Merriam Webster defines a human generation as the time from the birth of parents to that of their offspring. Typically, that time is 20 to 30 years. Thus, it has been 1 human generation from Andreas Gruntzig’s original description of balloon angioplasty in 1978 to its 30th anniversary in 2008. Three months after this report, one of us (B.P.O.) was born to a father (W.W.O.) who was starting his career in cardiac medicine. Thus, 2008 for us is a year of transition of a cardiac interventionalist from one generation to the next. At this time, it is fitting to reflect on the people, the procedure, and the practice in the first generation of angioplasty. In this issue of Circulation: Cardiovascular Interventions, Venkitachalam et al provide an overview of the changes that have occurred in practice and outcomes of the 1985–1986 National Heart, Lung, and Blood Institute (NHLBI) Registry and the NHLBI Dynamic Registry. The report highlights the remarkable distance we have covered with this procedure in a generation.

Imagine for a moment that you were a young investigator in 2008 and had invented a new device to treat coronary occlusions. You need to obtain millions of dollars in start-up funding and get institutional review board and Food and Drug Administration approval to initiate US clinical trials. The device is designed to treat young patients with stable angina, single-vessel disease, focal, concentric proximal lesions, and normal left ventricular function. The device has to be inserted through a 10F sheath and uses 9F guide catheters. Each procedure takes 3 to 4 hours to perform. Your success rate was 63% and the rate of myocardial infarction was 5%, with 24% of patients requiring coronary artery bypass (CABG) before discharge. How likely is it that funding would develop or that institutional review board or Food and Drug Administration approval to initiate US testing would occur today? How likely is it that US commercial sales would ever occur? Yet, these were the starting points for a field that now treats more than 2 million patients worldwide and generates in excess of 10 billion dollars per year in revenue to device companies. How did we get from such an inauspicious start to such a massive industry in 1 human generation?

The original NHLBI Registry3 in combination with the present report2 is a wonderful chronicle of the progress made in this field. Starting in 1977, the registry incorporated all original US and European centers that started performing balloon angioplasty. The scientific contributors to the registry were the original guiding force in nurturing and developing the field. Registry coauthors like Gruntzig, Bourassa, Detre, Jacobs, Cowley, Williams, Cohen, Wilensky, Faxon, Dorros, Mock, Kip, Block, Bentivoglio, Kent, King, and Myler made enormous seminal contributions to the field. Their talent and drive took this awkward, unpredictable procedure from a gimmick to a mainstay of cardiovascular health care in 1 generation.

NHLBI Registry observations set the agenda for research questions during the last 20 years. Differences in outcome between men and women, between young and old, and between stable and unstable angina were defined in the registry papers. The impact of a learning curve and lesion complexity were defined. The risks of acute occlusion and the need for emergency CABG were defined, and the incidence and the cause of restenosis was described. Progression of nonculprit lesion was discussed, and the long-term impact of incomplete revascularization was defined. For 20 years, ongoing observations from the registry have set a benchmark for practice that has been of enormous value to professional societies, hospital administrations, insurance plans, and government payors.

Although the NHLBI Registry encompassed 1 human generation, it spanned multiple technical generations. An unappreciated technical advance has been the change in imaging. Generation of x-rays is fundamental to percutaneous coronary intervention (PCI). A major revolution in x-ray imaging was propelled by the need for finer image resolution. At the dawn of angioplasty, most catheterization laboratories were equipped with exquisite hemodynamic recording instruments because valvular heart disease was such a large portion of catheterization laboratory business. X-ray image intensifiers really only needed to visualize large structures. Often, the gantry was fixed to the floor or ceiling, and angled projections were not available. In fact, many laboratories had cradles as tables so that patients could be rolled for right anterior oblique (RAO) and left anterior oblique (LAO) projections! Fluoroscopy quality was terrible. Instant replay could only occur on grainy video tape players. Many laboratories placed cellophone on the television monitors and drew crayon diagrams of vessels as guides for lesion location.

Today, pulsed digital fluoroscopy, digital angiography, instant replay with zoom capability, and flat-panel detectors have dramatically advanced the field of angioplasty. Many PCI techniques, including meticulous stent placement, jailed side-branch access, retrograde chronic total occlusion (CTO) recanalization, and complex bifurcation stenting, could not be possible with the first generation of coronary imaging.
Angioplasty hardware has also had multiple generations. Guide catheters have decreased from 9F to 5F or 6F. The procedure itself can be routinely performed transradially. Balloons have changed from fixed wire to over-the-wire steerable devices. Guide wires have markedly improved and decreased from 0.18 to 0.14 in, with the smaller balloon crossing profile and shaft diameter improving the ability of balloons to cross lesions. New coronary devices beyond “plain old balloon angioplasty” have even altered the name of the endeavor to percutaneous coronary intervention. Many methods of safely expanding coronary occlusions were pioneered. Lasers, rotational atherectomy, extraction atherectomy, and directional atherectomy have all been used extensively, but no method, except for intracoronary stents, has made a major impact. Technically, 3 major generations have occurred: first, the original fixed wire era, described in the 1977–1982 registry experience; second, the over-the-wire era, described in the 1985–1986 Percutaneous Transluminal Coronary Angioplasty Registry; and third, the stent era, described in the 1997–2006 Dynamic Registry.

Venkitachalam et al elegantly defines changes in patient profiles and improvements in outcomes for these 3 eras. The original NHLBI Registry from 1977 to 1981 constitutes the dawn of the procedure. It involved primarily the use of fixed-wire balloons and resulted in a 63% success rate, with 24% of patients requiring CABG before hospital discharge. In the early 1980s, steerable removable guide-wire technology evolved. The 1985–1986 Percutaneous Transluminal Coronary Angioplasty Registry found that success rates increased to 74%. Rates of emergency bypass were decreased to 6%.

The improvement in safety and predictability of PCI is nicely documented in the registry experience. Original PCI equipment was bulky and nonsteerable. The mode of failure of the procedure was largely related to the inability to reach lesions or cross. The high failure rate led to a 24% rate of CABG. As steerable wires and lower-profile devices became used, the 1985–1986 registry found that success rates increased to 82%. Because the mode of failure changed, abrupt occlusion and dissection became dominant modes of failure. The need for bypass surgery decreased to 6%. In the stent era, success rates increased from 94% to 97%. Even within the stent era, stent improvements led to more flexible and deliverable stents. Acute occlusion and occlusive dissection disappeared as a mode of failure. In a major clinical triumph, none of the 1244 patients treated in wave 5 of the Dynamic Registry required CABG. PCI had finally evolved to a point equal to that of the technical success and predictability of CABG.

The marked technical advances led to expansion of the patient population eligible for surgery. Patients older than 65 years increased from 28% to 47%. More women and minorities were treated. Severe comorbidities increased from 6% to 34%. Diabetes increased in frequency from 14% to 30%, and finally, acute myocardial infarction as the primary indication increased from 10% to 38%. It is striking that even as the patients treated were older, sicker, and markedly more often treated for acute myocardial infarction, overall mortality did not increase.

With one generation of coronary interventionalist ending (W.W.O.) and one about to begin (B.P.O.), what challenges and opportunities will the next generation face? There is no doubt that unimaginable advances will occur. It is conceivable that remote robotic-guided and magnetic-guided procedures will occur. Major new breakthroughs will occur in structural heart disease. Certainly, percutaneous aortic valve implantation will become routine. Percutaneous mitral valve repair or replacement lags behind aortic valve therapy but will also occur. Imaging will evolve to incorporate computed tomography, MRI, and echo imaging. Even basic training will fundamentally change as virtual reality simulations will make training much less of an apprenticeship and more of a predictable discipline. The widespread adoption of electronic medical records will make real-time national registries in the United States possible.

Not all changes will be for the good. The regulatory environment will become increasing more adverse to risk and cumbersome. When angioplasty first started, 60 patients treated and followed up for 6 months was all that was required for US Food and Drug Administration to provide approval for the device. Now, the Food and Drug Administration is pushing for treatment of tens of thousands of patients with years of follow-up. It is also pushing for rapid randomized trials. In the current regulatory environment, coronary angioplasty could never be developed like it was in 1977.

What lessons do the NHLBI Registry investigators leave for the next generation? First, patient safety is paramount. They learned that low-risk patients must be treated with early technology. The next lesson is that careful prospective registries are of enormous value in the early evolving stages of a technology and procedure. A field takes 15 to 20 years to mature, and premature attempts at randomized trials may kill a technology that could have value. Imagine if the Syntax trial had been attempted in 1977 rather than 2007. Premature randomized trials happened with directional atherectomy and transmyocardial laser revascularization. Both technologies never evolved beyond early stages after the initial randomized trials were unsuccessful. Finally, it is our fervent hope that the spirit of collegiality, the openness to share successes and failures, and the unblinking dedication to publication of unbiased outcomes that is the hallmark of the NHLBI Registry will be a legacy and a gift that is passed to the next generation. The lives of future patients depend on this.

Disclosures

None.

References


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