or as an alternative for preloading in ACS patients experiencing nausea and vomiting or reduced oral drug absorption due to impaired peripheral perfusion.

**Current role of dual antiplatelet therapy**

In the following section we will focus on open issues about DAPT: the role of preloading in acute coronary syndromes, the optimal length of treatment after PCI in stable coronary artery disease and ACS, and the role of extended DAPT after 12 months in selected patients.

**Preloading in acute coronary syndromes**

The rationale for P2Y\(_{12}\) receptor blocker administration before PCI in ACS arises from the observation that the risk of early thrombotic complications, such as re-infarction or acute stent thrombosis, is directly related to the level of platelet reactivity (fig. 3).

Several issues have to be addressed when considering preloading. First, the drug should be administered in a timely manner, early enough to allow complete inhibition at the time of PCI. Secondly, the delay between drug administration and its pharmacological action is related not only to the pharmacokinetics of the molecule, but also to some patient-specific clinical conditions (e.g., STEMI vs NSTEMI, low cardiac output syndromes, etc.) that may further delay absorption. Thirdly, the addition of a second antiplatelet agent on top of aspirin obviously increases the haemorrhagic risk, particularly in the subgroup of patients (5–10%) who might benefit from accelerated surgical revascularisation.

Given these premises, preloading with a P2Y\(_{12}\) inhibitor has been considered arationally appealing approach,
particularly in an era where clopidogrel, with its slow onset of action, was the first and the only available P2Y₁₂ inhibitor.

**ST-segment elevation ACS**

ST-segment elevation myocardial infarction (STEMI) is characterised by strong platelet hyper-reactivity and the need to achieve vessel reperfusion within 90 minutes from symptom onset, clearly requiring fast and adequate platelet inhibition. In this context, the synergistic action of heparin, aspirin and ADP receptor antagonists aims to reduce thrombotic activity at the site of plaque rupture and to minimise the thrombogenic impact of the percutaneous intervention.

The indications in guidelines have changed considerably over time, because of the introduction of newer drugs and of contrasting evidence on pretreatment in STEMI patients. Initial experience and, consequently, guidelines were strongly in favour of preloading [19, 20], but newer data challenged this concept [21, 22].

In particular, the recent ATLANTIC trial, the only available randomised study comparing out-of-hospital preloading with administration at the time of PCI in STEMI, failed to show any benefit of the upstream pre-treatment in terms of coronary reperfusion and outcome at 30 days, nevertheless with a small but significant reduction of definite stent thrombosis up to 30 days [21]. Even though the 2014 European society of Cardiology (ESC) guidelines on coronary revascularisation still recommend preloading in STEMI [2], recent evidence derived from the ATLANTIC trial weakened the concept of preloading in STEMI and will probably lead to future modifications of recommendations.

**Non-ST-segment elevation-ACS**

In contrast to STEMI, the therapeutic goal of antithrombotic treatment in the setting of non-ST-segment elevation-ACS (NSTEMI) is to stabilise the coronary plaque in view of mechanical revascularisation, which should take place within 24 to 48 hours [3]. Whereas previous guidelines warmly recommended preloading with a P2Y₁₂ inhibitor upstream [20], the only trial testing this hypothesis failed to demonstrate any advantage. In fact, the ACCOAST trial, published in 2013, which compared pretreatment with 30 mg of prasugrel (and a further 30 mg dose at the time of PCI) with prasugrel 60 mg given after diagnostic angiography, did not show any benefit in terms of cardiovascular death, recurrent myocardial infarction, stroke, urgent revascularisation and bailout use of GPIIb/IIIa inhibitors at 7 and 30 days. Instead, a significant increase in major bleedings in the pretreated group was observed [22].

Uncertainties about preloading are mirrored in the 2015 edition of the ESC NSTEMI guidelines, which clearly discourage pretreatment with prasugrel, and give no recommendation favouring or discouraging the use of clopidogrel or ticagrelor, clearly highlighting the lack of evidence to support either strategy [3]. A summary of the current recommendation is given in table 2.

**Optimal length of DAPT after stent implantation**

Current guidelines recommend routine use of DAPT for 6 months after DES implantation in stable patients and for 1 year after an ACS [2]. Several trials evaluated the hypothesis that a shorter duration of DAPT would guarantee good efficacy and safety after newer-generation stent implantation [23-27], and tested various regimens of DAPT differing in terms of drugs used or length of treatment. Pooled data from these trials, including more than 30 000 patients, concluded that a short course of antithrombotic treatment lasting 3–6 months provides a similar safety profile to longer treatment (12 months) (table 3) [28]. Regardless of different therapeutic options and guideline recommendations, the current trend is to shorten DAPT to the minimum period required according to patient and stent characteristics. So far, this approach has

---


**STEMI**

<table>
<thead>
<tr>
<th>Routine pre-hospital pretreatment cannot be recommended for patients with STEMI over the in-lab administration of the drug since the two strategies had similar outcomes. It can be advisable to administer potent and rapidly acting antiplatelet agents (prasugrel or ticagrelor) in the emergency department (i.e., ambulance) once the diagnosis of STEMI is confirmed and the patient proceeds to primary PCI.</th>
</tr>
</thead>
</table>

**NSTEMI**

| It is advisable to administer a potent and rapidly acting antiplatelet agent (prasugrel or ticagrelor) once the coronary anatomy is known (and the patient proceeds to immediate PCI). If prasugrel or ticagrelor are contraindicated, pretreatment with clopidogrel before coronary angiography may be advisable for patients with low bleeding risk and a high likelihood for immediate PCI, especially if radial access is planned. |

---

**Table 3**: Adverse events according to the length of treatment.

<table>
<thead>
<tr>
<th></th>
<th>DAPT 3–6 months</th>
<th>DAPT 12 months</th>
<th>RR</th>
</tr>
</thead>
<tbody>
<tr>
<td>ST* rate (%)</td>
<td>0.5</td>
<td>0.4</td>
<td>0.1</td>
</tr>
<tr>
<td>Pooled MI+ (%)</td>
<td>1.7</td>
<td>1.5</td>
<td>0.2</td>
</tr>
<tr>
<td>Major bleeding (%)</td>
<td>0.4</td>
<td>0.8</td>
<td>0.4</td>
</tr>
<tr>
<td>Death rate (%)</td>
<td>1.7</td>
<td>1.9</td>
<td>0.2</td>
</tr>
</tbody>
</table>

have been evaluated in the RESET [25] and OPTIMIZE (26) trials, which compared 3 and 12 months DAPT after implantation of a zotarolimus-eluting stent in patients with stable coronary artery disease. Both studies demonstrated noninferiority of the shorter treatment for the composite endpoint of all-cause death, myocardial infarction, stroke or major bleeding [26], as well as stent thrombosis and target vessel revascularisation [25]. In patients at high bleeding risk, the predefined DAPT period can be further shortened to 4 weeks when polymer-free drug-eluting stents are used. This is supported by evidence derived from the recent LEADERS FREE trial, which showed similar safety and superior efficacy with these stents as compared with conventional BMSs [29].

Factors that need to be considered in estimating bleeding (favouring shorter DAPT) and ischaemic risk (favouring longer DAPT) are listed in table 4.

DAPT beyond 12 months

Several studies [14, 24, 30–34] hypothesised that prolonged platelet inhibition might result in a better protection against recurrent cardiovascular events.

The first study evaluating this strategy, the CHARISMA trial (with more than 15 000 patients at risk of, or with established, cardiovascular diseases randomised to either aspirin alone or a combination of aspirin plus clopidogrel for a median of 28 months) failed to demonstrate any advantage of prolonged DAPT but raised some safety concerns in terms of bleeding [14]. A few years later, the DES-LATE study also failed to show any benefit associated with clopidogrel plus aspirin vs of aspirin alone in reducing the incidence of myocardial infarction or death from cardiac causes at 12 months [32]. More recently, the large Dual Antiplatelet Therapy (DAPT) study, compared the extension of DAPT up to 30 months after PCI vs the conventional approach in almost 10 000 event-free patients (30). Prolonged treatment after PCI significantly reduced the rates of stent thrombosis, myocardial infarction and major adverse cardiovascular events. Notably, the reduction in myocardial infarction was significant in both target and non-target lesions, suggesting a secondary prevention effect of long-term DAPT. However, in line with previous studies, a safety concern was raised owing to the increase in moderate to severe bleeding, all-cause mortality and deaths for non-cardiovascular causes in the treatment group.

Finally, the recent PEGASUS-TIMI 54 study, evaluating two different doses of ticagrelor (90 or 60 mg twice daily) plus aspirin vs aspirin alone in more than 21 000 stable high-risk patients (myocardial infarction 1–3 years earlier) with a median follow-up to 33 months, was reported [33]. Consistently with the previous observations, the study demonstrated a significant reduction in terms of the primary efficacy endpoint (combined death, reinfarction, stroke after 3 years). However, an increased risk of major bleeding for the two ticagrelor doses was also observed (2.6% for ticagrelor 90 mg vs 2.3% for ticagrelor 60 mg vs 1.0% for aspirin alone).

A summary of current evidence is available from an elegant meta-analysis, published in 2015 [35], which clearly showed that DAPT maintained well beyond 12 months (up to 24–30 months) reduces the incidence of thrombotic complications, in particular stent thrombosis and myocardial infarction, at the price of an increase in major bleeding and possibly in all-cause mortality. In other words, the dichotomy between efficacy and safety still represents the Achilles’s heel of this appealing, but challenging approach.

In conclusion, although 2014 ESC guidelines on myocardial revascularisation do not recommend routine extension of DAPT, on the other hand and in the light of the more recent results of the DAPT and Pegasus tri-

---

Table 4: Characteristics related to increased ischaemic/bleeding risk.

| Increased ischaemic risk or risk of stent thrombosis (may favour longer-duration DAPT) |
| Recurrent ischaemic episode on DAPT |
| ACS presentation in young patients |
| LV dysfunction |
| High vascular burden |
| Chronic stable kidney disease |
| Additional stent factors |
| First-generation DES |
| Stent undersizing |
| Bifurcation stent |
| Stent-in-stent |

| Increased bleeding risk (may favor shorter-duration DAPT) |
| Very old patients |
| Short life expectancy |
| Poor DAPT adherence |
| End-stage renal failure |
| Malignancy |
| Short term candidates for high risk surgery |
| Severe anaemia |
| History of prior bleeding |
| Major haematological disorders |
| Oral anticoagulation |
| Low body weight |

*Modified from Levine GL et al ACC/AHAGuidelines Focused Update on Duration of Dual Antiplatelet Therapy in Patients with Coronary Artery Disease.
als, treatment for more than 12 months can be considered in selected patients with a very high ischaemic burden (e.g., severe coronary artery disease in young patients with multiple risk factors, recurrent events) and at a very low bleeding risk.

**DAPT and oral anticoagulation**

Almost 6–8% of patients undergoing PCI have an indication for chronic oral anticoagulation (OAC) with vitamin K antagonists (VKAs) or new oral anticoagulants (NOACs), as a result of various conditions such as atrial fibrillation, mechanical heart valves and recent or recurrent venous thromboembolism. However, adding antiplatelet agents to warfarin increases nonfatal and fatal bleeding risk more than 3-fold as compared with DAPT [36]. Therefore, clinical judgment and regular reassessment of the indication for OAC is essential. Current guideline recommendations, derived from large registries [36], from rather small and underpowered randomised trials [37, 38] and from post-hoc analyses of the large randomised trials on atrial fibrillation, still recommend a pragmatic approach mainly based on a clear distinction between stable and acute coronary syndromes and on balancing the systemic bleeding risk by use of validated risk scores [3]. In patients with an acute coronary event and low bleeding risk (HAS-BLED score ≤2) extension of the triple therapy, consisting of aspirin, clopidogrel and either a vitamin K antagonist or NOAC, up to 6 months is recommended. In patients with stable coronary artery disease but at a high haemorrhagic risk (HAS-BLED score ≥2), a shortened triple therapy (1–3 months) and then a switch to a combination of one antiplatelet drug (either aspirin or clopidogrel) and one oral anticoagulant for up to 12 months is advised. In accordance with a joint consensus document [39], and in line with the most recent European Guidelines on atrial fibrillation [40], discontinuation of any antiplatelet agent at 1 year is encouraged irrespective of stent type, whereas dual therapy with oral anticoagulation and one antiplatelet agent (aspirin or clopidogrel) may be considered in very selected patients at high risk of recurrent ischaemic events. Prasugrel or ticagrelor as part of triple therapy should be avoided, since these potent P2Y12 receptor inhibitors generate an unpredictable risk of fatal bleeding. In addition, when VKAs are used, the prothrombin time international normalised ratio (INR) should be carefully maintained within a target of 2.0–2.5. In patients treated with NOACs, the lowest tested dose for stroke prevention should be applied (e.g., rivaroxaban 15 mg once daily).

The appropriate role of NOACs was investigated in the hypothesis-generating PIONEER AF-PCI [42], which enrolled 2124 patients with non-valvular atrial fibrillation who had undergone PCI. Patients were randomly assigned to receive low-dose rivaroxaban (15 mg once daily) plus a P2Y12 inhibitor for 12 months, very-low-dose rivaroxaban (2.5 mg twice daily) plus DAPT for 1, 6 or 12 months, or standard therapy with a dose-adjusted VKA (once daily) plus DAPT for 1, 6 or 12 months. Despite its complexity, the study showed a clear benefit in terms of bleeding rates and similar safety for the two rivaroxaban groups as compared with the standard treatment. Even though the trial was not powered to evaluate efficacy, it definitely opens new perspectives in this increasingly important area of antithrombotic treatment.

**Open questions and future perspectives**

One of the future directions being currently investigated is the potential role of a single antiplatelet treatment with one of the novel potent antithrombotic drugs as an alternative to the conventional DAPT approach.

The ongoing Global LEADERS trial, with more than 16.000 patients included and a 2-year follow up, aims to evaluate whether, after an initial short (1-month) DAPT period, ticagrelor monotherapy will provide similar antithrombotic efficacy without increasing the long-term risk of bleeding [43]. If this trial succeeds in demonstrating this, it could have a revolutionary impact on the clinical management of patients with ischaemic heart disease.

Moreover, the currently ongoing, large-scale COMPASS trial, which includes more than 20.000 patients with documented atherosclerosis, is currently investigating the role of a low dose factor X inhibitor (rivaroxaban 2.5 mg twice daily vs aspirin vs rivaroxaban 5 mg twice daily alone vs aspirin alone) in protecting against future cardiovascular events. Also in this case, if efficacy were proven, this would represent an important game-changer in the immediate future [44].

In other words, the antithrombotic perspective could considerably change in the coming years, according to the results of ongoing trials.

**Platelet inhibition following structural interventions**

The rationale behind platelet inhibition following structural interventions such as transcatheter aortic valve implantation (TAVI), transcatheter edge-to-edge mitral valve repair, left atrial appendage occlusion or patent foramen ovale / atrial septal defect occlusion is...
represented by both the need to prevent early thrombosis due to the loss of integrity of the endothelium at the time of the procedure and the need to prevent device thrombosis until complete endothelialisation is achieved.

Although there is a general consensus among cardiologists on the need for platelet inhibition, multiple empirical approaches are adopted in clinical practice. In the absence of clinical trials evaluating alternate antithrombotic regimens, especially after TAVI, no consensus on the optimal agent(s) or duration of therapy is yet available [45].

The recent WRITTEN survey highlighted that DAPT was the most common antithrombotic treatment prescribed at hospital discharge after TAVI. Nonetheless, significant differences were observed in terms of duration, this varying from 1 month in 14.3%, 3 months in 43.8%, 6 months in 35.5%, 12 months in 4.6% and indefinitely in 0.5% centres, while only a minority reported systematic use of single antiplatelet therapy with aspirin alone [46]. Even though some authors [47, 48] questioned the need for DAPT, we strongly support the current recommendation to consider DAPT for a minimum period of 1 to 3 months, as long as data from a large randomised trial are not available.

The concomitant presence of atrial fibrillation or alternative indications for oral anticoagulation clearly add complexity to complexity, and in fact it is not yet clear whether platelet inhibition is needed in the presence of oral anticoagulation.

The introduction of NOACs also opened new possibilities in patients undergoing TAVI. The currently running phase III GALILEO study, in which approximately 1 500 TAVI patients with no previous indication for OAC were randomly allocated to either rivaroxaban 10 mg plus aspirin once daily for 3 months followed by rivaroxaban 10 mg alone, or to standard DAPT with clopidogrel on top of aspirin for 3 months followed by aspirin alone, will most probably add new information and most probably impact on the current practice [49]. Concerning use and length of the dual antiplatelet therapy in the clinical context of structural interventions such as patent foramen ovale, atrial septal defect and left atrial appendage closure or after percutaneous mitral valve repair, the medical evidence is even more scanty and the current practice is still based on empirical recommendations which suggest combining aspirin with clopidogrel for up to 3 months followed by aspirin (or clopidogrel) alone for up to 6 months or as long as required by the clinical condition.

Conclusions

Dual antiplatelet treatment in the clinical context of coronary stent implantation is an evolving area with rapidly changing medical evidence and recommendations. On the basis of recent negative trials, preloading in ACS has been definitely called into question; concerning post-stent DAPT therapy, the current trend is to shorten treatment to the minimum required period and to stratify the approach according to patient and stent characteristics; finally, long term treatment for more than 12 months should only be considered in highly selected cases with a high ischaemic burden and a predicted low bleeding risk.

Ongoing large trials are currently investigating the role of single antiplatelet therapy with the new P2Y₁₂ inhibitors and the potential use of new oral anticoagulants both in the setting of coronary artery disease and as an adjunctive therapy after structural interventions.

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.
Rapidly changing world of cardiac surgery

Marko Turina
University of Zürich, Switzerland

Summary

Cardiac surgery developed rapidly in the seventies and eighties of the last century, followed by a period of stabilisation and finally a numerical decline in 21st century. Coronary bypass surgery has been largely supplanted by percutaneous interventions, arrhythmia surgery has been replaced by percutaneous ablation and implantable defibrillators, correction of simpler congenital anomalies is also accomplished by catheter techniques, and we are now observing the emergence of transcatheter aortic valve replacement, which is rapidly overtaking surgical valve repair. On the horizon are mitral and tricuspid repairs; even some short-term circulatory assistance devices are being employed by transcatheter approach. This development has important consequences for cardiosurgical training: minimally invasive procedures are becoming standard of care, catheter training in a heart laboratory (“wire skills”) is becoming essential, education in interpretation of advanced imaging techniques: magnetic resonance imaging, angio- and multislice computed tomography, and 2D and 3D echo must be introduced, and surgeons must be also trained in endoscopic and robotic surgery for advanced minimally invasive interventions.

Key words: cardiac surgery; TAVI; percutaneous interventions; surgical education

In surgery, as in many other medical disciplines, it is from time to time intellectually rewarding to look back and assess the changes in the profession at a larger time-scale. According to famous American philosopher of Spanish origin, George Santayana, “those who cannot remember the past are condemned to repeat it”. Having myself witnessed and participated in the rapid development, later stagnation and present major transformation of cardiac surgery, I feel that the time has come for a critical overview of the changes that have occurred in this field since its beginning in the late fifties and early sixties of the last century.

Cardiac surgery originated as correction of congenital anomalies in the forties and early fifties, first with closure of patent ductus arteriosus and resection of coarctation, later with palliative operations in tetralogy of Fallot and transposition of great arteries, and continuing with correction of atrial and ventricular septal defect and other anomalies. With the development of reliable pump oxygenators began the correction of various heart valve diseases, which grew into the large field of valve replacement and repair. But a real explosive growth of cardiac surgery came with the establishment of aorto-coronary bypass grafting, known as CABG, in the seventies, as clearly seen in the annual number of open heart procedures in Zurich through the eighties of the last century (fig. 1). With the development of cardioplegia, the risk associated with CABG in Zurich, as in many other large-volume centres, fell to less than 1% in this period.

The first major development in cardiology, which thoroughly changes the practice of cardiac surgery, was the development of percutaneous dilatation of coronary artery stenosis, known first as PTCA (percutaneous coronary angioplasty) and later as PCI (percutaneous coronary intervention) in Zurich in 1977/78 by Andreas Gruentzig. In spite of initial high complication rates [1], this revolutionary invention spread through cardiology like wildfire, creating a new specialist—the cardiac interventionist—and rapidly reducing the number of candidates for CABG. This is best shown by the statistics of the Swiss Society for Cardiac and Thoracic Vascular surgery and Swiss Society of Cardiology [2], which show that in recent years only about one fifth of patients with coronary artery disease are referred to surgery and the remaining four fifths undergo PCI.
In recent years, surgeons have observed that PCI was often used rather indiscriminately, and was indeed overused in some centres, which eventually led to legal proceedings and to punishment of the responsible cardiologists. PCI overuse was termed “ccculos tenotic reflex and iatrogenosis fulminans” [3] in a recent article in Circulation. Nevertheless, in 2004, one of the leading European cardiologists, Patrick Serruys, openly stated that “It is not a question if invasive cardiologist will replace the coronary surgeon, but only when.” In recent years it became obvious that only a small minority of patients with coronary artery disease will go to surgery, in spite of undeniable long-term advantages of arterial grafting, with its excellent long-term patency and certain protective effect on native coronary circulation, which prevents progression of distal disease in the native circulation [4].

New guidelines about coronary revascularisation, developed by the European Society of Cardiology and the European Association for Cardio-Thoracic Surgery surprisingly favoured CABG in a majority of coronary situations, given the better long-term outcome after CABG and similar risk with both procedures, but it does not seem that these guidelines are being followed by invasive cardiologists, as shown by frequency of PCI and CABG in the UK (fig. 3), and PCI remains the primary treatment of coronary artery disease in Western World [5].

In the last decade we have observed another revolutionary development in invasive cardiology, called “transcutaneous aortic valve implantation”, TAVI for short. Starting rather unsurprisingly in the 1990s, with only moderate success in percutaneous dilatation of aortic stenosis, it exploded, with the assistance of the biomedical industry, into a huge field, with numerous models of catheter-introduced aortic prosthesis, with various methods of fixation. TAVI addressed a major problem in the western world, aging of the population, with concomitant development of degenerative aortic stenosis in septuagenarians and octogenarians, a group of patients at higher surgical risk owing to their age and accompanying comorbidity. Spectacular, quick implantation with short, light anaesthesia, and fast postinterventional recovery, resulted in a rapid increase in the number of TAVI procedures, which in 2014 represented 57% of all aortic procedures in Germany [6]. Strangely enough, the number of surgical aortic valve replacements remained constant in the same period, showing that TAVI presently addresses a segment of the population that was, until now, denied treatment of their aortic valve disease. According to a recent analysis [7], mild, moderate or severe aortic stenosis is encountered in 12.4% of population and severe stenosis in 3.38%, indicating that invasive cardiology and surgery will have to devote considerable activity to this increasing population segment. According to EUROSTAT, the populations of the European Union is expected to include 24.8 million octogenarians by 2020.

Numerous problems arise from TAVI. Some asymptomatic cerebral and coronary embolisation seems to take place during the procedure, and the durability of this new type of prosthesis is still unknown, although they seem to function well up to 5 years after implantation. Treatment of coexisting coronary disease, which is very common in this advanced-age group, is still debated: do nothing, pre-dilate or post-dilate (difficult with a prosthesis in place)? TAVI endocarditis, a highly
lethal disease and almost unamenable to surgery, seems currently to be rather rare. But it is obvious that the biomedical industry is betting on the success of TAVI, with huge investments in this sector: they are projecting implantation of up to 289,000 units by 2025, with a projected global TAVI market of 5 billion US$ [8]. And TAVI still receives major attention in scientific publications, as shown by rising number of articles indexed in Medline that address this subject (fig. 4).

Figure 4: Annual incidence of scientific publications on transcatheter aortic valve implantation (TAVI), from Medline.

Innovations in percutaneous procedures have also reached the mitral valve. By use of a well-established surgical method, the Alfieri stitch, placed with a trans-septal catheter under echocardiographic control, reduction of mitral incompetence can be achieved, especially in the surgically difficult group with ischaemic mitral regurgitation, although results are presently still very inferior to surgical annuloplasty. Transcatheter mitral annuloplasty is already being tried clinically, and the same technique is also being applied to incompetent tricuspid valves. Transcatheter mitral valve replacement has had its first clinical trials, and transcatheter pulmonary valve replacement for pulmonary incompetence occurring late after surgical correction of Fallot’s tetralogy is already a clinical reality and is accepted as a standard procedure in properly selected cases.

New developments, especially when they challenge the prevailing routine, are subjected to increasing public scrutiny, and it is becoming difficult to develop a new surgical procedure, which in the beginning will be unavoidably saddled with an added risk. A classic example is the arterial correction of transposition of the great arteries (TGA). The original, atrial correction of TGA, designed and developed by Ake Senning [9], was achieving excellent results in the 1970s, without operative mortality [10]. When Adib Jatene first developed his alternative method of TGA correction, called arterial switch, his initial results showed a mortality of 71% (!), which improved later to 16.6% [11]. Such an effort would be impossible today, with continuous, widespread public scrutiny of surgical results: the surgeon would have been ostracised and indeed punished for his pioneering work. And today Jatene’s method is the only technique used in newborns with TGA, which needs correction in the first days of life, and it can be performed with minimal risk in experienced centres.

Another challenging cardiosurgical field was surgery of arrhythmias, beginning first with curative operations in Wolff-Parkinson-White syndrome, which was followed by electro-physiologically guided resection of arrhythmogenic zones in ischaemic cardiomypathy, and finally by surgical treatment of atrial fibrillation, pioneered by James Cox, with an operation which even today bears his name – the Cox procedure [12]. But all these procedures, which received wide exposure in Zurich and were used in many operations with good success rates, are today almost totally superseded by catheter-based interventions, albeit with a lower long-term success rate in atrial fibrillation, which are favoured by patients for their minimally-invasive nature, with short anaesthesia and one-day hospitalisation. Surgery for atrial fibrillation is nowadays only performed as an adjunct procedure during CABG or mitral and aortic valve operations. Ablation of atrial fibrillation and closure of the atrial appendage are today possible with minimally invasive, thoracoscopic procedures; nevertheless their numbers remain low.

Use of circulatory assist devices has long been a neglected area of cardiac surgery, with few institutions specialising in the use of total artificial hearts and modest long-term survival. The main problems remain thrombosis and infection of the device, embolisation, and large, often loud, extracorporeal devices. The intra-aortic balloon pump and, later, extracorporeal membrane oxygenation remain the principal, universally used assist devices. In the last decade, a number of very small, highly efficient pumping systems have been developed, with continuous flow pumps being in the foreground. Intermacs statistics [13] from the USA, reporting effectiveness of assist devices in 163 centres and in 20,659 subjects enrolled, show the attractiveness of left ventricular assist devices (LVADs), with total artificial hearts and isolated right heart assist being very rarely used (fig. 5). This also led to a change in attitude towards these devices: whereas they were previously used only for bridging the patient to transplantation, nowadays a substantial proportion of patients have LVADs as “destination therapy”, for keeping the patient alive and moderately
mobile and healthy without resorting to heart transplantation, because of either the patient’s age or polymorbidity (fig. 6). This destination therapy LVAD is achieving surprising survival rates of more than 50% after 3 years.

It is obvious that cardiac surgery is presently undergoing major changes, with loss of some areas, but promising developments in other fields. Clear changes include:

- A substantial proportion of CABG replaced by PCI
- Aortic valve replacement superseded by TAVI
- Mitral repair and replacement by catheter techniques
- Catheter closure of atrial septal defects, patent ductus arteriosus and even some ventricular septal defects
- Coarctation: balloon dilatation and covered stents
- Mitral and pulmonary stenosis: catheter dilatation
- Arrhythmia surgery: catheter procedures and automatic implantable cardioverter-defibrillators
- Pulmonary valve replacement: catheter technique
- Aortic aneurysms: endovascular aortic repair (EVAR) and thoracic EVAR

With changes in the nature of cardiosurgical activity, it is equally obvious that substantial changes must be made in the education of future cardiac surgeons: they must be trained in catheter technology to be able to interpret two- and three-dimensional echocardiography and magnetic resonance imaging, and they should become familiar with thoracoscopic techniques for minimally invasive heart operations.

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References
The full list of references is included in the online version of the article at www.cardiovascmed.ch.
The patient had a longstanding history of short episodes of dizziness and reduced effort tolerance

Atrial standstill
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Summary

Atrial standstill is a rare but serious condition, characterised by the absence of atrial electrical and mechanical activity. It potentially leads to syncope, congestive heart failure, stroke and sudden death. It can affect the atria partially or totally and in a transient or permanent way. There are three forms: idiopathic, inherited or secondary. It should be suspected if the ECG shows absence of P waves and a regular supraventricular bradycardic rhythm. The diagnosis can be confirmed through an echocardiogram revealing the absence of atrial contraction. The treatment of this condition is focused on its consequences and potential complications, and includes pacemaker implantation, heart failure management and anticoagulation therapy. We report a case of total atrial standstill, possibly idiopathic, in a young patient with a longstanding history of dizziness and reduced effort tolerance, and we review the literature about the subject.

Key words: atrial standstill; pacemaker

Case report

A 37-year-old male patient was referred to our cardiology division with a longstanding and worsening history of short episodes of dizziness and reduced effort tolerance. He denied any syncope, palpitations or chest pain. His medical history was unremarkable and he took no medication. Family history was negative for cardiac diseases at a young age or premature sudden death. On clinical examination, the patient appeared in good general condition. He was bradycardic at 40 bpm and normotensive; heart and lung auscultation was normal, the jugular veins distended. The resting ECG displayed a junctional rhythm at 35 bpm with complete right bundle-branch block and no atrial electrical activity (fig. 1). A chest X-ray showed cardiomegaly without pulmonary congestion. During a 24-hour Holter ECG, no atrial activity was discernible and a constant bradycardic junctional rhythm was noted, with a mean heart rate of 36 bpm. Moreover, 83 episodes of asystole lasting more than 3 seconds were recorded, of which 11 lasted more than 6 seconds, with the longest episode in the night being of 10.5 seconds duration (fig. 2). There were no serious ventricular arrhythmias and only 62 isolated premature ventricular beats were registered. An exercise stress test confirmed the reduced effort tolerance and absent atrial electrical activity, and revealed a severe chronotropic incompetence with maximum junctional heart rate of 88 bpm (fig. 3). The echocardiogram showed a moderate dilatation of all cardiac chambers (fig. 4) with normal biventricular systolic function, absent mechanical activity of both atria, and systemic congestion (as shown in figure 5 for the left atrium). Brain natriuretic peptide was moderately elevated (563 ng/l, reference range <100 ng/l), as were cholestatic enzymes (gamma-glutamyltransferase [GGT] 210 U/l, reference range <71 U/l). Cardiac magnetic resonance imaging confirmed the moderate dilatation of the heart chambers with normal biventricular systolic function and did not reveal ventricular myocardial fibrosis or evident atrial parietal thickening or fibrosis. An intracavitary thrombus was excluded. Electrocardiographically and genetic analysis were refused by the patient. Nevertheless, all clinical and paraclinical findings were consistent with a total atrial standstill, possibly idiopathic. Because of the severe symptomatic bradycardia, a pacemaker was implanted. During the procedure, no electrical activity was recorded in the whole right atrium and no atrial capture was obtained even at maximal output (10 volts, 1.5 msec.). Therefore, a single-chamber ventricular pacemaker was implanted. Oral anticoagulation therapy was considered, but we decided against it in the face of a CHA₂DS₂-VASc score of 0 and the absence of left atrial appendage thrombus. After the pacemaker implantation the patient felt better, effort capacity improved and no recurrence of dizziness was reported. At 18-month follow-up, he was well and asymptomatic with near normalisation of the brain natriuretic peptide concentration (135 ng/l) and of the cholestatic enzymes (GGT 113 U/l), proving that their increases were caused by hepatic congestion. Ventricular function remained normal without further dilatation of the heart chambers. No significant ventricular arrhythmia was recorded on the pacemaker ECGs. Family screening revealed that his parents, two sisters and 10-year-old son were all asymptomatic, with normal clinical examination and normal resting ECG.
Figure 1: Resting ECG showing a junctional rhythm at 35 bpm with complete right bundle-branch block. Note the absence of atrial electrical activity.

Figure 2: Three-channel continuous ECG tracing during Holter monitoring showing the maximal pause of 10.5 seconds. Note the irregular junctional rhythm and the absence of atrial electrical activity.
Figure 3: ECG at the maximum of effort showing a junctional rhythm at 88 bpm.

Figure 4: Parasternal long axis (A) and apical four chamber (B) echocardiogram views showing a moderate dilatation of all cardiac chambers (left ventricular end-diastolic diameter of 64 mm, right ventricular end-diastolic basal diameter of 50 mm, left atrial antero-posterior diameter of 52 mm). LV = left ventricle; RV = right ventricle; LA = left atrium; RA = right atrium; RVOT = right ventricular outflow tract.
Discussion

Atrial standstill, first described by Chavez et al. in 1946 [1], is characterised by the absence of electrical and mechanical activity of the atria. The ECG usually displays no discernible P waves and a regular bradycardic junctional rhythm [2, 3]. Effort-related chronotropic incompetence and transient asystole are common, as in our patient [4, 5]. The atrial mechanical dysfunction can be readily detected on an echocardiogram by the absence of an A-wave in transmitral or transtricuspid flow, by the lack of telediastolic opening of the mitral (or tricuspid) valve, as our case nicely showed, and by the absence of active atrial contraction in tissue Doppler imaging [2, 3]. Atrial standstill is a rare but serious condition, since the longstanding profound bradycardia and the loss of atrial function can have severe haemodynamic consequences, potentially leading to syncope, heart failure and, very rarely, sudden cardiac death. Cardiac arrest can be caused by extreme bradycardia or pause-related malignant ventricular arrhythmias, particularly when atrial standstill is associated with an underlying cardiopathy [6–9]. Moreover, the dysfunctional and dilated atria with consequent blood stasis can cause thromboembolic events, as in atrial fibrillation [5, 6]. Our patient complained of dizziness, effort intolerance and systemic congestion. It can sometimes be difficult to distinguish atrial standstill from atrial fibrillation with a slow ventricular rate, especially in patients with permanent atrial fibrillation, dilated atria and low amplitude fibrillatory waves treated with atrioventricular nodal blocking agents or with an associated atrioventricular block. Atrial standstill can be transient or permanent [4]. When transient, it is usually related to antiarrhythmic intoxication (especially with digoxin or quinidine), hy-

Figure 5: Transmitral pulse Doppler imaging (A) showing the absence of A waves and parasternal M-mode at the level of the mitral valve (B) showing the absence of the telediastolic opening of the mitral valve, demonstrating the absence of the mechanical activity of the left atrium. M-mode imaging of the inferior vena cava (C) showing systemic congestion. E = E-wave; IVC = inferior vena cava.
perkalaemia, hypoxia or acute myocardial infarction, situations which were excluded in our patient [10]. The rarer form of permanent atrial standstill has been reported in association with Emery-Dreifuss muscular dystrophy, Kugelberg-Welander syndrome, limb-girdle muscular dystrophy, various types of cardiomyopathies, valvular or congenital heart disease, Ebstein’s anomaly, Brugada syndrome, amylloydosis, acute myocarditis, diabetes mellitus, following open cardiac surgery or after longstanding atrial fibrillation [3, 4, 11, 12]. None of these conditions was evident in our case. Rare cases of familial atrial standstill have been reported and they are usually diagnosed between the third and the fifth decade of life, as in our patient. The genetic background of atrial standstill is not yet fully understood, mostly because of the extremely low prevalence of this condition. Nevertheless, the disease seems to be associated with mutations of the sodium channel SCN5A gene, which are also related to sinus node dysfunction, conduction disease, long QT syndrome type 3 and Brugada syndrome [3]. Moreover, atrial standstill seems to show complete penetrance only when atrial-specific gap junction connexin 40 (Cx40) polymorphisms are also present (around 7% of the population) [3, 11, 14]. Unfortunately, our patient refused genetic testing. However, screening of first-degree relatives through history, clinical examination and resting ECG turned out to be negative, making the genetic basis less likely. Therefore, our patient was possibly affected by an idiopathic form. Previous studies suggest that atrial standstill is a progressive disease, starting from the high lateral right atrium and later descending toward the lower right atrium and near to the tricuspid valve annulus. The left atrium seems to be the last to be affected [6]. This is why atrial standstill can also be classified into partial or total forms. Our patient had a total form, as demonstrated by the absence of mechanical activity of both atria (on the echocardiogram) and the absence of electrical activity of the right atrium (during pacemaker implantation). Pathophysiological hypotheses of atrial standstill, based on post-mortem examinations, include fibroelastosis and fatty infiltration of the atrial wall [10]. It is not surprising that magnetic resonance imaging did not clearly show the presence of atrial fibrosis or fatty infiltration, since it is very hard to detect these changes in the thin atrial wall. In biopsy samples, mostly from the right atrium, fibrofatty replacement is generally present in a severe and widespread state, especially in case of permanent atrial standstill [3, 5, 7]. Electrophysiological studies, and particularly electro-anatomical mapping, are employed to confirm the diagnosis and to assess the extent and the severity of the disease of the atrial wall [4, 15]. Unfortunately, our patient did not consent to these examinations.

The electrical and mechanical silence of the atrium characteristic of persistent atrial standstill can also be accompanied by an endocrinological silence, with a low plasma concentration of atrial natriuretic peptide, or, in patients with congestive heart failure, a lower increase in plasma atrial natriuretic peptide compared with the increase in brain natriuretic peptide, which is secreted by the ventricular myocardium [16, 17].

The treatment of atrial standstill is focused on the consequences and potential complications of this disorder, and can include pacemaker implantation, treatment of heart failure with diuretics and vasodilators, and prevention of thromboembolism with oral anticoagulation therapy [3, 18]. The indication for pacemaker implantation can be assumed to be similar to that for sick sinus syndrome [19]. In our case, symptomatic bradycardia with dizziness and heart failure clearly required pacemaker implantation. In atrial standstill, the electrical silence of the atria is accompanied by difficulty or impossibility of electrically stimulation, making it hard to find a suitable site for atrial lead placement. Therefore, in most of the cases reported in the literature, a single chamber ventricular pacemaker was finally implanted [4, 5, 7]. Our case was no exception, since it was not possible to detect atrial potentials or stimulate atrial tissue in the right atrium. As previously mentioned, through electro-anatomical mapping it would have been possible to localise atrial tissue with preserved electrical activity, where an atrial lead could have been placed, allowing haemodynamically better synchronous atrioventricular stimulation, as has been done in a few cases reported in the literature [4, 15]. Despite a single chamber ventricular pacemaker, the clinical improvement in our patient was remarkably good and he was asymptomatic with preserved ventricular function at a mid-term follow-up. Concerning thromboembolic prophylaxis, the pathophysiological basis seems to be similar to that for atrial fibrillation, with blood stasis due to the dysfunctional and dilated atria. Unfortunately, no study is available specifically for atrial standstill patients. Nevertheless, it seems logical to adopt the same risk stratification score as in atrial fibrillation. Concerning the prothrombotic state, the pathophysiological basis seems to be similar to that for atrial fibrillation, with blood stasis due to the dysfunctional and dilated atria. Unfortunately, no study is available specifically for atrial standstill patients. Yet, it seems logical to adopt the same risk stratification score as in atrial fibrillation. De novo atrial fibrillation [20]. In our case, the CHA2DS2-VASc score was 0, and no anticoagulation therapy was prescribed; no embolic event has occurred in 18 months of follow-up. Diuretics are indicated in cases of heart failure with fluid overload. In our patient, after pacemaker implantation the congestion signs rapidly resolved so that no diuretic therapy was needed. Vasodilators can be useful in cases of important remodelling of the heart with mitral regurgitation.
In conclusion, physicians should raise awareness of this rare but serious condition in order to provide the best therapeutic approach after the appropriate investigations.

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References
A lesion that can and should be removed through a minimally invasive approach

Minimally invasive excision of a papillary fibroelastoma

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A 51-year-old patient suffered from recurrent atypical thoracic pain. Clinical examination, cardiac biomarkers and electrocardiography were unremarkable. Transthoracic echocardiography revealed a normal ejection fraction, trivial mitral regurgitation and a mobile, echo-dense mass, 10 mm long and 6 mm in diameter, attached to the chordae tendineae of the P1/A1 segment of the mitral valve leaflet (fig. 1A, arrow).

Cardiac magnetic resonance imaging confirmed the presence of the mass, showing a mobile structure on the cine images, an isointense signal on T1 and T2 weighted images, as well as a hyperenhancement after late gadolinium administration (fig. 1B, cine image, arrow).

Given the appearance of the tumour, a papillary fibroelastoma of the mitral valve was suspected. Papillary

Figure 1.
fibroelastomas are rare primary cardiac tumours with a reported incidence of 0.002% [1]. Most patients are asymptomatic, but some are at increased risk of thromboembolic complications – in particular if the tumour is mobile and attached to the mitral valve apparatus [2]. We discussed the thrombotic risk with the patient and weighed it against the risk of minimally invasive surgery [3].

Because of the recurrent atypical thoracic pain experienced by the patient and the large diameter of the mobile mass, we chose surgery. Cardiopulmonary bypass was installed through a 2-cm right-sided groin incision. The heart was approached via a right-sided anterolateral minimally invasive incision. After cardiac arrest and opening of the left atrium, we found a tumour attached to a secondary chord at the P1 segment of the posterior leaflet (fig. 1C, arrow point on the tumour, posterior* and anterior** mitral leaflet). The tumour was completely excised without damaging the leaflets. The intraoperative course was uneventful, and echocardiography confirmed competent valve function. The postoperative course was uneventful and the patient discharged at day 7. Pathological diagnosis confirmed a papillary fibroelastoma.

Clinical follow-up at 3 months after surgery showed unremarkable wound healing (fig. 1D) and a full recovery.

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

References
Coronary vein visualisation during primary percutaneous coronary intervention

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A 66-year-old man presented with substernal chest pain of one hour’s duration and electrocardiographic evidence of acute inferior wall ST-segment elevation myocardial infarction. He underwent emergency coronary angiography that showed total occlusion of the mid right coronary artery (RCA) just beyond the origins of a right ventricular branch (RVB) and the sinus node artery (SNA), and significantly obstructive lesions in the distal left main coronary artery, the proximal left anterior descending artery and the obtuse marginal artery. Collateral circulation (Rentrop grade II) to the distal RCA branches from the left coronary artery was also noted (fig. 1B). Initial angiography of the RCA also showed a peculiar, faintly visualised vessel in an area corresponding to the acute margin of the heart, which was initially assumed to be the distal RCA being collateralised from the RVB (moving image 1). During subsequent percutaneous coronary intervention, the guide wire tracked up the distal RCA outside the faintly visualised vessel, which was seen as comprising two branches and a drain point (fig. 1C; moving image 2 and moving image 3); it was thus recognised as a coronary vein. Percutaneous coronary intervention was completed with delivery of three bare-metal stents across the mid RCA lesion and two bare-metal stents across a lesion from the distal RCA to posterior left ventricular branch. Final RCA angiography disclosed Thrombolysis in Myocardial Infarction (TIMI) grade III flow, occlusion of the RVB, sub-occlusion of the SNA and disappearance of the previously seen coronary vein (fig. 1D and moving image 4). The patient had an uneventful hospital course and was referred for surgical revascularisation of the left coronary artery lesions.

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Demonstration of a coronary vein in the distribution of an acutely occluded coronary artery is, in our experience, an unexpected and potentially misleading finding. To the best of our knowledge, there has to date been only one similar publication, by Anzai et al. [1], who reported a coronary vein following a course parallel to a proximally occluded RCA, giving the false impression of spontaneous reperfusion; the vein was no longer visible after recanalisation of the RCA. Scrutiny of the angiographic presentation of the portion of the coronary venous system described here, revealed that the trunk coursing parallel to the distal RCA in the right atrioventricular sulcus corresponded to the small cardiac vein, which received the right marginal vein at the area of the acute margin of the heart and terminated in the coronary sinus [2]. Like Anzai et al. [1], we initially misidentified the coronary vein as the distal RCA being collateralised from the RVB, and what made us recognise it was the observation of its draining point. The conus artery supplying the right ventricular infundibulum, the SNA supplying the sinus node and adjacent right atrial wall and a RVB supplying the anterior right ventricular wall arose proximal to the occlusion site of the RCA, thereby allowing uninterrupted perfusion of their dependent myocardial areas. The small cardiac vein drains most of the walls of the right atrium and the diaphragmatic surface of the right ventricle, whereas the right marginal vein drains the anterior wall of the right ventricle [2]. Furthermore, coronary sinus flow has been shown to decrease during acute RCA occlusion [3]; therefore, we presumed that clearance of contrast material from the small cardiac vein that drained the venous return from the walls of the right atrium and the anterior wall of the right ventricle being supplied by the patent proximal RCA branches was delayed, thereby facilitating its opacification. In addition to being an angiographic peculiarity, a coronary vein seen downstream of an acutely occluded coronary artery should not be misidentified as a collateralised culprit artery or lead to confusion regarding the position of the guiding wire.
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No financial support and no other potential conflict of interest relevant to this article was reported.

References
The Annual Scientific Congress of the Swiss Society of Cardiology in Baden, Switzerland, June 7–9, 2017

Last June the Swiss Society of Cardiology met for the first time, in the Trafo Center in Baden (fig. 1), for their Annual Scientific Meeting together with the Swiss Society for Cardio-Thoracic Surgery. The congress was extremely well received and attended by 974 participants from all over Switzerland, with a few participants from abroad (fig. 2). In addition, 347 exhibitors took part in the congress.

The scientific programme covered the entire field of cardiovascular medicine from blood pressure to anticoagulation, from coronary artery disease to heart failure and transplantation, and from prevention to acute coronary syndromes. As the Swiss Society for Emergency and Rescue Medicine was the special guest, there was a focus on cardiac emergencies. The faculty included participants from all major hospitals in Switzerland and a few foreign speakers; overall 238 speakers and 172 chairpersons contributed to the programme.

As always, the Andreas Grüntzig Award was a highlight of the programme, with a lecture of this year’s awardee Peter Buser from Basel who talked about “From functional to molecular analysis of heart disease. Steps into the future of cardiac imaging.” The Senning Lecture was given by Ulrich Althaus, former Director of Cardiovascular Surgery at the Inselspital in Bern on "Das Herz der Maler und Dichter.”

A particular focus was on younger colleagues as chairpersons and speakers. Indeed, the Swiss Cardiologists of Tomorrow contributed to the programme and held their own party on Wednesday night. The official get-together of the Congress was held in the Wettingen monastery on Thursday night. The congress was organised by the Congress President Prof. François Mach from the Hôpital Universitaire de Genève, together with a team of Board Members of the Swiss Society of Cardiology.

On Wednesday evening, the Annual Assembly of the Swiss Society of Cardiology took place under the chairmanship of the current President of the Swiss Society of Cardiology Prof. Michel Zellweger from the University Hospital Basel (fig. 3). Major topics were the current and future reimbursement policy of the Swiss government under the leadership of the current Health Minister Alain Berset. It became clear – as outlined by the representatives of the Swiss Society of Cardiology for these issues, Urs Kaufmann from Bern and Giovanni Pedrazzini from Lugano – that most reimbursements, particularly for interventions, but also for diagnostic procedures, will decrease by on average between 5 to 10% in 2018 (range –1 to –28% in the overall reimbursement), which will certainly affect the Swiss cardiologist community as a whole, regardless of whether they work in private practice or hospitals.

A large number of new members and junior members have been welcomed to the Society, showing that the Swiss Society of Cardiology is well and alive. At the end of the General Assembly a controversial topic was discussed: the creation of subspecialty certifications, for example, in interventional cardiology and interventional electrophysiology. Some participants argued in favour of such a strategy, which would be in line with developments in Europe and North America, whereas some, particularly practicing cardiologists, raised concerns about such a step.

On Friday morning, 9 June 2017, the traditional Young Swiss Investigators Session took place under the chairmanship of Prof. Thomas F. Lüscher from the University Hospital Zurich and Prof. François Mach from the Hôpital Universitaire de Genève (fig. 4). Five awardees presented their excellent work. Indeed, all participants and the chairmen, as well as Prof. Augusto Gallino, board member of the Swiss Heart Foundation and Prof. Hans Rickli from the Swiss Society of Cardiology, were impressed by the quality of the research presented. David Nanchen from the Centre Hospitalier Universitaire Vaudois received the Swiss Heart Foundation Research Award for his work on familial hypercholesterolaemia in patients with acute coronary syndromes, an analysis of the Swiss SPUM ACS cohort of the University Hospitals Berne, Geneva, Lausanne and Zurich supported by the Swiss National Research Foundation. The neurologist and stroke physician David Seiffige from the University Hospitals Basel shared this prize with him for his work on thrombosis in patients on anticoagulants, in particular novel oral anticoagulants. The Swiss AMGEN Cardiology Award of the Swiss Society of Cardiology, a prize that has changed its name over the years, but has been in place now for more than two decades, went to the cardiologist...
Christoph Gräni for his work at the University Hospital Zurich in nuclear cardiology, under the leadership of Prof. Philipp A. Kaufmann, on anomalous coronary arteries, work reported in three papers published in the European Heart Journal, the Journal of Nuclear Cardiology and the Swiss Medical Weekly. Finally, two awardees of the Otto Hess Trainee Award presented their work: Panagiotis Antiochos, MD, from the Centre Hospitalier Universitaire Vaudois in Lausanne, “Association between anti-apolipoprotein A-1 antibodies and cardiovascular disease in the general population – results from the CoLaus study;” and Nicolas Johner, MD, from the Hôpital Universitaire de Genève, “Electrophysiologic properties in the coronary sinus of sustained versus non-sustained atrial fibrillation: a retrospective study and prediction model.”

Prize Winners Joint Congress SSC/SSCS 2018, Baden

Abstract Prizes

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<tr>
<th>Topic Nr.</th>
<th>Abstract Topic</th>
<th>Abstract Title</th>
<th>Winner</th>
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<tr>
<td>1</td>
<td>Cardiovascular biology (Including all abstracts with in vitro or in vivo investigations)</td>
<td>Sirtuin 5 mediates brain damage and neurological deficits in the mouse model of cerebral ischemia – reperfusion injury</td>
<td>Ms. Candela Diaz Canestro, Zurich</td>
</tr>
<tr>
<td>2</td>
<td>Pacemaker, defibrillator and electrophysiology</td>
<td>Association between genotype and ventricular involvement patterns in arrhythmogenic right ventricular cardiomyopathy/dysplasia</td>
<td>Ms. Deniz Akdis, Zurich</td>
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<tr>
<td>3</td>
<td>Cardiac failure, valvulopathies, cardiomyopathies, heart transplantation</td>
<td>Severe retinal endothelial dysfunction in patients with ischemic cardiomyopathy</td>
<td>Mr Jens Barthelmes, Zurich</td>
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<td>4</td>
<td>Acute coronary syndrome (ACS), percutaneous coronary intervention (PCI), coronary artery bypass graft surgery (CABG)</td>
<td>Effect of pre-test probability on diagnostic and prognostic performance of high-sensitivity cardiac troponin for acute myocardial infarction</td>
<td>Mr Patrick Badertscher, Basel</td>
</tr>
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<td>5</td>
<td>Epidemiology, risk factors, rehabilitation, thromboembolic disease</td>
<td>Whole Blood Omega-3 Fatty Acid Concentrations Are Associated With Lower Blood Pressure in Young Healthy Adults</td>
<td>Mr Mark Georg Filipovic, Baden</td>
</tr>
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<td>6</td>
<td>Cardiac imaging, congenital and paediatric cardiology</td>
<td>Echocardiographic predictors of midterm outcome after MitraClip implantation</td>
<td>Mr Ioannis Kapos, Zurich</td>
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<tr>
<td>7</td>
<td>Clinical cases</td>
<td>Leaflet thrombosis following transcatheter mitral valve replacement</td>
<td>Mr FlorianFranzeck, St Gallen</td>
</tr>
<tr>
<td></td>
<td>Best abstract “Congenital”</td>
<td>Left heart failure after double switch operation: The dilemma of preventing systemic right heart failure in congenitally corrected transposition of the great arteries</td>
<td>Ms Francesca Bonassin Tempesta, Zurich</td>
</tr>
</tbody>
</table>

Research Prizes and Honorary Lectures

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<tr>
<th>Prize</th>
<th>Title</th>
<th>Winner</th>
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<tbody>
<tr>
<td>Andrea Grünzig Award</td>
<td>From functional to molecular analysis of heart disease. Steps into the future of cardiac imaging.</td>
<td>Mr Peter Buser, Basel</td>
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<tr>
<td>Senning Lecture</td>
<td>Das Herz der Maler und Dichter</td>
<td>Mr Ulrich Althaus, Bern</td>
</tr>
<tr>
<td>Amgen Swiss Cardiology Research Award</td>
<td>Noninvasive evaluation, prevalence and outcome of middle-aged individuals with anomalous origin of the coronary artery from the opposite sinus</td>
<td>Mr Christoph Gräni, Zurich</td>
</tr>
<tr>
<td>Medtronic Young Investigators Award</td>
<td>Improving skeletonised internal thoracic artery harvesting: A low thermal electrosurgical knife provides endothelial integrity and avoids vessel wall injury</td>
<td>Ms. Alicia Zientara, Zurich</td>
</tr>
<tr>
<td>Research Prize Swiss Heart Foundation</td>
<td>Prognosis of patients with familial hypercholesterolemia</td>
<td>Mr David Nanchen, Lausanne</td>
</tr>
<tr>
<td>Research Prize Swiss Heart Foundation</td>
<td>Recanalization therapies in acute ischemic stroke patients</td>
<td>Mr David Julian Seiffge, Basel</td>
</tr>
<tr>
<td>Otto Hess Trainee Award</td>
<td>Electrophysiologic properties in the coronary sinus of sustained versus non-sustained atrial fibrillation: a retrospective study and prediction model</td>
<td>Mr Nicolas Johner, Geneva</td>
</tr>
<tr>
<td>Otto Hess Trainee Award</td>
<td>Apolipoprotein A-1 autoantibodies as a risk factor for coronary artery disease and all-cause mortality in the general population</td>
<td>Mr Panagiotis Antiochos, Lausanne</td>
</tr>
</tbody>
</table>
Two Awards on Clinical Excellence in Lipidology 2017:

- Walter Riesen Award for the best publication by a young researcher: The prize recognizes the best publication on lipidology and/or atherosclerosis by a young researcher in the ongoing or previous year. The prize is endowed with CHF 5000 donated by Sanofi.
- Award for Research Abroad, supporting a young researcher’s work abroad: The prize is awarded to a young researcher to support his/her visit of a research facility abroad to carry out a scientific project on lipidology/atherosclerosis. The prize is endowed with CHF 10 000 and is donated by Sanofi-Aventis (Suisse) SA.

Requirements

- Applicants for the Walter Riesen Award/ Award for Research Abroad must be under 45 years of age at the deadline of submission and must be working in a hospital or another institution in Switzerland.
- The prize winner will be selected by an independent prize jury, consisting of the AGLA president and some of its board members.
- The winners will give a short presentation of their research publication or project, respectively, at the AGLA Update Meeting on January 11, 2018 in Bern.
- For further information, please visit www.sanofi-atherosclerosis-research.ch

Neuer Chefarzt Kardiologie am Kantonsspital Aarau

Die Spitälleitung des Kantonsspitals Aarau hat per 1. Januar 2018 PD Dr. Laurent M. Haegeli, Oberarzt an der Klinik für Kardiologie am Universitäts-Herzzentrum Freiburg – Bad Krozingen, zum Chefarzt Kardiologie und Nachfolger von Dr. André Vuilliomenet ernannt.


Ehrungen

Prof. Dr. Thomas F. Lüscher, Zürich, wurde von der Peruanischen Gesellschaft für Kardiologie (Sociedad Peruana de Cardiologia) an ihrer diesjährigen Jahrestagung zusammen mit Val Fuster, New York mit der «Conferencia Magistral» ausgezeichnet und zum Ehrenmitglied ernannt.

For further information, please visit www.amgen-swiss-lipid-research.ch.