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Editorial

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Interventional cardiology on a roll

The year 2007 marks the 30th anniversary of percutaneous transluminal coronary angioplasty (PTCA), more recently called percutaneous coronary intervention (PCI). It also marks the 20th anniversary of the annual comprehensive poll of catheter-based cardiac procedures in Switzerland. The analysis of the 18th poll pertaining to 2005 is published in this issue. These yearly registries have the longest history worldwide and still the second-best degree of detail and precision (after Austria).

PCI has not initiated interventional cardiology but it is its most prominent representative. In fact, the first interventional therapy of heart disease was carried out by Rubio-Alvarez in 1951. He was using a crude instrument to crack a congenital pulmonary valve stenosis [1]. Of note, percutaneous closure of an atrial septal defect (ASD) also preceded PCI by a couple of years [2]. These were procedures in the realm of pediatric cardiology. The adult cardiologist woke up to mechanical therapeutic procedures with the first case of PCI performed on September 16th, 1977, at the University Hospital (Kantonsspital at that time) of Zurich, Switzerland.

This procedure kicked off an unprecedented success story in modern medicine. PCI is currently the most common medical intervention dealing with a prognostically important disorder. It is a direct descendent of peripheral catheter angioplasty introduced with an article of Dotter and Judkins in 1964 [3]. Their method to improve blood flow through narrowed peripheral arteries by passing the stenosis with catheters of increasingly large diameters was moderately successful and highly impractical. It implied a hole at the puncture site commensurate to the largest catheter used. Porstmann in Germany tried to improve the method by using a Latex balloon confined to a maximal diameter because it was inflated within the longitudinally split plastic catheter [4]. However, the disadvantage of catching plaque material during deflation of the device prevented a wider application of the method. The breakthrough came with the polyvinyl chloride (PVC) balloon of Grüntzig. PVC was suggested to Grüntzig by a retired plastic expert of the Technical University of Zurich (ETH) who continued to occupy a small office just a stone-throw away from Grüntzig's place of work as a resident in the Angiology Division of the adjacent hospital [5]. The fact that the PVC balloon grew to a certain diameter with a low pressure of 1 bar and then retained a fairly constant shape while increasing the pressure up to about 6 bar (rupture pressure of the PVC balloons of the time) predestined it for the treatment of atherosclerotic cardiovascular disease.

After using this type of balloon successfully in several hundred peripheral arteries, Grüntzig managed to miniaturise it for the use in the coronary arteries together with a small local company specialising in medical equipment (Schneider Medintag). In 1976, the balloon was ready for a first attempt but a patient was nowhere to be found. At that time in Switzerland, coronary angiography was restricted for patients refractory to conventional triple anti-anginal therapy. This was imposed by a dearth in facilities for coronary angiography which created a long waiting list. Thus, patients finally undergoing diagnostic cardiac catheterisation were typically found to have advanced triple vessel disease. Grüntzig was looking for a patient with a single stenosis.

On March 22nd, 1976, Grüntzig decided against his initial plan to try his method on a patient with terminal triple vessel disease and unstable angina. The patient had been turned down by the cardiac surgeons and was in desolate and moribund condition. Grüntzig was

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unable to reach the coronary orifice with the primitive guiding catheter of the time having to use an arm artery for access because of an occluded abdominal aorta. The procedure was abandoned before a balloon catheter came into play. The patient died two days later [6].

A year later, in March 1977, still short of a suitable patient, Grüntzig travelled to San Francisco, invited by Richard Myler, an American cardiologist, who had been intrigued by a poster Grüntzig had displayed at the American Heart Association Meeting in Miami, 1976, explaining PCI in a canine model. Together with a cardiac surgeon, the threesome dilated a few coronary stenoses intraoperatively before implanting the bypasses. Early follow-up angiography was encouraging.

The historical first PCI finally took place in September 1977, when Grüntzig returned rather frustrated from yet another week spent in San Francisco without finding a suitable patient for the percutaneous technique. I had the pleasure to present him with an age-mate of his (38 years) who just had had a coronary angiogram for unstable angina showing a single proximal stenosis of the left anterior descending coronary artery. Years before ethical committees and consent forms were to be introduced to Switzerland, Grüntzig had a brief talk with the patient and the case was scheduled for the next day with the blessing of Ake Senning, head of cardiac surgery and his right arm, Marko Turina. The handful of us witnessing this case were impressed but none of us (including the operator) had the faintest idea of how big the avalanche launched that day was going to be. The first intervention was a splendid success and the patient is still doing well 30 years later, having survived the fatal plane crash of his benefactor by more than 20 years. This splendid success was subsequently replicated millions of times. Of course, failures and complications also occurred. While already the 7th patient had to undergo emergency bypass surgery (a new indication for cardiac surgery to become quite common albeit only for about a decade), it was not until more than a thousand patients had been treated by Grüntzig and his closest collaborators that an in-hospital death occurred.

Sobered by the tedious search for the first patient, Grüntzig projected, that ideally some day 15% of patients needing coronary revascularisation would be able to benefit from PCI. By the end of 1980 he had treated not even 200 patients, reason for him to emigrate to the United States, where coronary angiography was being offered to patients with coronary artery disease at an increasing pace much in contrast to Europe with a persistently conservative attitude.

Continued improvement of material furthered the expansion of the method. More instrumental was a gradual change in attitude towards coronary artery disease. The availability of a percutaneous procedure not much more uncomfortable than fixing a tooth to amend blocked coronary arteries begot the development of diagnostic facilities. Although frowned upon at first, when the quality of fluoroscopy was still quite poor, “ad hoc” procedures (PCI during the initial diagnostic session) insidiously became the standard. This is exemplified by the fact that over 90% of PCIs in Switzerland are currently done as “ad hoc” procedures.

The coronary stent introduced in 1986 was the only add-on to balloon angioplasty with a potential to improve safety. Unfortunately this advantage was forfeited by blatant overuse. About 25% of PCI procedures can possibly benefit from a stent, that is, the 30% that would either have an abrupt closure (about 5%) or a significant restenosis (about 25%) minus about 5% of stent failures because of thrombotic occlusion or in-stent restenosis. In stark contrast to that fact, stents are currently intentionally used in all cases. The problems with stents (side branch occlusion, distal embolisation, stent thrombosis) in the 75% of patients receiving but not needing them all but annihilate the prognostic benefit that stents would afford if they were used more judiciously. Although not usually acknowledged, the disappointing failure of the coronary stent to impact beneficially on prognostic endpoints (survival and freedom of myocardial infarction), prevented what had been foretold with the introduction of the coronary stent, the gradual replacement of bypass surgery by PCI in multivessel disease. The current registry attests to 22% multivessel PCI procedures, higher than the 15–20% reported in the yearly European registry [7] but far from the 50–80% projected by experts asked for a 20-year-outlook in 1987, after coronary stents had been introduced.

Not only the restenoses persisted as a problem even with default stenting but also did in-stent restenosis prove more difficult to treat than post balloon restenosis. More precisely, the need for intervention was only reduced from about 25% to 15% with the introduction of general stenting and this reduction was further compromised by the fact that in-stent restenosis was a more daunting problem

to resolve than the recurrent lesion after plain balloon angioplasty. Brachytherapy flickered up as an option for a moment but it turned out that 10 patients had to be irradiated to keep one of them from needing a reintervention, This can hardly be considered a bargain. Brachytherapy was doomed before its bane of late thrombosis became apparent and before the drug-eluting stent (DES) offered a much more user-friendly remedy for the in-stent restenosis problem.

With DES (active stents), for the first time in cardiovascular medicine a new method was introduced that (at least a first glance) only had upsides but no downsides, the higher purchase price notwithstanding. It looked like a win-win situation for doctor and patient (improved result but no change in technique and no new side effects) and the industry (higher revenue even before the increase in numbers). The initial concern voiced by some, that the thinning of the neointimal stent coverage would reduce restenosis but also increase the risk for stent thrombosis [8] was hushed by cleanly conducted randomised trials showing no such increase in risk. However, paradise is for heaven and not for earth. Late thrombosis turned out to be indeed more common with DES than with the bare metal (passive) stents albeit only by about 0.5% per year over the first years. While some farfetched theories for this have been offered, the most likely cause is the thin coat on the stent surface. This thin coat can be compared to the thin-cap plaque in unstable angina with a propensity for fissure or rupture and subsequent thrombosis. The fact that the Taxus stent with the somewhat thicker coat has a thrombosis rate similar to that of the Cypher stent with a thinner coat can be explained an inhomogeneous coverage of certain active stents. An overall thicker coat may be extremely thin at the very stent strut while a somewhat thinner coat may be more homogeneous and comparatively thicker at the stent struts (while thinner between the struts). This can explain a lower restenosis rate and at the same time a better safety profile. The thienopyridines are once again profiting from a misinterpretation of processes and data. Already with the introduction of the stent they had garnered only partially deserved merits. They had been introduced in parallel to the transition from bail-out stenting (stenting only in case of a poor balloon angioplasty result) to default stenting, and the marked reduction in stent thrombosis going along with these changes was credited to the thienopyridines alone, while it was mostly due to the change in indications and techniques. Again, the fact that late stent thrombosis usually occurred after the traditional limited period of thienopyridine use was misinterpreted in the sense, that the lack of the thienpopyridine was considered the cause of the stent thrombosis. It was ignored, that most patients without late stent thrombosis were off thienopyridines as well. Having said that, it is certainly wise to associate the thienopyridine clopidogrel to acetylsalicylic acid in patients with drug-eluting stents, in patients with bare metal stents, in patients after balloon angioplasty, and even in patients with coronary artery disease but no intervention. Yet the role of clopidogrel in preventing stent thrombosis (or causing it when stopped) is overrated. If a patient who has received (drug-eluting) stents recently needs to undergo major surgery and clopidogrel is stopped for that reason, the stent thrombosis that may occur during or immediately after the surgery is more due to the hyperthrombogenicity induced by the insult of surgery than by the discontinuation of clopidogrel. In other words, most of these unfortunate patients would have had no stent thrombosis if clopidogrel had been stopped but no surgery performed or the same stent thrombosis if they had undergone surgery without stopping clopidogrel before.

The train has left the station. PCI will be done with stenting and active stents will completely supplant passive stents in not so far future even where they have not already done so. PCI will continue to perform best in early coronary artery disease but this will be more and more the typical stage that coronary artery disease is documented in. Hence, instead of the 15% of coronary revascularisation procedures by PCI projected by Grüntzig in the early eighties, coronary bypass surgery will be reduced to about that percentage before the end of this decade. Again, this is not so much due to an expansion of indications for PCI but to a drastic reduction of patients with full-grown multivessel disease when they first come to the attention of a heart specialist.

Once a technique has reached 30 years, only few people still care about where it came from; and cross your heart, it is more fitting to rejoice the current potential and role of PCI and its brilliant future than to sentimentally reminisce about its past. Let us celebrate and then move on.

Abstracting from electrical ablation therapy in electrophysiology, another giant branch of interventional cardiology worthy of an editorial on its own by another editorialist, two

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procedures have what it takes to even challenge PCI in its primacy.

Closure of the patent foramen ovale (PFO) is calculated to be needed yearly in a number of patients representing about 10% of those undergoing PCI if the stringent and irrational by restrictive current recommendations are honoured. Once we wake up from our intellectual delusion that the PFO only needs to be considered after all other stroke causes were excluded, indications will at least quadruple. Why should a PFO only be a potential cause of a stroke, if the stroke has been termed cryptogenic by exclusion of all other causes? The search for the PFO should be the first thing to do in young patients and a simultaneous part of the work-up in older patients. The PFO is a potential cause for stroke, not more and not less. It is more dangerous in elderly people because the presence of small clots in the venous systems steeply increases after the age of 50 years. Of course there are more competitive causes in the elderly, but this does by no means acquit the PFO. Once the idea spreads that the PFO should possibly be closed before it causes havoc (think of the horrid fate of a young person losing sight or speech to a stroke while being likely to live "healthily" for another 50 or more years), at least the 4% of people with a PFO and a flimsy septum primum (atrial septal aneurysm) will become targets for a once in a lifetime procedure. Finally, if 4% of the population have to undergo a procedure, it will be further refined to come close to a "mechanical vaccination" (which it almost is already today). This might then open the indication field to the full 25% of PFO carriers, because even a small PFO can potentially have disastrous consequences or even kill the person, not to mention that migraine may be improved and diving or climbing may be safer. Companies and institutions with interest in PFO closures are currently hastily conducting migraine trials just to get the foot in the door. While it takes about a year to prove (or disprove, which is unlikely) that closing the PFO improves migraine, it will take between 10 and 20 years to prove that it is prognostically beneficial via prevention of paradoxical emboli. Companies producing PFO closure devices want supporting data before they run out of venture capital and physicians offering the technique want recognition before they retire.

Every year, Switzerland sees more than 20 000 new PFOs (25% of about 80 000 births plus immigrants). Should screening for and closure of the PFO in the teens become as accepted as putting braces to the teeth, these 20 000 would represent the annual number of procedures plus a few re-interventions for incomplete results, once an estimated backlog of 1.5 million PFOs have been taken care of. Should PCI figures level off at about 20 000 per year, PFO closure has the potential to briefly dominate and subsequently at least rival PCI numerically as the most common procedure.

While closure of the PFO already is an outpatient procedure, requiring a venous stick and 15 minutes of easy catheter manipulation with the patient able to go back to a normal physical life within a couple of hours, the second runner-up of PCI, aortic valve replacement, is and will remain a delicate and risky challenge for both the patient and the operator. However, senile aortic stenosis, and by the same token, aortic regurgitation, are common problems in our aging population. It is foreseeable, that percutaneous aortic valve replacement, already ushered in a number of countries but not yet performed in Switzerland, will become the third most common catheter-based cardiac (non-electrophysiologic) intervention within 5–10 years. This should already impact on the type of aortic valves implanted surgically today in the sense that tissue valves be preferred. By the time they will need replacement (in about 10 years), the percutaneous approach is almost certain to be a routine technique. Mitral valvuloplasty, closure of atrial or ventricular septal defects, alcohol ablation of obstructive hypertrophic cardiomyopathy, and other corrections of congenital defects will remain niche procedures. Their numbers have remained stable for the past 10 years in the Swiss registry and there is no reason to believe that this will change. Neither is there reason to believe that inoculation of stem cells or growth factors into cardiac tissue will bring about any clinical benefit to write home about before the millennium becomes a teenager (or ever).

Let us worship interventional cardiology. It has turned a handsome specialty into the beauty queen of modern medicine. It has fostered independency of cardiology and independency has fostered cardiology exemplified by the fact that the only university hospital with an independent cardiovascular department boasts the highest efficiency in Switzerland. It has turned cardiology as a whole and in particular some cardiology subspecialists from thinkers into (hopefully thinking) doers. It has created a fruitful symbiosis between doctors and the device industry, it has nurtured curricula and careers, and it provides a

large number of jobs (engendering salaries but also satisfaction); and all that was not to be foretold 30 years ago.

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