The Mechanism of Balloon Impact in Percutaneous Transluminal Coronary Angioplasty in Eccentric Coronary Artery Narrowings

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In the early days of percutaneous transluminal coronary angioplasty (PTCA) and in particular before the stent era, the selection of the appropriate balloon diameter was crucial for risk and success of the intervention. With larger balloon diameters the risk of vessel wall dissection was increased but the rate of restenosis was much higher when smaller balloons were used. In retrospect, it is surprising how few histopathological studies have been performed during this time period to study the mechanism of PTCA. A main reason for this may have been that PTCA has been working well in most cases and was very effective for the relief of angina symptoms. This lack of basic research led even to the erroneous assumption by the PTCA pioneer Andreas Gruentzig, that the angioplasty procedure be characterized "by a concentric expansion of the vessel over a suitable portion of its length." This view has been challenged by Professor Jesse E. Edwards, a distinguished cardiovascular pathologist from Minneapolis, MN/USA, with a world-wide reputation. The disagreement was based on the finding that 70% of coronary stenoses have been found to be eccentric and only 30% to be concentric narrowings. Jesse E. Edwards therefore initiated a histopathological study about the mechanism of balloon angioplasty in coronary arteries of freshly autopsied hearts. The study was performed in 1982 by one of the authors (HS), then a young cardiology fellow in the laboratories of Professor Kurt A. Amplatz. Kurt A. Amplatz was in an early stage of his career to later become a world famous pioneer for the development of a variety of catheters, wires, instruments, and devices for the closure of the patent foramen ovale, atrial and ventricular septal defects, and the left atrial appendage. The study documents were unavailable for almost 40 years but have recently been made accessible again. Conclusion: This manuscript discusses the main findings of the histopathological study on the mechanism of coronary balloon dilatation and is dedicated to 2 giants of cardiovascular research, Jesse E. Edwards and Kurt A. Amplatz. **(Am J Cardiol 2021;146:128−131)**

Coronary atherosclerotic lesions have been found to be eccentrically located in 70% and concentrically located in 30% of histological series of coronary arteries.[1] The presence of a normal arterial wall opposite to an obstructive coronary artery has important implications for the mechanism of the balloon impact in percutaneous transluminal coronary angioplasty (PTCA). However, there are only few studies about morphologic changes of coronary arteries after PTCA in human hearts.[2-5] This study reports the results of angiographic and pathological examinations of coronary arteries after PTCA in post-mortem human heart specimens and presents a histological classification.

Eleven postmortem human hearts (7 female, 4 male, age 57 to 91 years) were examined within 4 hours after autopsy and within 24 hours after death. It was tried to avoid significant postmortem changes of the bioelastic properties of the arterial wall with a potential impact on the results of the PTCA as much as possible by the procedure protocol. After assessment of coronary calcifications using a special soft tissue film, the coronary arteries were filled with Renographin 76 under controlled pressure conditions for assessment and grading of stenotic arterial segments and for grading of luminal narrowing. Dilatation was performed using commercially available coronary balloon catheters (BARD, Murray Hill NJ/USA) with 5 sequential balloon inflation-deflation cycles with water at a maximum pressure of 5 atmospheres. Balloon diameter was selected according to the diameter of the nondiseased vessel proximal to the stenosis. In preparation for histological examination, the coronary arteries were flushed and perfused with 10% formaldehyd solution under constant pressure and temperature conditions. Coronary arteries were filled with a gelatine-barium sulphate mixture. After careful dissection, the coronary arteries were cut transversally at 2 to 5 mm intervals and processed for light microscopy. Hematoxylin-eosin and elastic tissue stain preparations were prepared to assess nature and extend of vessel damage. A total of 57 stenotic coronary arteries underwent balloon angioplasty and in 42 segments exact correlations between angiographic and histological findings could be established. They pertained to 14 left anterior descending, 8 left circumflex, and 20 right coronary arteries. Coronary artery stenoses of >50% were

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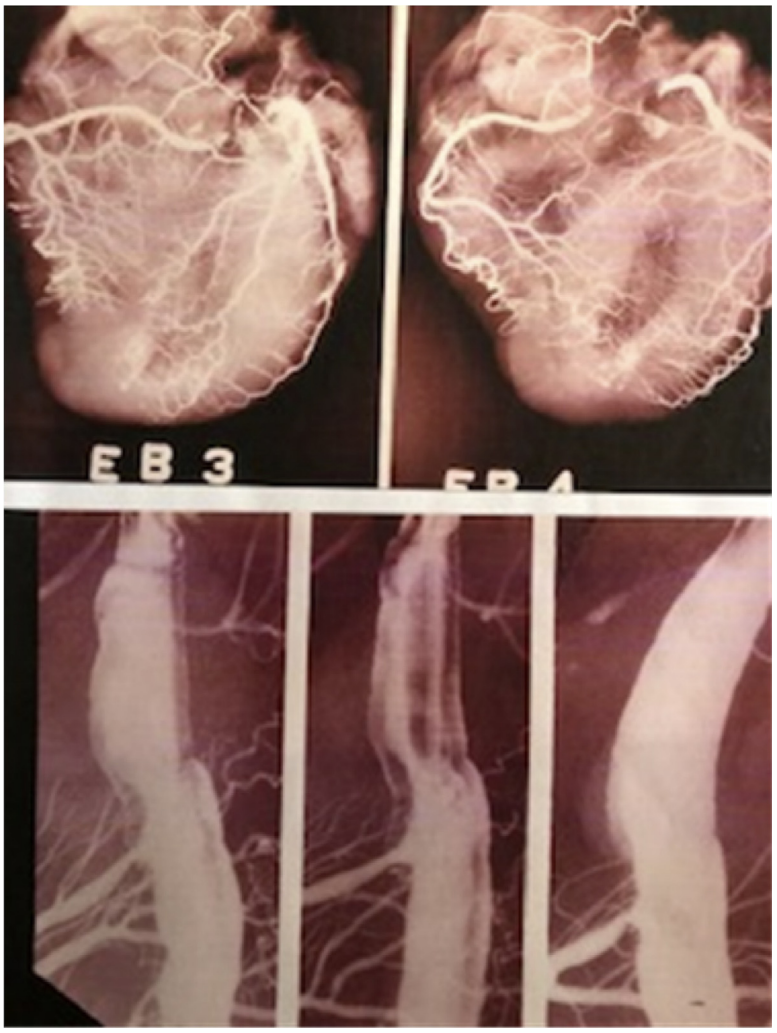

Figure 1. Autopsy specimen of a human heart after perfusion of the coronary arteries with a gelatine-barium sulphate mixture (upper panel) and during the balloon dilation procedure (lower panel).

present in 7/14 left anterior descending, 6/8 left circumflex, and 10/20 right coronary arteries segments. The mean diameter of coronary arteries proximal to the dilated segments was 3.2 mm. An increase of the transluminal diameter could be observed in 33 (78%) of the 42 segments after PTCA (Figure 1).

Superficial intima splitting, intimal tears, and focal intima denudation were common findings in all 42 segments. Rupture of the internal elastic membrane was observed in 9 segments (21%), tears in the media in 5 segments (12%), rupture of the media in 7 segments (17%), and rupture of the adventitia in 8 segments (42%). No signs of compression, remodelling, or redistribution of the atherosclerotic material were found. Except for areas of detachment from the media, fibrous and fatty plaques in markedly dilated vessels were structurally indistinguishable from control segments. Components of well-developed plaques such as cholesterol clefts were similar in size, shape, and orientation in dilated and nondilated vessels. However, plaque dehiscence and fracture were seen in several eccentric atherosclerotic lesions. One lesion appeared to be successfully dilated angiographically but proved histologically to have a media dissection.

Histological changes have been classified according to the ruptured wall structure as grade I (intima), grade II (media), and grade III (adventitia). There was a significant correlation between balloon size and grade of histological changes: The correlation between balloon size and diameter of the stenosis was 1.48 ± 0.2 in grade I, 1.61 ± 0.2 in grade II, and 1.82 ± 0.2 in grade III lesions ($r = 0.99$). Examples for each of the 3 stages are shown in Figure 2.

Results of the investigation indicate that the relation between balloon size and the diameter of the stenosis seems to be more important for the degree of morphologic changes than the relation between balloon size and vessel diameter proximal to the stenosis. The risk of dissection of the vessel wall increases in an almost linear fashion with increasing balloon size. The main histopathological result was that there were no signs of compression, remodelling, or redistribution of the atherosclerotic material. Except for areas of detachment from the media, fibrous and fatty plaques in markedly dilated vessels were structurally indistinguishable from control segments.

The initial theory of percutaneous angioplasty pioneers about the mechanism of lumen gain after catheter impact

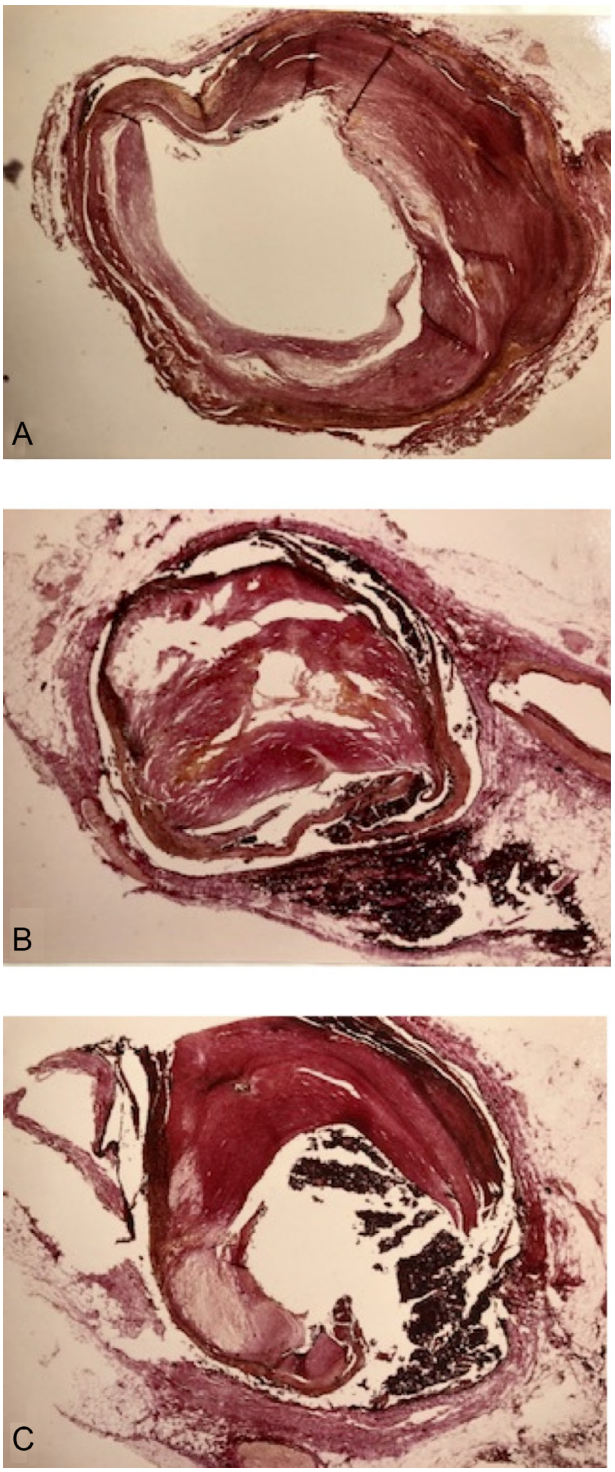

Figure 2. *Histological changes. Grade I:* Rupture of the internal elastic membrane (A), *Grade II:* Rupture of the media (B), *Grade III:* Rupture of the media and the adventitia with contrast medium exit into the paravalvular tissue (C).

on peripheral vessels[6] or balloon impact on peripheral or coronary vessels[7] based on vessel distention and plaque compression (footprint in the snow). Histology refuted that and dissection of one or several layers of the vessel wall quickly moved into the limelight as acting mechanism of lumen enlargement. However, dissection heralded abrupt closure, the most dreaded acute complication of PTCA before coronary stents. Interventional cardiologists intuitively and effectively reacted by undersizing balloons to minimize dissection. They were readier to accept later restenosis than abrupt closure. The first was typically blamed to them, the second to nature. Restenosis rates climbed from about 30% in the initial era when appropriate size balloons were employed to 50% and more in the era of undersized balloons. This happened more conspicuously in the United States of America with an established culture of malpractice litigations than in the rest of the world. Based on this obvious and understandable trend, word passed around in the 1980s that American PTCA operators dilated more lesions less whereas European PTCA operators dilated less lesions more. The advent of coronary stents put an end to that trend. Dissections were tacked back to the wall, initially only in obviously threatening cases (bail-out stenting) and eventually in all cases (default stenting). Pathological findings like the ones described here went to the museum. There we found them and undusted them to present them here as a tribute to old times and their luminaries Jesse E. Edwards and Kurt A. Amplatz.

This manuscript is dedicated to Prof. Jesse E. Edwards und Prof. Kurt A. Amplatz from Minneapolis MN/USA in memory of their great contributions to the basic understanding of cardiovascular pathology and interventional cardiology

Jesse E. Edwards, MD, (July 14, 1911 – May 18, 2008) was an American cardiac pathologist whose pioneering work substantially influenced the course of modern cardiology, advanced open heart surgery, and enhanced understanding of both, congenital and acquired heart diseases. He served as president of the American Heart Association in 1968 and was awarded the organization's Gold Heart Award, among many other honors. He assembled a formidable collection of over 22,000 human hearts, vessels, and lungs to let physicians study coronary artery disease, congenital defects, and trauma (picture by courtesy of the Edwards family). The collection became a principal resource for his three-volume illustrated reference "An Atlas of Acquired Diseases of the Heart and Great Vessels" (1961).

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Kurt A. Amplatz, MD (left, February 25, 1924 – November 6, 2019) was a great pioneer in interventional radiology and cardiology. His inventions have helped millions and saved countless lives. He provided scientists and health care professionals with concepts and tools for the treatment of cardiovascular disease. He introduced transfemoral percutaneous left heart catheterization in 1958, developed the first vascular injector in 1960, modified the Seldinger technique for percutaneous vessel access, and developed the Amplatz coronary artery catheters, an array of guidewires, and a gamut of other devices, such as the Amplatz Gooseneck Snare, Amplatzer septal and left atrial appendage occluders, and Amplatzer Vascular Plugs. He received numerous awards including the Gold Medal

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Declaration of Competing Interest

Nothing to disclose.

1. Saner H, Gobel L, Salomonowitz E, Erlien DA, Edwards JE. The disease-free wall in coronary atherosclerosis: Its relation to degree of obstruction. *J Am Coll Cardiol* 1985;6:1096–1099.
2. Block PC. Mechanism of transluminal angioplasty. *Am J Cardiol* 1984; 63:69C–71C.
3. Castaneda-Zuniga WR, Sibley R, Amplatz K. The pathologic basis of angioplasty. *Angiology* 1984;35:195–205.
4. Kohchi K, Takebayashi S, Block P, Hiroki T, Nobuyoshi M. Arterial changes after percutaneous transluminal coronary angioplasty. *J Am Coll Cardiol* 1987;10:592–599.
5. Farb A, Virmani R, Atkinson JB, Kolodgie FD. Plaque morphology and pathologic changes in arteries from patients dying after coronary balloon angioplasty. *J Am Coll Cardiol* 1990;16:1421–1429.
6. Dotter CT, Judkins MP. Transluminal treatment of arteriosclerotic obstruction: description of a new techic and a preliminary report of its application. *Circulation* 1964;3:654–670.
7. Grüntzig A. Perkutane Dilatation von Coronarstenosen – Beschreibung eines neuen Kathetersystems. *Klin Wschr* 1976;54:543–545.