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Contents

Stent supported carotid angioplasty: A Gordian knot to be unraveled

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Conflicts of interest statement

The author has or has had equity positions in numerous medical vendors who are involved in various aspects of carotid angioplasty: Boston Scientific Corporation, Medtronic, Embolic Protection Inc., ArteriA, Inc., Endotex, and Johnson & Johnson Inc.

Introduction

During the last 23 years, angioplasty has been an integral part of my existence. Its ever-changing form and direction continually stimulated, excited, challenged me. Angioplasty has demanded that I learn how to critically think along with re-visitation, re-thinking, and re-addressing ideas, procedures, methodologies, techniques, and protocols. Clinical endpoints, patient inclusion and exclusion criteria, an investigator's responsibility, informed patient consent, and data collection were topics, which were no longer insignificant, unimportant, or secondary issues. The meaning and limitations of data only became understandable during the challenge of creating comprehensible, scientific concise written and oral communications. The privilege to peer review colleagues' data communications broadened my appreciation of the scientific method, quality data, physician adherence to protocol, appropriate statistical utilization as well as the distinctions between interpretation (explanation), interpolation (insertion), and extrapolation (inference). These edifying experiences helped to shape my patient care perspectives.

Today, balloons, stents, and embolic protection devices, as treatment for extracranial obliterative disease have created a predicament, not dissimilar to the percutaneous interventions of coronary angioplasty and mitral valvuloplasty. The latter two procedures, using observational data, supplanted standard surgeries, and these successions occurred without the imprimatur of a large, expensive, "randomized" trial, which juxtaposed the percutaneous against the surgical procedure.

Historical Perspective

My introduction to angioplasty's potential use in the cerebrovascular circulation occurred in 1980, in Zurich at the 3rd Gruentzig Angioplasty Course. A patient with recurrent symptoms of basilar artery insufficiency, which could not be resolved despite multiple surgeries, underwent surgical exposure of the left vertebral at the base of the skull, which facilitated balloon catheter insertion, advancement, and dilatation of the obstructing posterior circulation lesion. This daring maneuver produced symptom resolution, after a presumed arterial spasm induced period of "transient" quadriplegia [1]. My extracranial bifurcation carotid angioplasty experience began in 1988; an 88-year-old man with severe aortic stenosis, congestive heart failure, a severe right internal carotid artery stenosis, and daily recurring transient ischemic attacks, could not be managed with standard anticoagulant therapy. Two senior cardiovascular surgeons refused the patient for endarterectomy, with one surgeon reaffirming his opinion during a second consultation. The patient, under these circumstances, was considered to be a candidate for the compassionate use of balloon angioplasty. The patient and family were meticulously informed about the unusual clinical setting, and the minimal experience of angioplasty within this setting, nevertheless, the patient and family elected to undergo the angioplasty procedure, which was performed without incident, using coronary angioplasty equipment. Post-operatively, the patient had no further TIA's, and was discharged within a few days. About 4 months later, although the patient was neurologically asymptomatic, follow-up angiography showed a still significant lesion, which was uneventfully dilated with a larger peripheral angioplasty balloon. This therapy, despite the patient's clinical success, created a furor among the hospital's surgeons.

Two years and tens of thousands of dollars were required to obtain approval of a physician sponsored investigational device exemption (IDE) carotid balloon angioplasty protocol for high-risk surgical patients from the Food and Drug Administration (FDA), and the hospital institutional review board (IRB). The first case, under this IDE, was a symptomatic 60 year-old man with occlusion of the left carotid and vertebral arteries whose balloon dilation was complicated by a flow obstructing intimal tear. The patient lost consciousness and seized. With no other immediate options of re-establishing flow available, a Palmaztm biliary (P204) stent was deployed. Antegrade flow was restored; the patient regained consciousness without neurological impairment. This protocol deviation (i.e., use of a stent) led to a cessation of the study, with an inexplicable assertion advanced that the proper care for this unconscious, convulsing patient, with an acute carotid artery occlusion, should have been an emergency carotid endarterectomy. No thought was given to what had actually occurred, and the implications of the immediate clinical result. The patient did well, remained asymptomatic, and follow-up angiography at 6 and 24 months showed no lesion recurrence. Subsequently, after numerous correspondence and verbal

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exchanges with the FDA and the IRB, an agreement was reached that permitted recommencement of the IDE. A codicil, outlined in a letter, allowed peripheral stent placement in a limited number of patients if a flow-limiting lesion resulted after balloon angioplasty. This was the inception of stent supported carotid angioplasty; subsequently, balloon-expandable-stent deployment was used judiciously. One subsequent experience defined the necessity to convert from balloon- to self-expanding stents. A symptomatic 52-year-old man, 1 month after successful Palmaztm biliary stent supported angioplasty of a severe internal right carotid had recurrence of neurologic symptoms. A crushed Palmaztm stent was detected, and no plausible explanation could be deciphered [2]. The deformed stent was successfully re-expanded and the patient became asymptomatic. The lack of any reasonable explanation for this occurrence made everyone believe that a self-expanding, resilient stent might have avoided this situation, and future problems.

"Changes in attitude and changes in latitude"

During the last two decades, opinions concerning the seminal and creative work of Theron [3-9] have dramatically changed. Editorials [10-19] have been disparate. Some physicians spoke of caution, while others advanced passionate diatribes against the "unconscionable and uncontrolled" usage of stent-supported carotid angioplasty. A few physicians, loudly, and clearly, made unsubstantiated pronouncements of its virtue as the primary treatment for extracranial carotid bifurcation obliterative disease. The subsequent verbal jousts often focused upon why should endarterectomy, "the gold-standard", be challenged let alone potentially be eliminated from the surgeon's repertoire; and, interrogatories often centered about the appropriateness of cardiologists entering this surgical fiefdom of vascular disease. These interactions were not pleasant, however, the persistence, perseverance, tenacity, openness, and forthrightness by these daring physicians has enabled this endovascular therapeutic application to evolve. Thus, the numerous recent publications [20-26] have prompted my revisitation of this issue.

Cardiologists, spurred onwards by their successful endovascular treatments of a variety of cardiac pathologies, have vigorously championed the proposal that their talents should not be restricted to a specific anatomic region. Such pronouncements disturbed interventional radiologists and surgeons, who perceived this posture to be self-serving, gratuitous, as well as demeaning of these surgical specialties, their accomplishments, perspectives, and concerns. However, the vociferous outcries of foul by these same specialties fortuitously not only failed to acknowledge the cardiologists' successes but also, often, summarily dismissed these contributions [27-30]. Furthermore, the scientific communications, effective oral presentations and illustrative, instructive live-case demonstrations made more obvious and less veiled the cardiologists' intent, as well as the extant and significant interdisciplinary tensions. Strained relations were often compounded by the surgeons' and radiologists' angst about the blurring of previously "clearly" defined specialty boundaries, contractual arrangements, their medical future, a loss of specific procedural activity, and a reduction in compensation. The cardiologist's effective communication and research skills often cornered surgeons and radiologists into posturing which occasionally resulted in passionate, and unattractive responses. Perhaps, the final straws, which made these interdisciplinary tensions more taut, were not only the cardiologists' early extrapolations that stent-supported carotid angioplasty was superior to carotid endarterectomy but also the numbers of cardiologists who would be doing these procedures.

The utilization of the unorthodox technique of stent-supported carotid angioplasty was considered apropos for unusual and extreme clinical situations; and, its employment in ordinary, regular clinical situations, outside of well-designed and carefully monitored experimental protocols, was deemed inappropriate and even unethical. While the rationale for this position seemed reasonable and appropriate, there also co-existed a more Machiavellian position, which was that carotid endarterectomy was not going to be removed from the surgeon's repertoire. However, time has moved forward. Experience, time, and observational data accumulation now requires a re-consideration of the initial positions. The crucial interrogatory presently to consider is does "carotid angioplasty data indicate that stent-supported carotid angioplasty should be limited to only extra-ordinary clinical situations or should stent supported carotid angioplasty be utilized for symptomatic and asymptomatic patients with severe extracranial carotid bifurcation obstructive disease, who are reasonable surgical candidate?" A positive answer to this query has far reaching implications.

Data Assessment

For the last two decades, interventional cardiologists have routinely introduced new, unique, and brilliant therapeutic ideas, many of which supplanted standard procedures or therapies; the novel therapy had better immediate results, fewer complications, and superior outcomes. Stent supported carotid angioplasty has been not only successful in the odd situation but also has been recognized as an enabling procedure, since the treatable population has been expanded beyond that cohort of reasonable carotid endarterectomy candidates. Carotid angioplasty's immediate results and complication rates, even in the most difficult cases, remains equivalent if not superior to those achieved by carotid endarterectomy, and its follow-up results demonstrated prevention of subsequent ipsilateral neurologic events. Roubin and Iyer's non-randomized observational data [17, 18, 20-25, 32-34] underscores this position. Five hundred twenty eight consecutive patients, in whom 604 hemispheres were treated by stent revascularization of the stenotic carotid artery, underwent the procedure with a mortality of 1,6%, and a 0,6% fatal stroke and a 1% non-stroke death rate at 30 days. The major stroke rate was 1%, and the minor stroke rate was 4,8%. The overall 30-day stroke and death rate was 7,4%. Over the 5-year study period, the 30-day minor stroke rate improved from 7,1% for the first year to 3,1% for the fifth year ($P<0,05$). The best predictor of 30-day stroke and death was age >80 years. After the 30-day period, the incidence of fatal and nonfatal stroke was 3,2%. The 3-year freedom from ipsilateral or fatal stroke was 92+1%. These are exceptional data.

In the past, the quick and flippant dismissal by some cardiologists of carotid endarterectomy, the benchmark, against which carotid angioplasty had to be measured was irritating because of the superficial dismissal of carotid endarterectomy data. Furthermore, the numerous trials and publications concerning carotid endarterectomy data, for symptomatic and asymptomatic patients [35-45] employed by opponents of carotid angioplasty, were considered and presented as unimpeachable data. Initially, all attention was directed towards procedural outcomes. When it became apparent that angioplasty could be performed as simply and safely as CEA, then the argument metamorphosed into the fact that angioplasty had not demonstrated the long-term prevention of subsequent ipsilateral neurologic deficit(s). However, the cardiology procedural proponents, in creating their protocols, had demanded independent neurologic patient assessment, which was appropriate as well as clever and fortuitous; but what was initially not readily gleaned from the surgical literature was the absence of independent, immediate, and long-term neurologic assessment.

Recent publications have indicated that actual endarterectomy complication rates were far different than those quoted. Wennberg [46] detailed the variation in 30-day risk of stroke and death associated with carotid endarterectomy among 113,300 Medicare patients treated in 2699 non-federal hospitals, during 1992 to 1993, of which 86 institutions (TRIAL hospitals), had participated in the NASCET and ACAS trials, and 2613 institutions (non-TRIAL hospitals) had not been involved. Retrospectively, these two institutional groups' perioperative mortality data of 113,300 carotid endarterectomy patients was compared. The 30-day mortality (Figure 1) was 1.9% in TRIAL and 1,7% in NON-TRIAL hospitals. NON-TRIAL hospitals were stratified according to procedural volumes, which revealed mortalities of 1,7% in high, 1,9% in average, and 2,5% in low volume cohorts. When comparing TRIAL to NON-TRIAL institutions, the mortality risk reduction was 15% for high volume (1,4% vs. 1,7%), 25% for average volume (1,4% vs. 1,9%), and 43% for low volume (1,4% vs. 2,5%) institutions. TRIAL hospitals had the best results, and procedural volume directly impacted perioperative mortality. However, these mortality (not stroke) statistics were higher than generally quoted by surgeons. Thus, the mortality risks recorded for a patient in the carefully controlled endarterectomy trials probably do not correspond to those mortality risks, which a patient must face when undergoing carotid endarterectomy by low or medium volume surgeons. If these major carefully controlled trial results represented the best surgeons, with the best track records, operating on the most carefully chosen patient cohort, then what makes an "occasional carotid-endarterectomy-surgeon" believe he/she can utilize them when addressing a patient, while failing to disclose his/her data?

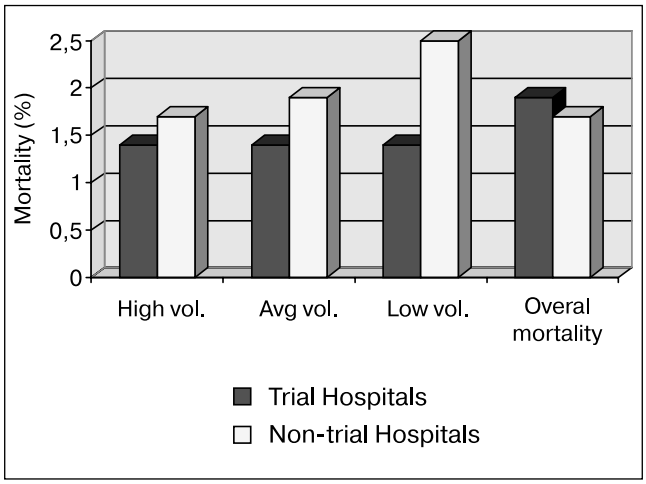

Figure 1. CEA Procedural Volume as it Relates to Operative Mortality

Furthermore, the generalized quoted statistics rarely are appropriate for the vast majority of potential surgical patients. Goldstein [47] assessed the impact of potential perioperative risk factors on carotid endarterectomy results in 12 academic centers. A random sample of 1160 asymptomatic endarterectomy patients had their charts abstracted with regard to perioperative complications. The perioperative stroke and death rate was 2,8% with the risk being similar for patients with cerebrovascular symptoms (1,8% vs. 4,2%; p=0,21). However, the postoperative stroke and death rate was more than 3 times higher in women (5,3% vs. 1,6%; p=0,02), more than 4 times higher in patients >75 years (7,8% vs. 1,8%; p=0,01), nearly 4 times higher in patients with congestive heart failure (8,6% vs. 2,3%; p=0,03), and nearly 9 times higher in patients who had undergone combined endarterectomy and coronary bypass surgery (18,7% vs. 2,1%; p<0,001). In addition, Rothwell and others have verified these conclusions [55-62] that a much higher incidence of stroke existed post endarterectomy, when independent neurological examination is performed.

Data "check"

Roubin and Iyer's numerous and carefully monitored studies [17, 18, 20-24, 32-34], all with independent neurologic assessment, never focused upon or included patient assessment of the aforementioned cognitive domains. However, their meritorious studies included many patients excluded from the major surgical trials (NASCET, ACAS, and ECST). As such, their data demand indagnation with regard the poor surgical candidates category. Observers have assumed that these patients were excluded from the trials because their potential surgical risk was high, and, by implication and extension, that the angioplasty procedure risks were increased. This conclusion is a misinterpretation of the protocols' intent. These patients were excluded, by en-large, from the surgical trials because their co-morbidity (ies) could potentially result in stroke. The difficulty avoided was the subsequent determination of whether a stroke was clearly attributed and causally related to the concomitant co-morbidity or the endarterectomy. Thus, inclusion of NASCET and ACAS ineligible patients into any study evaluating subsequent occurrences of neurologic events should be counterproductive. This is precisely the reason that Roubin and Iyer's data demands examination, especially with regard to the extremely low incidence of neurologic deficit during the nearly 5 years of follow-up. Despite the presence of a larger number of NASCET excluded patients, their data, with regard to acute procedural outcome and freedom from subsequent neurological events, were excel-

lent and superior to that of carotid endarterectomy, especially considering their patient cohort.

The Carotid and Vertebral Artery Transluminal Angioplasty study (CAVATAS) [48], involving 504 patients with high-grade symptomatic carotid stenosis who were randomized to carotid angioplasty [with stenting only in the case of a suboptimal result (only 55 /251 patients received a stent)] or carotid endarterectomy demonstrated no difference in procedural and long-term outcomes although, not unexpectedly, fewer complications were recorded with the interventional technique: cranial neuropathy (0 vs. 9%), and major groin or neck hematoma (1% vs. 7%). Amusingly, the angioplasty results were not better than anticipated, but the surgical results were worse than expected. These data were consistent with those of Wennberg and Goldstein.

The American Heart Association's guidelines for performance of carotid endarterectomy [63] imply that certain levels of risk are acceptable to reestablish carotid blood flow. However, the actual surgical data numbers do not appear to be synchronous to the guideline recommendations. In fact, those of stent-supported carotid angioplasty appear to clearly be better than those of minimal acceptable values outlined. Since the carotid artery is widely patent using stent-supported carotid angioplasty, and the follow-up data indicate that subsequent ipsilateral neurologic deficit is prevented, why should carotid endarterectomy be used in its place?

Randomization is the only true methodology

The premise that randomization is "the only valid and proper scientific" way in which an appropriate conclusion can be determined is nonsense. Many correct conclusions are obvious and or intuitive. Randomized trials' results cannot and should not be extrapolated as applicable for all patients and all medical situations. In fact, most medical problems can be resolved without the need of a randomized trial. A knife lying within a wound must be removed before repair; a lacerated blood vessel must be repaired to prevent further hemorrhage, and non-obstructed, antegrade arterial blood flow is better than impeded or absent flow. While the idea of not performing a randomized trial for stent-supported carotid angioplasty may be abhorrent to some, to me, today, this requirement is burdensome, absurd, and farcical. The espousement that these trials are absolutely and categorically necessary for the establishment of stent supported carotid angioplasty's primacy is erroneous; and, furthermore, the demand that certain trials must be done so as to gain governmental approval for re-imbursement for routine physician and hospital payments is horrific. While some small closed end randomized trials may elucidate specific issues, the pronouncements that all issues, to be adequately resolved, require randomization are flawed. Who are making these demands for us to do these trials, and upon what basis? Are these trials necessary for us to determine what is the best care for our patients? Are the physicians promulgating these positions using this platform for self-aggrandizement, to maintain their patient base, or to gain power and notoriety?

Clinical trials and clinical endpoints:

"The Acronym Studies"

Appropriate study endpoints were necessary to be determined so that conclusions based upon data collected appropriately addressed the hypothesis of whether these devices were beneficial. Presently, data indicate that the risks of performing carotid angioplasty in the vast majority of cardiologists' hands are similar if not superior to that of historical carotid endarterectomy series. Thus, why do we need to have these numerous acronyms entered into our vocabulary: CREST [72-74], SAPPHIRE, ARCHER, CARESS, SPACE, EVA-3S, or CAVATAS-2 or ICSS? For whose benefit are these trials? (Before answering the questions, see how they are designed.) CREST (carotid revascularization endarterectomy versus stent trial) addresses symptomatic low risk surgical patients. SAPPHIRE and ARCHER are registries that address stenting and angioplasty with distal protection in patients at high risk for endarterectomy. CARESS is an exegesis of asymptomatic or symptomatic patients within a registry format. SPACE is a randomized trial comparing stent-protected percutaneous angioplasty and carotid endarterectomy. EVA-3S compares endarterectomy versus angioplasty in patients with severe symptomatic carotid stenosis. CAVATAS-2 (or ICSS) compares primary stenting and endarterectomy. However, all these C-PTA studies have defined stroke, myocardial infarction, and death as the appropriate primary end-points. Why? If the compelling data of Roubin and Iyer are accurate, and substantiated by other observational series, and if major and minor stroke occur so infrequent in skilled hands with present C-PTA techniques, then why were the above endpoints of these studies chosen, and not since redefined? The response to this query of ,"it was too late and much too costly" seems unacceptable. Stent supported carotid angioplasty non-randomized observational series have shown that their success, morbidity and mortality rates were comparable, if not superior to CEA in all subsets of patients. Since a very large cohort will be required to demonstrate a significant difference between angioplasty and surgery, and if what we know is accurate, then why even do those studies? CREST will incur enormous costs, reaffirm the extant work, at some point "way into the future", and, most painfully, subject numerous unsuspecting patients unnecessarily to the complications of carotid endarterectomy.

Embolic Protection Devices

The long-term studies regarding neurologic problems resulting from coronary bypass graft surgery (CABG) [49-53] provide insight into why the above major studies might reconsider their endpoints, especially with regard small particulate debris embolization. Vanninen's [49] conclusions from a study in which preoperative and postoperative CABG magnetic resonance imaging (MRI) of the brain, quantitative electroencephalography, and detailed neuropsychological and neurologic examinations were that small vessel ischemic lesions were detected and that alterations occurred in the quantitative electroencephalograms. Selnes [50-52], utilizing standardized neuropsychological tests preoperatively, and at 1 and 12 months postoperatively, detailed diminution in cognitive function. The decline in the neuropsychological tests, which assessed cognitive domains

(attention, language, verbal and visual memory, visuoconstruction, psychomotor and motor speed, and executive function), found a significant late cognitive deterioration with postoperative neurologic and cognitive complications: stroke (2-5%), delirium (10-30%), and cognitive deterioration [short-term 33-83% (involving primarily memory); and long-term 42% (involving more subtle problems dealing with following directions, mental arithmetic, and planning complex actions as well as a lower frustration threshold, and broader mood swings)]. The late decline in the cognitive performance was attributed to manipulation and or cannulation of the aorta that resulted in a showering of atheroembolic debris within the cerebral circulation that resulted in occlusion of both small and large vessels. If a significant stroke had not occurred postoperatively, then, the small vessel occlusions, potentially resulting from embolic debris, could have been responsible for the subsequent cognitive decline.

The rationale for use of these adjunctive embolic protection devices appears specious unless the neurologic and cognitive data points are included into these randomized study design. Why introduce a protection device into the protocol schema to prevent embolization, if it would or could not have a significant, potential, positive impact upon the defined endpoints? Are there other motivations? Have we forgotten that any additional device introduced into the carotid angioplasty procedure would have its own distinct set of complications? A study focusing upon the clinical impact of debris embolization after carotid angioplasty would be a long and expensive study, which does not appear to be in the plans of any of the medical vendors, any division within the National Institutes of Health, device inventors, or their proponents. Why? If embolic protection devices could possibly reduce the incidence of procedurally related stroke (very difficult to detail) as well as preclude possible late cognitive decline, would that not be an important and crucial reason for a randomized trial?

Physician Training and Experience

Curiously, why did radiologists not enthusiastically or even cautiously support and rally round the seminal works of Theron [3-9], Kachel [64, 65], and Mathias [66, 67]? Why have vascular surgeons only recently proclaimed their sovereignty over peripheral vascular disease and endovascular interventions, which can treat these problems, and, which, until recently, they preemptively dismissed? What has prompted them to change their posture? Why do these physicians now believe that fiat or divine fate has provided them with the requisite skills necessary to readily perform these procedures, with little imaging and angiographic experience as well as minimal catheter based training? Why do surgeons readily dismiss the guidewire and technical skills as well as the adjunctive catheter based procedures, which cardiologists and radiologists have learned through coronary and peripheral angiography and angioplasty? Why have surgeons perfunctorily minimized the conclusions reached by interventional cardiology and radiology that excellent imaging systems with the facile ability to achieve oblique views and road-mapping, along with specialized training is necessary to attain those interventional skill sets so as to assure patients minimum levels of competence and expertise? How can physicians utilize imaging equipment in the operating theater, would be unacceptable in any modern cardiac catheterization facility or radiology-imaging special procedures suite. Operating theater imaging systems exist, including cantilevered, moveable and rotational, radiolucent operating tables, which can provide the same level of quality as found in the catheterization laboratories and radiology special procedure suites. Why are they not being put into the operating theatres? Should patients be subjected to procedures using inferior equipment because of politics or finances? Furthermore, there is equivalently no justification for the routine use of general anesthesia to perform any of the standard interventional procedures including carotid angioplasty.

Furthermore, video transmitted live procedures should allow teaching-leaders to display to their audience readily available interventional equipment, standard techniques and methodologies, as well as the methods of successful extrication from an unforeseen occurrence, i.e. complication. Guidewire techniques should be emphasized: steering rather than pushing the guidewire through severe, tortuous, ectatic lesions; guidewire's whose tips are bent or kinked or otherwise damaged should not be advanced, but rather removed; knowledge and vision of distal guidewire position must be emphasized before insertion of a catheter or stent delivery system; and, avoidance of procedures or techniques which have an associated unsatisfactory complication record, i.e., direct carotid cannulation. These are some of the obligations that the physicians who teach procedures must abide by, and they must forgo the opportunity of primarily demonstrating their unusual prowess and skill often to unsophisticated or novitiate audiences. Experimental or unusual devices may be displayed, but not at the expense of showing to the audience what are the standard methods of operating.

All physicians are not equally gifted, and this fact was underscored at the 2001 American College of Cardiology Congress. A surgeon detailed his [68] carotid angioplasty experience (mortality: 4,4%; stroke rate: 10,0%; TIA: 7,8%), and stratified his data with regard procedures in which distal protection devices were used (mortality: 2,5%; stroke rate: 7,5%; TIA: 5,0%) and those procedures without their use (mortality: 5,0%; stroke rate: 12,0%; TIA: 10,0%); the conclusion advanced was that carotid angioplasty was more dangerous than carotid endarterectomy (mortality: 0%; stroke rate: 2,0%; TIA: 1,0%). An alternative interpretation of these data, when comparing it to those presented by other cardiologists [69,70], might have been that the requisite skills necessary to perform carotid angioplasty were lacking. Shawl's [69] study of 225 patients under the age of 80 years had a mortality of 0%, a minor stroke rate of 3,0%, and a major stroke rate of 0,9%; and, for the 74 patients >80 years, the mortality was 0%, the minor stroke rate was 1,3%, and the major stroke rate was 0%. Henry [70] reported on 164 protected interventional procedures on 148 high-risk patients that there were 3 neurological complications (1,8%) of which two (1,2%) were major, and no procedurally related deaths. Since these data further demonstrate that physician skill levels may be very disparate, as such should not patients be advised of the physician's actual level of expertise? Patients

have the absolute right to know if someone else can perform a procedure more effectively, efficiently, and safer.

These facts underscore all our fears about inadequately trained and educated physicians performing procedures. Physicians must have not only the necessary cognitive skills to determine which patients are procedural candidates, a level of technical proficiency necessary to adequately perform such interventions, the capacity to anticipate, manage, and/or overcome the majority of difficulties encountered [71], and dedication. Somehow, a few unschooled physicians, for whatever motivation and without a skill set or knowledge base, including a paradigm to successfully extricate their patient from a predicament, have declared their intention to obtain privileges to perform carotid angioplasty, regardless of their capabilities and their patients' needs. Perhaps, they believe that a celestial warrant rather than "training" would knight them with necessary technical and cognitive abilities. Should we permit this to occur?

Conclusions

As this nascent period of endovascular carotid procedures draws to an end, what is clear, crystal clear to me, is that a significant conundrum exists. The Gordian knot to be unraveled is not whether stent-supported carotid angioplasty is the standard of care, but rather how will physicians adequately develop the cognition and skill to safely perform these procedures. The tools will define themselves. However, the image of an inexperienced interventionist (cardiologist, radiologist, or surgeon), having limited or minimal diagnostic angiographic imaging and catheter skills, let-alone, the necessary interventional cognitive and technical skill, performing carotid angioplasty with inadequate imaging systems is disconcerting. Scalpel experience does not miraculously transfer and impart to the surgeon the average interventionist's skills and ability without dedication, education, study, and work. The unbridled and cavalier use of stents or any devices within the extracranial carotid bifurcation, as standard care by such unskilled physicians is inappropriate, and should not be condoned. Without a resolution of this quagmire, trained physicians, from whatever specialty, will be precluded from best caring for patients.

Presently, some segments of the medical community are not sufficiently perplexed as to the equivalency of carotid endarterectomy and stent-supported carotid angioplasty. Spokes-persons for each contingent vigorously and passionately detail their perspectives, often referencing their observational experiences as evidence of their unbiased, and logical conclusions. However, clinical equipoise, a genuine state of doubt regarding the equivalence of each procedure or the superiority of one procedure over another, does not exist. The point of perplexity has passed. While some members of the medical community may not share this view, their opposition and disagreement appears more likely to be lack of familiarity with the extant data, obstinacy, self-interest, and/or an inflexible need for a randomized trial to demonstrate the statistical merit of the therapy, rather than an assessment of the data.

Disabling, debilitating, devastating, and deadly complications can result from both surgery and angioplasty, and, as such, testimonials and limited observational experiences or waiting seven years for the results of an antiquated study with FDA imprimatur should not be the avenue, which impedes progress. Stent supported carotid angioplasty, subjects the patient to an immediate lower complication rate than carotid endarterectomy, with less trauma, a minimal postoperative recovery period, and precludes subsequent ipsilateral neurologic deficit. While neurologic deficit can and will occur with both procedures, the incidence of such deficits appears significantly less likely to occur with stent-supported carotid angioplasty, as such, all physicians should remember this when they make their therapeutic recommendations.

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Decreasing hospital mortality in patients with acute myocardial infarction

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The authors have studied the dynamics of mortality rate and other severe complications, as well as the alterations having occurred in course of treatment of 4077 patients with acute myocardial infarction (AMI), undergoing hospital treatment in the Cardiological Department N6 of Municipal Clinical Hospital No 15 and Moscow City Centre of Interventional Cardioangiology from 1993 to 2002. During those years both clinics were headed by D.G. Iosseliani and followed the common strategy in the management of acute myocardial infarction. The mentioned period was accompanied by a decrease in the AMI-related mortality rate from 16,7 % (1993) to 4,7 % (2002).

In order to reveal the factors influencing the mortality rate and other severe complications, we used such indices as the duration of hospital stay, age, sex, concomitant diseases, a history of prior MI, AMI size and localization, and the type of treatment used.

The AMI-related mortality rate during 1993-2002 was noted to decrease significantly on the background of wider use of endovascular and surgical methods of myocardial revascularization in treatment of AMI.

Key words

Acute myocardial infarction (AMI), percutaneous transluminal coronary angioplasty (PTCA), stenting.

Unfortunately, mortality from cardiovascular diseases amongst the Russian Federation population younger than 65 years is 3-3,5 times as high as the similar average value for the European countries [1]. Namely, in the 1990s increased mortality from cardiovascular diseases resulted in increased indices of total mortality of the population of the Russian Federation [2]. Cardiovascular diseases account for approximately 60 % in the structure of the Russian Federation population mortality, with AMI accounting for about 70 % of deaths from all cardiovascular diseases [3].

High mortality gave stimulus to a permanent search of more efficient methods of diagnosis and treatment of patients with cardiovascular diseases, especially those suffering from AMI. The last 15 years brought considerable positive shifts in this direction, accompanied by substantially improved general principles of treatment of patients with acute disorders of the coronary circulation. Along with the broadening of the choice of pharmacological agents, such as nitrates used for infusion therapy, cardioselective β-blockers, thrombolytics, desaggregants, ACE inhibitors, endovascular and surgical methods of coronary blood flow restoration got wider use in clinical practice of certain therapeutic facilities. These methods include: intracoronary (selective) thrombolysis, PTCA and stenting of coronary arteries, and coronary arteries bypass grafting (CABG), making it possible in the majority of cases to successfully restore the blood flow in the infarct-related artery (IRA), which, according to the opinion of many authors, is an important condition for a favourable clinical course of the disease [4-7]. All the above-mentioned measures made it possible to decrease significantly AMI-related mortality in many developed countries all over the world. Similar trends are also observed in certain clinics of Russia. Therefore, it seems necessary to identify those methods and drugs playing a leading part in increasing survival and improving the prognosis in patients with AMI, and to promulgate a wider and universal use thereof in treatment of acute myocardial infarction.

The present study was aimed at determining the factors influencing a decrease in hospital mortality in patients with AMI.

Material and methods

In this study we analysed the experience of the Cardiological Department N6 of Municipal Clinical Hospital № 15 (prior to 1996 this Department was the clinical base of the Bakoulev Institute for Cardiovascular Surgery, then it became the basic Department of the Moscow City Centre of Interventional Cardioangiology) and Moscow City Centre of Interventional Cardioangiology of Moscow. These clinics headed by Professor D.G. Iosseliani followed the same diagnostic and therapeutic strategy in the management of AMI. Starting from 1995, the information concerning all the patients undergoing treatment in both these clinics, namely: case history, complaints, clinical status, carried out treatment and examination came to and was archived in the net computer-assisted system (DIMOL) [8], making it possible to store all the required information concerning the patients, and to obtain, on demand, these data, as well as to carry out statistical selection of the indices of interest [8]. The present study was carried out retrospectively basing on the data of the archive materials. We analysed a total of 4077 patients (1318 females, 2759 males) treated at the Cardiological Department N6 of Municipal Clinical Hospital №15 and Moscow City Centre of Interventional Cardioangiology from 1993 to 2002, who had endured a total of 4439 AMIs. The diagnosis of AMI was made in accordance with the categories 1.1=1.2.7 of the Minnesota Code [9], also taking into consideration the cases of recurrent AMI.

The diagnostic criteria of AMI were as follows:

1) Prolonged anginal pain not relieved by nitroglycerin;

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2) Changes of ST-T segment and deviation and appearance of the Q wave on the ECG;

3) A reliable increase in the cardiospecific enzymes – creatinphosphokinase (CPK) >120 IU/ml and MB fraction > 5-7%.

The localization of AMI was determined by the data of ECG, EchoCG and left ventriculography. When analysing the obtained data, we took into consideration a history of previous myocardial infarction, diabetes mellitus, and arterial hypertension. In the coronary care unit, the patients with AMI underwent proper treatment in accordance with a specially worked out protocol, including infusion therapy with nitrates during the first 12 – 24 hours after the onset of the disease; β-adrenergic receptor blockers; aspirin; ACE inhibitors; in some cases – calcium antagonists. The patients admitted to the hospital within 6-8 hours from the onset of the anginal pain episode were subjected to emergency coronary angiography, and if a stenotic or occlusive lesion of the coronary arteries was revealed, they were subjected to endovascular procedure aimed at restoring the blood flow in the infarct-related artery (IRA). All the patients with MI underwent monitoring of the ECG, as well as of arterial pressure, heart rate, respiration rate, pulse oximetry. After being stabilised, the patients were transferred to the department for treatment of the patients with AMI.

The obtained findings of the study were statistically processed using the standard non-parametric statistical methods: Mann-Whitney criterion for the comparison of the mean values; Fischer's exact criterion, and correlational analysis according to Spearman (significance level $p < 0,05$).

Results and discussion

The yearly number of the patients with AMI treated in the Cardiological Department N6 of Municipal Clinical Hospital №15 and Moscow City Centre of Interventional Cardioangiology during the studied period was subjected to certain fluctuations. The maximal number of admissions was observed in 2001 – 491 patients with AMI, and the minimal one – in 1999 – 324 AMI patients.

The number of patients aged 70 years and more during the whole period of the study was about 30 % of the total number of the patients. The number of the male patients with AMI was nearly two times greater than that of female patients, which fully corresponds to the average statistical correlation of the MI incidence in men and women. The percentage of the diabetic and hypertensive patients, as well as of patients with previous infarctions during the studied period varied insignificantly. No reliable variations were observed in the localizations of LV myocardial infarction.

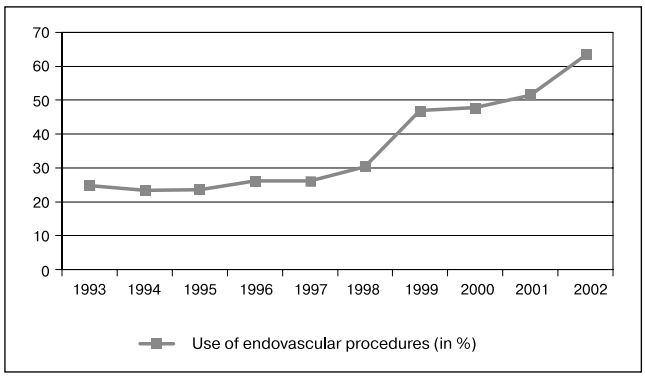

Figure 1. Dynamics of the number of endovascular procedures performed in patients with AMI in 1993-2002

The strategy of drug therapy over those years had endured certain changes due to the introduction of new drugs and therapeutic techniques into the clinical practice of AMI treatment. Special mention should be made that implementation of coronary arteries stenting into clinical practice of treating AMI in 1996 resulted in the respective changes in the drug therapy now consisting in a combination of aspirin at a dose of 325 mg and ticlopidine at a dose of 500 mg daily. The percentage ratio of the patients having received aspirin, nitrates and β-adrenergic receptor blockers did not change substantially, however the drugs themselves underwent considerable changes. From 1997, new-generation selective β-adrenoblockers with less side effects were used more frequently. Over the examined period, we saw a reliable trend towards increased incidence of prescribing ACE inhibitors to the patients with acute MI complicated by cardiac insufficiency, LV postinfarction aneurysm, a considerable decrease in both the segmental and global contractility (prevention of myocardial remodelling) and/or concomitant arterial hypertension.

Over the whole period studied, we noted a clear-cut trend toward an increase in endovascular procedures aimed at restoring the blood flow in the infarct-related artery (IRA) (Fig. 1).

A specially considerable increase was seen from 1998 on, with a sharp rise of the number of endovascular interventions carried out in patients with AMI both within the first hours after the admission, and in the follow-up period of hospital treatment and examination (in patients with early postinfarction angina pectoris or silent myocardial ischemia).

In 2002, 63 % of the AMI patients underwent successful procedures of angioplasty of IRA, performed both within the first hours of the disease, and in later terms,

Table 1. Main clinical and historical characteristics of the examined patients with AMI (by years)

Variables, %	1993 (354)	1994 (389)	1995 (416)	1996 (435)	1997 (409)	1998 (488)	1999 (324)	2000 (343)	2001 (491)	2002 (428)
Age < 70 years	68	70	66	71	72	74	69	68	73	77
Males	70	67	70	65	68	64	69	66	73	65
A history of myocardial infarction	19	22	24	25	24	21	18	24	22	19
Diabetes mellitus	11	14	12	9	12	15	11	12	10	11
Arterial hypertension	55	64	57	60	61	58	60	54	56	56
Anterior localization of MI	49	56	59	52	60	57	62	60	54	52
Posterior localization of MI	37	30	30	35	29	34	30	30	36	38
Lateral localization of MI	10	9	7	9	7	4	5	7	6	7
Circular MI	4	5	4	4	4	5	3	5	4	3
Early postinfarction angina pectoris	24,2	23,7	22,2	21,4	19,1	18,7	13,4	11,5	9,0	8,3
Mortality rate	16,7	17,2	16,8	16	16,6	13	6	6,2	5	4,7

Таблица 2. Methods of treatment of patients with AMI from 1993 to 2002

Variables, %	1993 (354)	1994 (389)	1995 (416)	1996 (435)	1997 (409)	1998 (488)	1999 (324)	2000 (343)	2001 (491)	2002 (428)
Emergency PTCA and/or stenting	7,6	8,3	8,9	9,2	9,3	10,6	21	23,6	34,4	40,8
Intracoronary thrombolysis	6,5	4,6	5,3	6,2	5,8	5,7	5,3	3,8	1,2	2,1
Delayed PTCA and/or stenting	10,7	10,5	9,4	10,8	11	14	20,6	20,4	15,8	20,3
Total amount of pts with endovascular procedures	24,8	23,4	23,6	26,2	26,1	30,3	46,9	47,8	51,4	63,2
Referred to CABG	6,8	7,9	9,3	14	14,1	18,8	23,1	25,6	27,3	26,2
Nitrates	94,2	95,4	97,3	97	98,1	97,4	97,8	98,3	97,9	98,1
β-blockers	78,4	77	81,3	82,4	80,5	83,7	85,1	86,6	87,7	87,9
Desaggregants	96,2	97,4	96,9	97,1	95,4	96,8	96,5	97	97,2	96,8
ACE inhibitors	60,2	58,3	61,2	64,3	64,8	73,4	75,3	77,2	82,4	81,2
Mortality rate	16,7	17,2	16,8	16	16,6	13	6	6,2	5	4,7

which reliably differed from the indices for 1993 (24,8 %) ($p < 0,00001$).

During the whole period studied (1993 – 2002), we noted a reliable decrease in the hospital mortality among the patients with myocardial infarction from 16,7% to 4,7% ($p < 0,01$), hence, over the studied period the AMI-related mortality rate in the mentioned clinics decreased by 3,5 times. In order to reveal the factors which could have positively influenced the decrease in the AMI-related mortality at the hospital stage, we carried out a statistical analysis of the larger part of the clinical, laboratory and historical data of these patients. The following parameters were analysed: age, sex, presence of diabetes mellitus, arterial hypertension, previous MI, localisation of acute myocardial infarction, presence of early postinfarction angina pectoris (PIAP), used methods of treatment (intracoronary thrombolysis, PTCA, stenting). The carried out correlation analysis showed a statistically reliable inverse relationship between the indices of hospital mortality and the number of endovascular procedures successfully performed at early stages of AMI, ($r = -0.95$, $p < 0.00003$), as well as between the incidence of development of early postinfarction angina pectoris and the number of endovascular procedures ($r = -0.95$, $p < 0.00003$) (Fig. 2).

The number of the elderly patients, patients with concomitant diabetes mellitus, those with a history of arterial hypertension, MI, as well as the number of the male patients stayed at the same level along the years during the whole studied period, and no reliable dependence between these indices was revealed. The studied period was accompanied by a decrease in the number of the carried out procedures of intracoronary thrombolysis, to be more frequently substituted by PTCA and stenting of the IRA.

The duration of the hospital stay of the patients with AMI averagely amounted to 14.8 days. A clear-cut trend was noted toward a decrease in this index during the whole period of study from 19,2 days to 12,1 days, i.e., the duration of the hospital stay of patients with AMI over that period decreased by 37%. At present maximal duration of in-hospital stay of an AMI patient is 10 days.

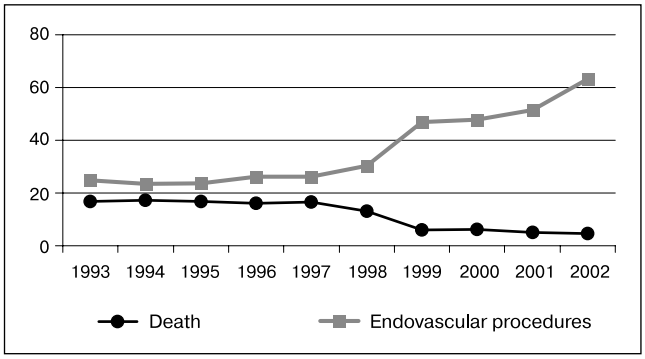

Figure 2. Diagram reflecting the dynamics of endovascular interventions growth and the mortality level in patients with AMI in 1993-2002 (in %)

Studies of Dellborg M. et al. (1994) showed that in-hospital mortality following myocardial infarction decreased by 40 % during the period from 1979 to 1990. According to their opinion, this decrease is explained by a set of the following factors: wide use of monitoring of important indices of the patient's state; early use of β-blockers, nitroglycerin, aspirin; systemic thrombolytic therapy [10]. Gheorghiade M. et al. (1996) compared two groups of patients with myocardial infarction, followed up from 1981-1984 and from 1990-1992, with the latter having receive considerably more thrombolytics, aspirin, heparin, warfarin, nitrates, β-blockers, and less antiarrhythmic drugs. In the patients followed up by these researchers from 1990 to 1992, the hospital mortality decreased two-fold as compared with that of the patients studied earlier, and according to the summary logistic model of regression the difference between these indices was explained by increased therapy with β-blockers, use of coronary angioplasty and thrombolytic therapy, along with decreased use of lidocaine [11].

In our study, therapy with nitrates, β-blockers, desaggregants had been carried out in most patients with AMI at all stages of the period studied. The basic limitations for β-blockers administration in patients with AMI were as follows: acute LV failure, presence of the bronchoobstructive syndrome, sick sinus syndrome. Contraindications to aspirin included: gastroduodenal ulcer in the acute exacerbation stage or unstable remission and presence of aspirin-related asthma. The number of the patients with the given diseases was not large and did not exert any reliably influence upon the results of the study. The use of calcium antagonists was necessitated by treatment of arterial hypertension and early postinfarction angina pectoris in the patients with AMI, as well as by antispastic properties of these drugs, since the patients with AMI in the acute exacerbation stage often develop coronary arteries spasms. As was noted earlier, the use of calcium antagonists did not exert any reliably effect on the mortality rate. We revealed a reliable inverse correlation between the indices of mortality and increased frequency of using ACE inhibitors ($p < 0,01$), as for the remaining indices, the dependence was not reliable, with only a trend being noted. Mention should be made that a wider use of ACE inhibitors also began from 1998. In our study, we also

revealed no correlation between mortality and the patients sex, the survival rate improved similarly both in men, and in women. Similar data were obtained in various years by Lincoff A.M. et al. (1993), Dittrich H. et al. (1988), Robinson K. et al. (1988), who did not find out any dependence of mortality from the sex of the patients with AMI [12-14]. On the contrary, Greenland P. et al. (1991), studying a group of AMI patients, consisting of 1524 women and 4314 men revealed that the female gender is associated with higher in-hospital mortality [15]. Similar results were obtained in the studies of Wilkinson P. et al. (1994), Tofler G.H. et al (1987) [16-17].

Our study showed that diabetes mellitus, early postinfarction angina pectoris and circular myocardial infarction were independent factors of increased risk of death amongst the patients with AMI. However, no reliable correlation between a decrease in the AMI-related mortality and previous history of myocardial infarction, diabetes mellitus and arterial hypertension was revealed. Special mention should also be made that we observed a considerable improvement of the mortality indices in all the age-specific groups. The group of patients aged over 70 showed a considerable decrease in the mortality rate during the follow-up period, but this decrease was less pronounced than that in the 50-to-70-year-old patients. In a similar study of the dynamics of nosocomial and 2-year mortality following MI during the period from 1994 to 1991, Abrahamsson P. et al. (1998) drew an important conclusion that the dynamics of decreased mortality and incidence of cardiac complications at the hospital stage of treatment also persists in the follow-up (2-year) period, and does largely depend on the efficiency of the primary treatment carried out in the acute stage of myocardial infarction [18].

Hence, the study convincingly showed that over the 10-year period (1993-2002) in the studied emergency cardiology clinics headed by D.G. Iosseliani (Cardiological Department N6 of Municipal Clinical Hospital №15 and Moscow City Centre of Interventional Cardioangiology) we observed a considerable decrease in the mortality from acute myocardial infarction, which, along with improved and enhanced drug therapy largely depended upon a wide use of endovascular procedures of myocardial reperfusion, both within the first hours of the disease, and later on during the whole hospital stage of treatment (presence of postinfarction angina pectoris and other manifestations of continuing myocardial ischemia). All this was accompanied by a considerable decrease in the duration of the hospital stay of the patients with AMI.

Conclusions

1. The period from 1993 to 2002 was characterised by a reliable decrease in the AMI-related mortality, which fell from 16,7% to 4,7%, thus constituting a 3,5-fold drop.

2. During the studied period, the mortality rate amongst the patients with myocardial infarction had a reliable inverse correlation with the number of the endovascular interventions performed. We also noted a reliable trend towards a decrease in mortality as the number of the patients treated with ACE inhibitors increased.

3. Over the studied period, the patients with AMI showed a reliably decreased incidence of early postinfarction angina pectoris. The incidence rate of postinfarction angina pectoris also correlated inversely with the number of the endovascular interventions performed.

4. The studied period was characterised by a manifested trend towards a decrease in the duration of hospital stay of AMI patients, amounting to 37 %.

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Systemic Administration of Chemotherapy for Concurrent Cancer Therapy Decreases the Clinical Restenosis after Coronary Stent Implantation

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Key words
Restenosis, stent, cancer

Abstract

Background: Local treatment with antiproliferative agents via drug-eluting stents has significantly reduced coronary in-stent restenosis (ISR). We investigated the rate of clinical ISR in cancers patients treated concurrently with percutaneous coronary intervention (PCI).

Methods and Results: Seventy-eight patients who underwent PCI with stent implantation while being treated for their tumors were divided into two groups: non-chemotherapy group (control, n=38) and chemotherapy group (n=40). Clinical ISR was defined as either a stenosis >50% of the luminal diameter at follow-up coronary angiography or a thallium stress test documenting at least moderate myocardial ischemia in the territory previously treated with a stent. The clinical ISR rate was 5% in the chemotherapy group versus 26% in the non-chemotherapy group, p<0,01. No clinical ISR was observed in patients treated with polyfunctional alkylating agents, anthracycline antibiotics, or plant alkaloids.

Conclusions: After PCI with stent implantation, cancer patients who receive systemic chemotherapy appear to have very low clinical ISR in comparison to cancer patients who did not receive systemic chemotherapy.

Introduction

In-stent restenosis (ISR) remains an important problem and continues to limit long-term success of bare metal stent implanation [1, 2]. ISR results mainly from neointimal proliferation in response to inflammatory mediators released after local vessel injury [2]. Similarities have been found between tumor cell growth and intimal hyperplasia [3]. This has led to recent biological approaches to prevent ISR, including radiation therapy and drug-eluting stents. Because of its immunosuppressive and antimitotic properties, the sirolimus-eluting stent markedly decreased the angiographic evidence of neointimal hyperplasia and restenosis as well as the need for repeat revascularization [4, 5]. The paclitaxel (an antineoplastic agent) – eluting stent, which inhibits cell division, has also shown promising clinical results [6]. Yet the use of systemic chemotherapy agents in preventing ISR has not been studied. Because of the parallel pathobiology between tumor cell growth and intimal proliferation in the vessel wall, we investigated whether systemic chemotherapy confers similar protective results from ISR. We tested this hypothesis in a population of cancer patients undergoing anti-tumor therapy who required percutaneous coronary intervention (PCI) with stent implantation.

Methods

The tumor board and interventional cardiology registries of Lenox Hill Hospital were queried to identify 78 cancer patients who underwent PCI with stent implantation while being treated for their tumors. Retrospective medical record review was approved by the Institutional Review Board. For the purposes of comparison and data analysis, patients were divided into two groups. The control group (n=38) represented cancer patients who did not receive chemotherapy, and the drug group (n=40) were patients who received systemic chemotherapy for their tumors. The follow up period ranged from 6 months to 3 years.

Clinical ISR was defined as either a stenosis >50% of the luminal diameter evaluated by follow-up coronary angiography or a thallium stress test documenting at least moderate myocardial ischemia in the territory previously treated with a stent.

The type of bare metal stents placed was left at the discretion of the operator.

Continuous variables are expressed as percentage mean +1SD and compared with Student's *t*-test. Categorical variables are expressed as frequencies and compared with Fisher's Exact Test. The level of significance was set at p<0,05.

Results

There were no significant differences between the chemotherapy and control groups with respect to the baseline characteristics (Table 1). The mean age of patients was 64+14 years. The majority of patients (88%) had ≤2 vessel coronary artery disease. Diabetic patients represented 23% of the study population. The chemotherapy group did not have a history of previous myocardial infarction or coronary bypass surgery. Type of cancer for each group is listed in Table 2.

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Table 1. Baseline Characteristics of the Study Population

	Chemotherapy Group (n=40)	Non-Chemotherapy Group (n=38)	p-Value
Age (years)	66 ± 12	62 ± 16	NS
Sex (male)	50%	56%	NS
Hypertension	60%	71%	0,35
Diabetes	18%	29%	0,28
Current Cigarette smoking	20%	8%	0,2
Dyslipidemia	55%	45%	0,5
Diabetes	18%	29%	0,28
Body Mass Index, kg/m2	30 ± 5,8	29 ± 6,0	0,04
Systolic blood pressure, mmHg.	135 ± 12	130 ± 10	0,4
Diastolic blood pressure, mmHg	80 ± 10	78 ± 10	0,45
Total Cholesterol, mg/dL	201 ± 35	210 ± 45	0,2
High Density Lipoprotein, mg/dL	50 ± 16	52 ± 12	0,5
Low-Density Lipoprotein, mg/dL	115 ± 44	119 ± 35	0,66
Triglycerides, mg/dL	158 ± 115	148 ± 105	0,7
Myocardial Infarction	0	5	
CABG	0	8%	
One Vessel CAD	52%	32%	0,07
Two Vessel CAD	40%	52%	0,36
Three Vessel CAD	8%	16%	0,30

The clinical ISR rate was 5% in the chemotherapy group versus 26% in the non-chemotherapy group; odds ratio = 0.15, 95% confidence intervals 0.03-0.7, p<0.01 (Figure 1).

Table 3 summarizes the clinical ISR rates observed with each type of chemotherapy administered. Patients who received polyfunctional alkylating agents, anthracycline antibiotics. or plant alkaloids showed no clinical ISR, compared to 12.5% and 25% (respectively) for patients who received antimetabolites or steroid chemotherapy.

Discussion

The problem of clinical ISR accounts for 20-30% of patients treated with PCI [7-9]. Intracoronary radiation represented the first considerable improvement in attempts to decrease the ISR recurrence rate [11-16]. One of the complications of brachytherapy was the development of late thrombosis, especially in patients receiving a new stent at the time of intracoronary radiation [13, 14, 17, 18]. Restenosis seemed to reoccur at the margins of the irradiated segment [19, 20].

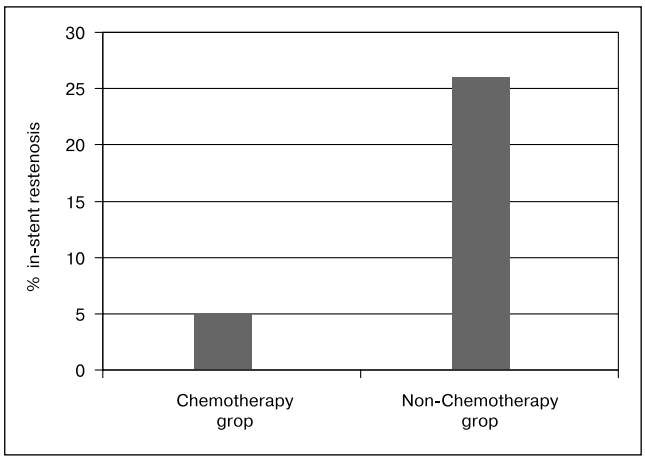

Figure 1. Incidence of in-stent restenosis

Finally, the logistics involved in delivery of brachytherapy has limited its wide adoption.

Recently, drug-eluting stents have shown remarkable success in preventing ISR; sirolimus, a cell-cycle inhibitor [21] that also possesses immunosuppressive and inflammatory properties [22], as well as the antiproliferative agent clinically approved for therapy of gynecological and other cancers paclitaxel [6] have produced very promising data [4-6].

The above observations with stents eluting cytostatic and antiproliferative agents and the pathobiologic similarity between the tumor cell growth and intimal proliferation [3] led us to inquire whether systemic chemotherapy administration might have similarly beneficial effects in prevention of intimal proliferation and clinical ISR after stent implantation in the coronary arteries. To our knowledge, this study represents the first one to have investigated this subject. In this present report we found a very low ISR rate in the systemic chemotherapy group: 5% versus 26% in the control group. The most powerful impact in reduction of ISR was in patients treated with polyfunctional alkylating agents, anthracycline antibiotics, and plant alkaloids (0% restenosis). The less aggressive chemotherapy agents (steroids) appeared to exert no significant effect on prevention of ISR (25% versus 26% in the control group).

The impact of systemic chemotherapy on ISR observed in this study appears to be similar to the results of drug-eluting stents trials, most likely involving the same mechanism of inhibition of intimal proliferation by antiproliferative, antimigratory, and anti-inflammatory properties. Systemic chemotherapy allows a broader drug delivery on the coronary arterial bed as compared to drug-eluting stent; this potentially allows treatment of a broader peri-stent vessel segment, while the current drug-eluting stents are almost strictly limited to the stent segment. This approach may be useful in a selected population of high risk patients for ISR possibly including diabetic patients, diffuse coronary artery disease and small vessel disease. However, further studies are needed to confirm this initial observation and better define differences in effica-

Table 2. Types of Cancer

Chemotherapy Group (n=40)		No-Chemotherapy Group (n=38)	
Breast Cancer	8 (20%)	Skin Cancer	
Lung Cancer		a) Squamous cell cancer	13 (32,5%)
a) Squamous Cell Cancer	5 (12,5%)	b) Basal cell cancer	14 (37%)
b) Small Cell Cancer	5 (12,5%)	c) Melanoma	1 (2,6%)
c) Large Cell Cancer	2 (5%)	Prostate Cancer	7 (18%)
Hodgkins Lymphoma	2 (5%)	Renal Cell Cancer	1 (2,6%)
Non-Hodgkins Lymphoma	1 (2,5%)	Colon Cancer	2 (5,3%)
Acute Myeloblastic Leukemia	3 (7,5%)		
Chronic Lymphblastic Leukemia	2 (5%)		
Colon Cancer	7 (17,5%)		
Ovarian Cancer	4 (10%)		
Bladder Cancer	1 (2,5%)		

Table 3. In-stent restenosis rates according to chemotherapy agent subgroups*

	N	Restenosis Rates	P-value vs. control
No Chemotherapy (Control group)	38	26%	
All Chemotherapy (Drug group)	40	5%	0,01
Polyfunctional Alkylating Agents (e.g. Cyclophosphamide, Cisplatin)	29	0	0,0001
Anthracycline Antibiotics (e.g. Doxorubicin, Mitomycin, Bleomycin)	20	0	0,03
Plant Alkaloids (e.g. Vinblastine, Vincristine, Paclitaxel)	25	0	0,0074
Antimetabolites (e.g. Methotrexate, 5-Fluorouracil, Cytarabine)	8	12,5%	NS
Steroid Hormones	4	25%	NS

* Patients usually received > Chemotherapeutic 1 agent; but no patient treated with antimetabolites or steroids also received polyfunctional alkylating agents, anthracycline antibiotics, or plant alkaloids

cy and therapeutic windows of the various chemotherapy agents. Furthermore, the appropriate dose and frequency of systemic chemotherapy are important to determine in order to avoid side effects. Lastly, this approach might be less expensive compared to new drug-eluting stents, especially if multiple stents are required for complete revascularization.

Study limitations

This was a retrospective analysis, and therefore, the results are limited by bias inherent to this type of study. In addition, the study population was small. Therefore, the association observed between systemic chemotherapy and the low ISR rate needs to be confirmed in larger series. We assessed the clinical ISR rate; this study does not include an assessment of angiographic restenosis, major adverse cardiac events, and mortality. Nonetheless, previous vascular brachytherapy studies showed that clinical ISR correlates closely with angiographic restenosis within the treated vessel and vessel segment (23). Finally, the nature of this study did not allow determining the appropriate dose and frequency of the systemic chemotherapy.

Conclusion

In this study, we found a relationship between systemic chemotherapy (especially with polyfunctional alkylating agents, anthracycline antibiotics, and plant alkaloids) and a very low ISR rate in cancer patients also treated with stents. Further trials are needed to investigate agent and dosage considerations and the practical utility of this therapy with bare metal and drug-eluting stents.

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Stenting of CAD patients with restenosis of primary PTCA

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Twenty five years have passed after implementation of A. Gruentzing's method of PTCA into the clinical practice, and since then permanent perfection of the tools and experience gained by cardiologists have made it possible to perform the procedures with high incidence of success (>94%) and low risk of severe complications (<2%). However, restenoses in the follow-up after balloon dilatation still remain the main limiting factor for wider clinical application of the method. For example, in the USA annually more than 100 thousands patients require secondary myocardial revascularization for restenoses after primary PTCA, with the yearly expenditures for treatment of restenoses amounting to over 2 billion dollars [1].

Restenosis developing within various terms after PTCA is one of the main indications for the stenting of coronary arteries. Before the appearance of stents, secondary PTCA remained the only invasive intracoronary procedure for treatment of post-PTCA restenoses. However, secondary restenosis occurs in more than 25% of cases after repeated PTCA [2].

Whether stenting prevents development of subsequent restenoses after previously developed secondary post-PTCA narrowing remains insufficiently studied so far.

Purpose of this study - comparative evaluation of long-term outcomes of stenting and secondary PTCA in patients with restenosis following primary PTCA.

Aims of the study

1) Comparative assessment of the state of coronary circulation in the follow-up after stenting and secondary PTCA carried out for restenosis;

2) To carry out a comparative evaluation of the state of coronary arteries, as well as of clinical and functional state of the patients in the follow-up after stenting and secondary PTCA carried out for restenosis;

3) To reveal clinical and angiographic factors influencing the incidence of restenosis in the follow-up in patients after stenting and secondary PTCA carried out for restenosis.

Material and methods

The study comprised patients with coronary artery disease (CAD) (n=66), who underwent primary PTCA in the Moscow City Center of Interventional Cardioangiology from January 1996 to July 2002; repeated coronary angiography revealed post-PTCA restenosis in all of them. The patients were subdivided into two groups. Group 1 consisted of the patients who were subjected to secondary PTCA (PTCA group; n=36). Group 2 consisted of the patients subjected to implantation of a stent into the site of post-PTCA restenosis (stent group; n=30).

After the clinical examination including ECG, echocardiography, ambulatory 24-hours ECG monitoring and stress test with dosed physical load, all the patients underwent selective coronary angiography. The findings of the examination are shown in Table 1.

As one can see from Table 1, Group 1 consisted of 36 pts (34 males) whose mean age was 51,7 ± 8,3 years. The average duration of CAD was 14,4 months. In 11 pts (30,6%) clinical manifestations of CAD persisted for less than 1 month, in 16 pts (44,4%) – up to 12 months, in 9 pts (25%) – for more than 12 months. 61,1% of patients have previously experienced acute myocardial infarction (AMI), with 86,1% of the patients suffering from arterial hypertension, 58,3% of patients having hypercholesterolemia, and 22,2% of patients having hypertriglyceridemia. Two patients

Table 1. Clinical and laboratory characteristics of Group 1 and Group 2 patients

Variables	PTCA group (1)	Stent group (2)	P
Males	34/2 (94,4%/5,6%)	26/4 (86,7%/13,3%)	0,274
Age (years)	51,7±8,3	55,4±6,66	0,050*
Angina pectoris:	36 (100%)	30 (100%)	0,248
Functional class 2	6 (16,7%)	9 (30%)	
Functional class 3	24 (66,7%)	14 (46,7%)	
Functional class 4	6 (11,1%)	7 (23,3%)	
Arterial hypertension	31 (86,1%)	26 (86,7%)	0,561
History of AMI	22 (61,1%)	18 (60%)	
Q- MI	14 (63,6%)	8 (26,7%)	0,294
Positive stress-test	22 (84,6%)	14 (87,5%)	0,810
Non-informative stress-test	1 (3,8%)	1 (6,25%)	
Stress test load (watts)	70,0±25,0	61,7±22,9	0,299
LV ejection fraction, %	57,4±9,8	56,7±9,0	0,777
Hypercholesterolemia	21 (58,3%)	17 (56,7%)	0,127
Blood serum cholesterol level, mmol/l	6,1±0,91	5,6±0,9	0,071
Hypertriglyceridemia	8 (22,2%)	14 (46,7%)	
Blood serum triglycerides level, mmol/l	2,1±0,79	2,3±1,1	0,687
Type 2 diabetes mellitus	0 (0%)	3 (10%)	0,052
Smoking	13 (36,1%)	6 (20%)	0,150

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(5,6%) had previously undergone PTCA. In this group there were no patients with type 2 diabetes mellitus.

Group 2 consisted of 30 patients (26 males) whose mean age was 55,4 ± 6,66 years. The duration of CAD in this cohort of patients amounted to 30,7 months in average. In 2 patients (6,7%) clinical manifestations of CAD persisted for less than 1 month, in 11 pts (36,7%) - up to 12 months, in 17 pts (56,7%) - for more than 12 months. 60% pf patents had history of AMI, 86,7% of patients suffered from arterial hypertension, 56,7% of patients had hypercholesterolemia, and 46,7% - hypertriglyceridemia. Type 2 diabetes mellitus was revealed in 3 (10%) patients of this group. Three patients had previously been subjected to PTCA.

Table 2. Baseline data of left venrtriculography and selective coronary angiography of patients from Groups 1 and 2 (prior to the first PTCA procedure)

Variables	PTCA group (1)	Stent group (2)	P
LV ejection fraction (%)	64,8±13,0	661,9±10,4	0,359
End-diastolic volume (ml)	175,7±68,7	143,4±71,9	0,090
E-systolic volume (ml)	66,9±35,6	52,6±28,7	0,103
LV anterior wall contractility hypokinesia akinesia dyskinesia hyperkinesias	 5 (13,9%) 4 (11,1%) 2 (5,6%) 1 (2,8%)	 6 (20%) 2 (6,7%) 0 (0%) 0 (0%)	0,505
LV apical contractility hypokinesia akinesia dyskinesia hyperkinesias	 4 (11,1%) 2 (5,6%) 5 (13,9%) 0 (0%)	 1 (3,3%) 2 (6,7%) 1 (3,3%) 0 (0%)	0,264
LV posterior wall contractility hypokinesia akinesia dyskinesia hyperkinesias	 5 (13,9%) 3 (8,3%) 1 (2,8%) 1 (2,8%)	 5 (16,7%) 2 (6,7%) 0 (0%) 0 (0%)	0,763
Number of affected segments	49 (100%)	38 (100%)	0,340
Left anterior descending artery (LAD) proximal segment median segment	27/49(55,1%) 10 13	24/38 (63,2%) 15 4	
Diagonal branch distal segment occlusion	4 0 4	5 0 2	
Intermediate branch (IB)	1/49 (2,04%)	0/38 (0%)	
Circumflex artery (CA) proximal segment median segment	6/49 (12,2%) 2 4	8/38 (21,1%) 1 2	
Marginal branch distal segment occlusion	0 0 0	5 0 2	
Right coronary artery (RCA) proximal segment median segment distal segment occlusion	15/49 (30,6%) 5 8 2 3	6/38 (15,8%) 1 4 1 3	
Type of coronary circulation right left balanced	 28 (77,8%) 0 (0%) 8 (22,2%)	 26 (86,7%) 2 (6,7%) 2 (6,7%)	0,075
Type of lesion to the dilated segment A B1 B2 C	 1 (2,8%) 10 (27,8%) 18 (50%) 7(19,4%)	 0 (0%) 9 (30%) 15 (50%) 6 (20%)	0,834
Eccentricity	26 (86,7%)	24 (80%)	0,463
Percentage of stenosis of the dilated segment	84,1±10,9	83,8±9,7	0,931
Target segment length, mm	13,6±3,9	15,2±4,6	0,131

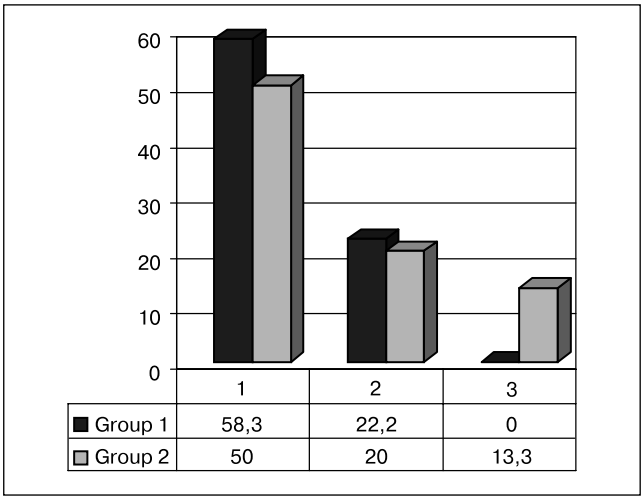


Diagram 1. Prevalence of one-vessel lesion of the coronary bed in patients from both groups

Left ventriculography and selective coronary angiography were carried out by means of percutaneous femoral access according to the standard technique. The data of patients from both groups are shown in Table 2.

The lesions leading to over 50% lumen narrowing were considered as hemodynamically significant. An isolated lesion of one coronary artery was observed in 21 (58.3%) patients in Group 1, and in 15 patients (50%) in Group 2, two-vessel lesion in 8 (22,2%) Group 1 patients, and in 6 (20%) Group 2 patients, three-vessel lesions were seen only in 4 patients from Group 2 (13,3%). The intergroup differences were not statistically reliable (p > 0,05) (Diagram 1).

Stenotic lesions were most commonly observed in the left anterior descending artery in both isolated and combined variants (55,6% in Group 1, 73,3% in Group 2), less often - in the intermediate branch (2,8% in Group 1 and 0% in Group 2), marginal branch (0% in Group 1, 3,3% in Group 2), in the right (25% in Group1, 13,3% in Group 2) and circumflex (11,1% and 10%, respectively) arteries (p = 0,340) (Diagram 2).

In total, the complicated lesions of B2 and C types prevailed in both groups (Group 1: B2 – 50%, C – 19,4%; Group 2: B2 – 50%, C – 20% (p = 0,834).

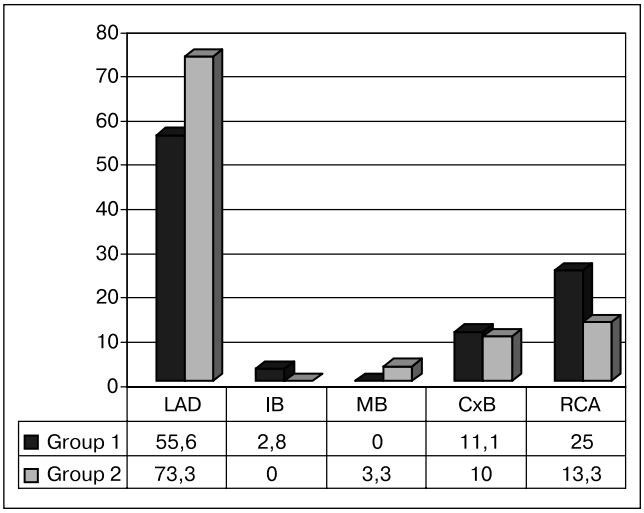


Diagram 2. Prevalence of left anterior descending artery lesions in patients from both groups

As one can see from those data, there were no reliable differences in the volume of coronary lesions, the number of diseased arteries and the morphological type of coronary lesion between the patients in both groups.

Neither did the studied groups differ by the type of the coronary circulation (p=0,075). Twenty-eight patients (77,8%) in Group 1 and 26 patients (86,7%) in Group 2 had showed the right type of the coronary circulation, the left type was seen in 2 patients (6,7%) in Group 2, the balanced type of coronary circulation in 8 patients (22,2%) in Group 1 and in 2 patients (6,7%) in Group 2. However, the following trend was observed: in Group 1 the percentage of patients with the balanced type of coronary circulation was higher than in Group 2 (22,2% vs 6,7%). Besides, in the PTCA group there were no patients with the left type of coronary circulation (0% vs 7,1%).

All patients from both groups were formerly subjected to the procedure of primary PTCA on the base of the clinical and instrumental studies. The procedure was considered successful if a satisfactory angiographic outcome was obtained (residual stenosis less than 30%) in all the segments of dilated coronary arteries, in the absence of complications.

The procedure of primary PTCA was distributed as follows: Group 1: LAD – 20 (55,6%), 1st diagonal branch (1-DB) - 2 (5,6%), circumflex artery (CA) – 4 (11,1%), intermediate branch (IB) – 1 (2,8%), right coronary artery (RCA) – 9 (25%); Group 2: LAD – 22 (73,3%), CA – 3 (10%), marginal branch (MB) – 1 (3,3%), RCA – 4 (13,3%) (Diagram 3).

In Group 1 the procedure was performed for arterial occlusion in 7 cases (19,4%), in 5 (71,4%) cases occlusion's age was less than 3 months (recent occlusions). In Group 2 the procedure was carried out for arterial occlusion in 5 cases (16,7%), in 2 cases (40%) recent occlusion was revealed.

After the successful primary PTCA, all the patients from both groups received approximately similar drug therapy, as well as disaggregants (aspirin, 100 mg daily).

Control coronary angiography performed 6-7 months later showed restenosis of the dilated artery in all the patients, so we decided to perform either repeated PTCA, or stenting of coronary arteries. The clinical findings of the second examination of the Group 1 and Group 2 patients are shown in Table 3.

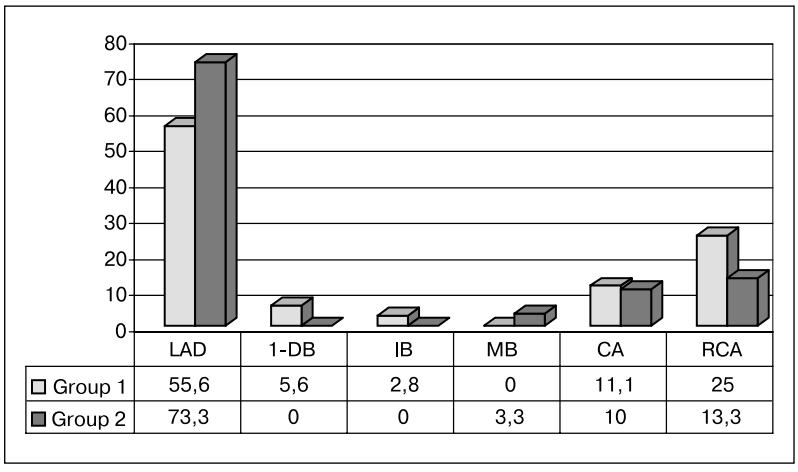


Diagram 3. Procedure of primary PTCA in patients in both groups

Table 3. Clinical and laboratory indices of the studied groups of patients

Variables	Group 1 (n = 36)	Group 2 (n = 30)
Angina pectoris	29 (80,6%)	29 (96,7%)
NYHA class I	2 (6,9%)	0 (0%)
NYHA class II	10 (34,5%)	4 (13,8%)
NYHA class III	14 (48,3%)	17 (58,6%)
NYHA class IV	3 (10,3%)	3 (10,3%)
Positive stress-test	16 (59,3%)	11 (84,6%)
Negative stress-test	8 (29,6%)	2 (15,4%)
Non-informative stress-test	3 (11,1%)	0 (0%)
Stress test load, watts	72,2±25,3	62,5±24,6
LVEF, %	60,2±10,7	57,4±7,1
Hypercholesterolemia	22 (61,1%)	12 (40%)
Blood serum cholesterol, mmol/l	5,7±1,2	5,4±0,8
Hypertriglyceridemia	13 (36,1%)	7 (23,3%)

In the stent group (gr.2), a total of 30 stents was implanted, including: Angiostent C1 – 5 (16,7%), Bx Sonic – 2 (6,7%), Bx Velocity – 2 (6,7%), Crossflex – 8 (26,7%), BiodYvisio SV – 3 (10%), BiodYvisio OC – 3 (10%), BiodYvisio AS – 1 (3,3%), Be Stent 2 Med – 1 (3,3%), Multilink Tetra - 2 (6,7%), JoStent – 2 (6.7%), MiniCrown - 1 (3,3%) (see Diagram 4). As for the design, the stents were distributed as follows: coil stents – 15 (50%), matrix stent – 8 (26,7%), module stent – 7 (23,3%). The average stent's diameter after implantation amounted to 3,03 ± 0,34 mm, and its length to 15,47 ± 3,7 mm. The average implantation pressure amounted to 12,4 ± 2,2 atm. The stent was implanted into LAD in 73,3% of cases, into CA - in 10% of cases, into MB in 3,3% of cases, into RCA - in 13,3% of cases. In the majority of patients, the procedures were performed in the proximal and middle segments of the arteries (in 66,7% of cases – in the proximal segment, in 33,3% of cases – in the middle segment).

The short-term angiographic outcome of PTCA was assessed immediately by the computerized quantitative analysis. The obtained result was considered angiographically successful when the residual stenosis after the procedure did not exceed 30% of the vessel's diameter.

After the second procedure, all the patients from Group 1 and Group 2 were given symptomatic therapy and antiaggregants, while the stented patients additionally received Ticlid (ticlopidin) at a daily dose of 500 mg for a month.

The clinical result was considered successful if after the procedure clinical manifestations of angina pectoris decreased by at least two functional classes in the absence of acute complications (myocardial infarction, emergency CABG, or death).

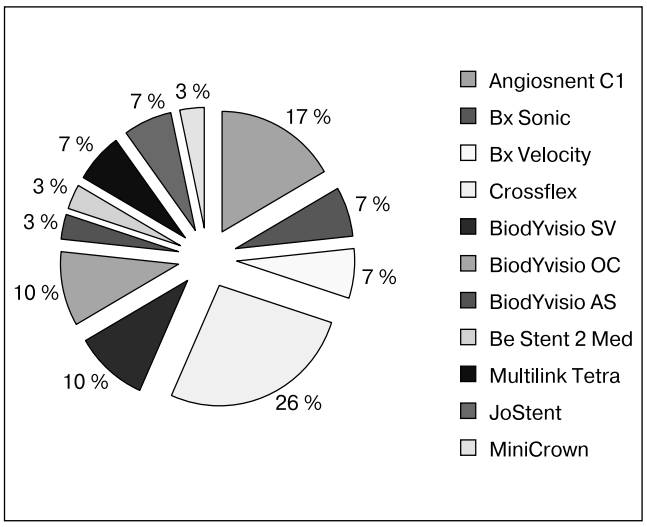


Diagram 4. Types of stents in Group 2 patients

At least 6 months after the procedure (average, 7,6 months after repeated PTCA; 6,9 months after stent implantation) all the patients were re-examined with ECG, echocardiography, continuous ECG monitoring, stress test with dosed physical load and selective coronary angiography. The clinical and angiographic findings are shown below.

Statistics

The obtained data were statistically processed using the software SPSS version 10,0 (SPSS Inc., Chicago, Illinois) [3, 4]. The data analysis included determination of the frequencies and average values with the standard deviations. To compare the mean values of the quantitative signs of independent samples we used the Student's t-test, and for those of qualitative signs - the χ^2 test. The p value of less than 0,05 was considered statistically significant. The interrelation between the signs was assessed as follows: for the quantitative criteria – by Pearson's correlation coefficient, for the qualitative criteria – by Spearman's correlation coefficient.

Results

The angiographic success of the repeated PTCA, as well as that of the coronary arteries stenting amounted to 100% in the both groups. The clinical and functional characteristics of the patients from both groups are given in Table 1.

As one can see from the presented data, the patients in Group 1 and Group 2 did not reliably differ by age, sex, presence of risk factors for development of CAD or concomitant diseases, the number of the previous myocardial infarctions, diagnosis at the moment of the first procedure and carried out drug therapy (Diagram 5). However, the duration of clinical manifestations of CAD in Group 2 patients was significantly greater as compared with Group 1 (duration over 12 months in 56,7% of patients vs 25% in Group 1, r = 0,253, p = 0,04).

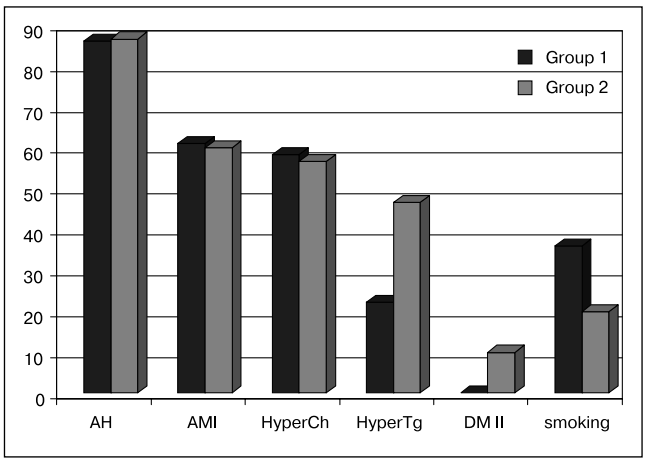


Diagram 5. Clinical characteristics of the patients in both groups

The drug therapy in the postprocedural period after primary PTCA did not differ significantly in the patients from two studied groups (p > 0,05) (Table 4). However, as one can see from this Table, the prevalence of patients having received Ca channels antagonists was higher in Group 2 after primary PTCA (53,3% vs 25%, p = 0,018*).

The procedures of repeated PTCA and stenting of restenosis following primary PTCA were successfully completed in 66 patients (100%). As a result of treatment, complete revascularization (i.e., complete freedom from hemodynamically significant lesions) was achieved in 34 patients in Group 1 (94,4%) and in 25 patients in Group 2 (83,3%) (the differences between the groups NS, p = 0,144). The acute complications in the form of occluding dissection or thrombosis of the stent didn't develop in any case.

Table 4. Drug therapy in patients of both groups following

Drug	After primary PTCA		In the follow-up	
	Group 1	Group 2	Group 1	Group 2
Nitrates	80,6%	73,3%	72,2%	46,7%
β-blockers	72,2%	73,3%	88,9%	80%
Ca-blockers	25%*	53,3%*	52,8%	53,3%

In-hospital survival rate after the procedures amounted to 100%; there were no cases of development of AMI, stroke, or necessity of emergency myocardial revascularization.

During the post-procedural period clinical manifestations of angina pectoris decreased.

All the patients were properly examined in the follow-up period. The findings of the follow-up examination are represented in Table 5. The clinical course of the disease in the follow-up period after interventional procedures was

Table 5. Long-term outcomes (n = 66)

Outcome	PTCA group (n = 36)	Stent group (n = 30)
Death	0 (0%)	0 (0%)
Survival	36 (100%)	30 (100%)
Acute myocardial infarction	0 (0%)	0 (0%)
Angina pectoris (prior to the control angiography)	26 (72,2%)	9 (30%)
CABG	9 (25%)	3 (10%)
Repeated endovascular procedures (PTCA)	2 (5,6%)	3 (10%)
Drug treatment: aspirin nitrates calcium antagonists β-blockers	 36 (100%) 26 (72,2%) 19 (52,8%) 32 (88,9%)	 30 (100%) 14 (46,7%) 16 (53,3%) 24 (80%)
Restenosis	22 (61,1%)	8 (26,7%)
Reocclusions	0 (0%)	2 (6,7%)

assessed by three main criteria: survival, presence of angina pectoris, and AMI. Besides, we also took into consideration the dynamics of left ventricle ejection fraction, stress test load, necessity of drug, repeated endovascular, or surgical treatment.

During the follow-up period the need of repeated procedures for myocardial revascularization (CABG and PTCA) in Group 2 was significantly lower than in Group 1 (20% vs 30,6%, respectively, p = 0,017*) (Diagram 6).

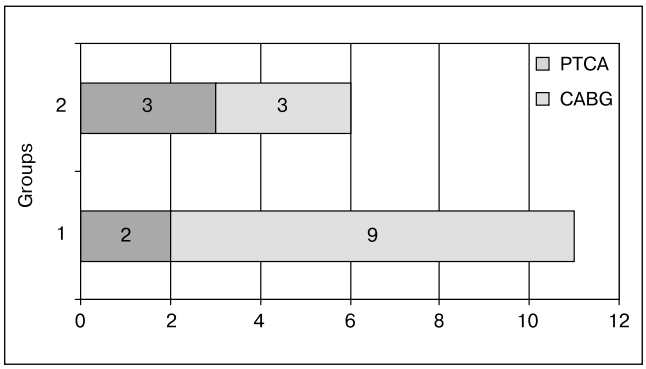


Diagram 6. Myocardial revascularization in the patients from both groups in the follow-up period

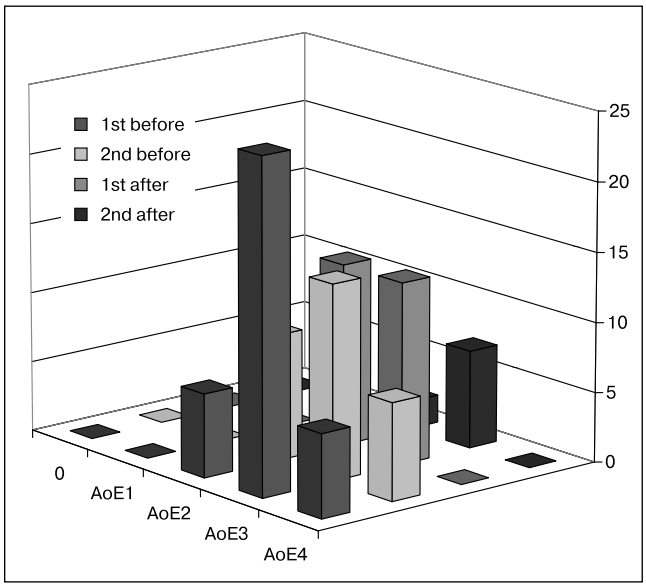


Diagram 7. Comparison of the clinical state of both groups' patients prior to the primary procedure and in the follow-up period

The control clinical examination carried out in the follow-up period revealed clinical signs of angina of effort in 72,2% of patients from Group 1 and in 30% of patients from Group 2 (p = 0,001). As one can see, in Group 2 the percentage of patients free from angina pectoris is significantly higher (p = 0,001) (Diagram 7).

In order to determine the reserve capabilities of the coronary blood flow and the effect of the successful myocardial revascularization thereupon, we used stress test. Veloergometry (VEM) at the control examination was performed in 32 (88,9%) Group 1 patients, and in 24 (80%) Group 2 patients. At the moment of the second examination, the majority of the Group 2 patients (14; 58,3%) having performed the stress test yielded a negative result (as compared with only 10 (31,3%) patients from Group 1 (p = 0,188) (Diagram 8).

The drug therapy in both groups consisted in the following: nitrates – 72,2% vs 46,7 (p = 0,034), calcium channels blockers – 52,8% vs 53,3% (p = 0,964), β-blockers – 88,9% vs 80% (p = 0,316), respectively. In the late follow-up we noted a reliable decrease of the number of Group 2 patients needing nitrates, while the percentage of the Group 1 patients taking β-adrenoblockers and Ca-channel antagonists increased. Aside from nitrates, the patients from Group 1 and Group 2 did not differ significantly in the scope of the therapy performed.

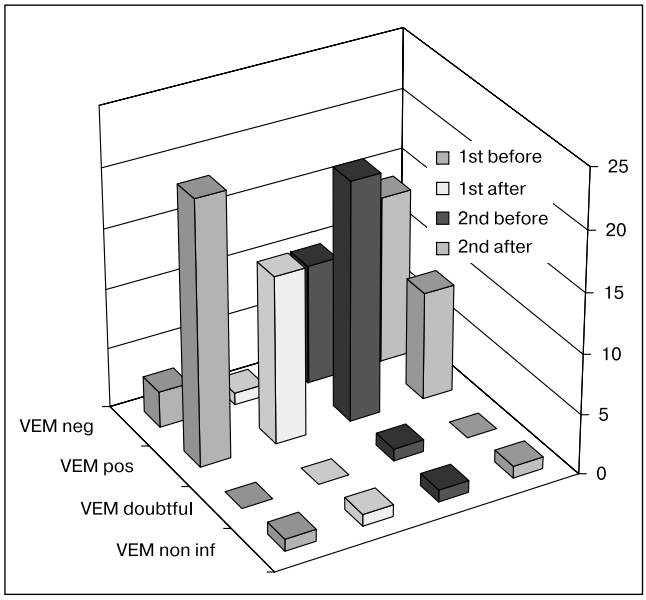


Diagram 8. Comparative assessment of the stress test results in both-groups' patients before the primary procedure and in the follow-up period

Restenosis at the control examination was diagnosed in 61,1% of the patients in Gr. 1, and in 26,7% of patients in Gr. 2 (p = 0,005*).

Several months after the second procedure the functional indices of the left ventricle (LV) were noted to improve in both groups (Table 6).

According to the data of control examination left ventricular ejection fraction improved reliably in both groups (from 57,4 ± 9,8% to 62,6 ± 8,7% in Group 1 (p = 0,0001) and from 56,7 ± 9,0% to 62,7 ± 18,4% in Group 2 (p = 0,0001) (Diagram 9). Stress test load also increased significantly: in Group 1- from 70 ± 25 Wt to 82,03 ± 223,96 Wt (p = 0,0001); and in Group 2 - from 61,7 ± 22,9 Wt to 78 ± 26,4 Wt (p = 0.0001) (Diagram 10).

In the follow-up period, the average value of blood serum cholesterol in the patients of Gr. 1 amounted to 5,7 ± 0,97 mmol/l, and in Gr. 2 - to 5,4 ± 0,8 mmol/l (NS, p = 0,213). The average value of blood serum triglyceride

Table 6. Functional indices of the LV in the follow-up period in the studied

Indices	PTCA group	Stent group	P
Stress test load	82,03±23,96	78,3±26,4	0,584
LVEF, %	62,6±8,7	62,7±10,4	0,972
EDV, ml	170,4±57,1	128,96±33,6	0,001*
ESV, ml	58,7±30,9	54,1±31,3	0,560

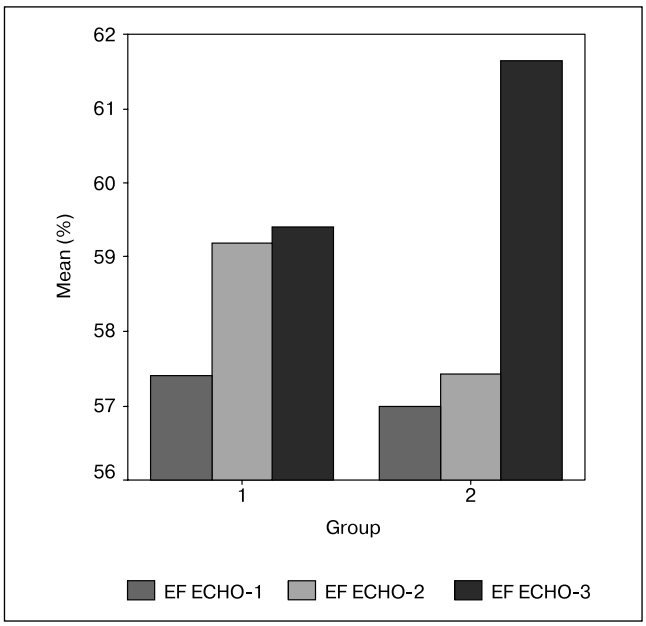


Diagram 9. Significant increase of LVEF in both groups

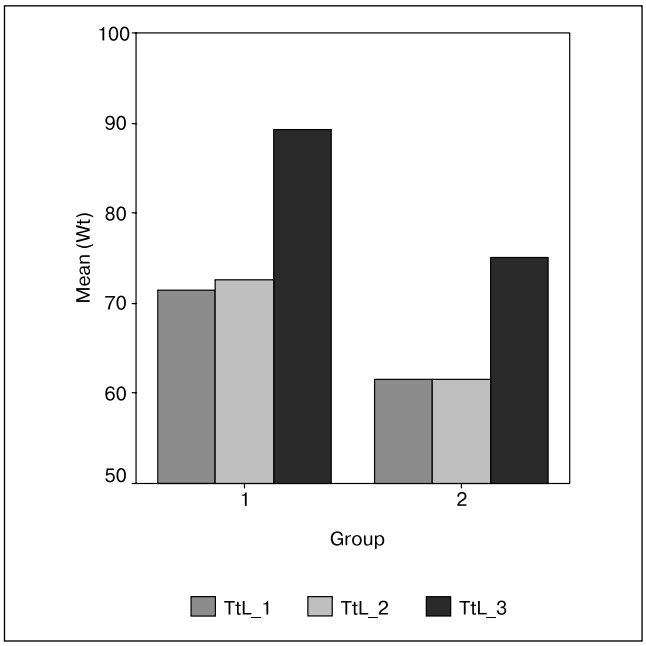


Diagram 10. Significant increase of stress test load in both groups

amounted to 1,6 ± 0,8 mmol/l and 1,97 ± 0.8 mmol/l for the patients of the Groups 1 and 2, respectively (NS, p = 0,108). We also noted a reliable decrease in blood serum cholesterol prior to the primary PTCA and in the follow-up period in Group 1 patients from 6,1 ± 0,9 mmol/l to 5,7 ± 0,97 mmol/l (p = 0,0001), and in Group 2 patients from 5,6 ± 0,9 mmol/l to 5,3 ± 0,8 mmol/l (p = 0,0001) (Diagram 11). Besides, we revealed a reliable decrease in blood serum triglycerides at first examination and in the follow-up period: Group 1 - from 2,1 ± 0,8 mmol/l to 1,6 ± 0,8 mmol/l (p = 0,0001), Group 2 - from 2,3 ± 1,1 mmol/l to 1,7 ± 0,6 mmol/l (p = 0,0001) (Diagram 12).

The data obtained in the follow-up period were assessed by means of the correlation analysis (for the qualitative criteria we chose Spearman's coefficient, and for the quantitative ones – Pearson's coefficient).

The analysis of the data revealed the following patterns for the patients in both groups: patients with type 2 diabetes mellitus predominantly had a more severe lesion of the coronary arteries (Spearman's coefficient r = 0,330, p = 0,007*); type B2 and C lesions of the coronary arteries and incomplete myocardial revascularization more often correlated with high functional class of angina of effort (Spearman's coefficient r = 0,281, p = 0,022*; Spearman's coefficient r = 0,317, p = 0,01*, respectively).

Longer lesions of the coronary arteries were noted to yield higher values of blood serum cholesterol and triglycerides (r = 0,312, p = 0,018* and r = 0,311, p = 0,04*, respectively).

We also studied possible predictors for restenosis in the follow-up periods after interventional procedures.

Neither age, nor sex of the patients from both groups influenced reliably the rate of restenosis (p > 0,05).

Risk factors for CAD such as hypertension, type 2 diabetes mellitus, smoking, hypercholesterolemia, hypertriglyceridemia did not exert a reliable influence on the incidence of restenosis development in both groups (p > 0,05).

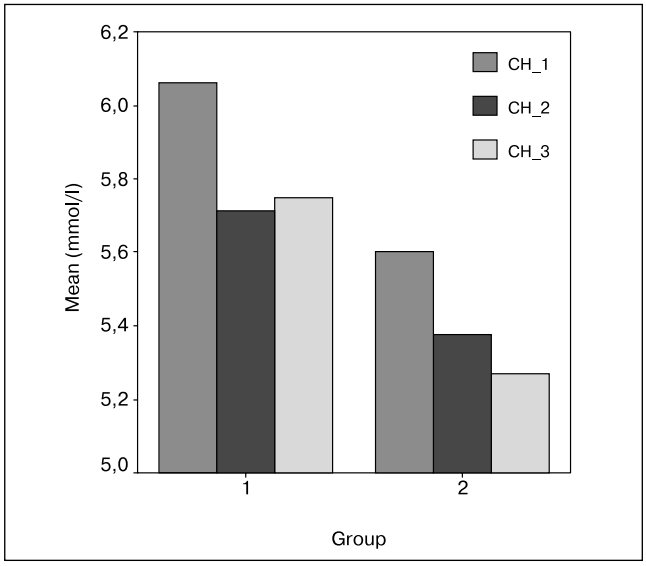


Diagram 11. Significant decrease in blood serum cholesterol in both groups

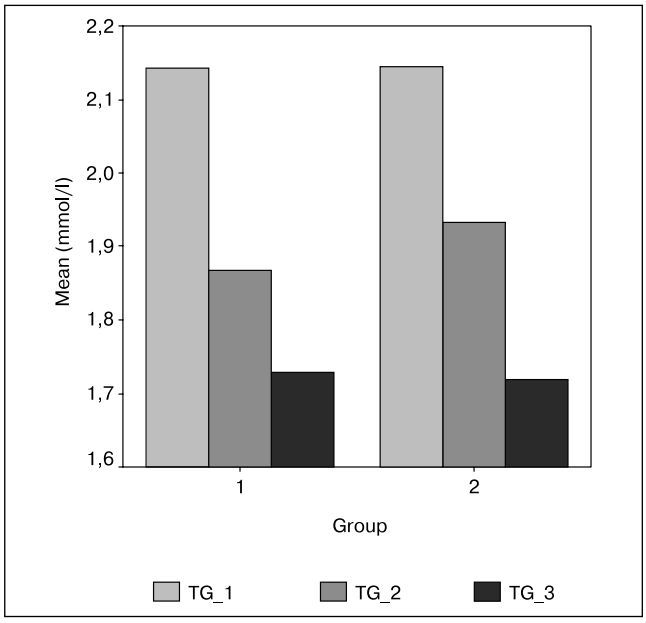


Diagram 12. Significant decrease in blood serum triglycerides in both groups

However, in the stented patients, blood serum cholesterol and triglycerides before the primary procedure did significantly influence the rate of late restenosis (r = 0,532, p = 0,005*; r = 0,525, p = 0,015*, respectively). It was revealed that the blood serum cholesterol levels ≥ 5,5 mmol/l in the follow-up period in the patients of Group 2 correlated with higher rate of restenosis (p = 0,027*).

Restenosis or occlusion in the site of procedure were mostly often revealed in the LAD (72,7% in Group 1, 75% in Group 2), less often - in the RCA and CA, with the differences being statistically not significant (p = 0,615) (Diagram 13).

In case of proximal lesion localization, restenosis was revealed more often in Group 2 patients (6/8 patients (75%),

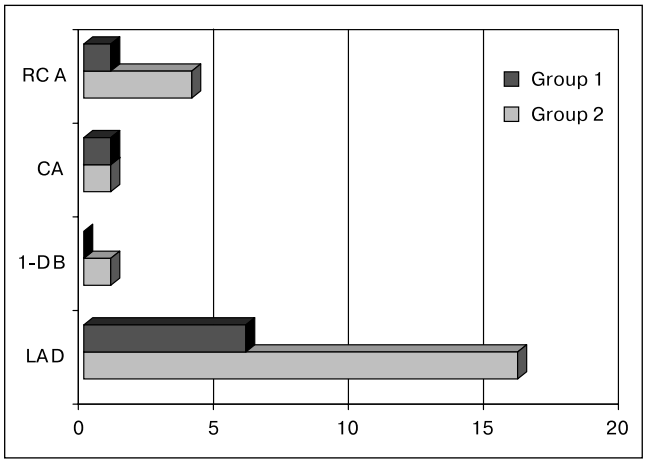


Diagram 13. Lesion of coronary vessels in patients with restenosis in the follow-up period

p = 0,559); on the contrary, in Group 1 patients, restenosis was diagnosed in a larger percentage of cases of lesion localization in the middle segment (14/22, 63,6%, p = 0,697).

The morphological characteristics of a stenosis (eccentricity, length, percentage, type) did not influence significantly the incidence of restenosis in the follow-up period for the entire cohort studied (p = 0,875; p = 0,724; p = 0,493; p = 0,372, respectively). However, in both groups most patients with restenosis had more complicated morphological characteristics of the stenotic lesion (type B2 and C, eccentricity) (Diagrams 14 and 15). It is worth mentioning that the length of the lesion amongst the stented patients exerted a significant influence on the prevalence of restenosis in the follow-up period (r = 0,578, p = 0,001*). It has been proven that restenosis is revealed reliably more often in patients with the length of the affected portion ≥ 18 mm (p = 0,001*).

The stent's length was observed to reliably influence the prevalence of restenosis (r = 0,398, p = 0,029*). Restenosis was revealed in 3 patients in whom a 15-mm long coronary stent was implanted (37,5%), in 3 patients with a 20-mm long stent (37,5%), in 1 (12,5%) patient with a 25-mm long, and in 1 (12,5%) with a 13-mm long stent. Hence, using a coronary prosthesis ≥ 20-mm long is reliably more often followed by restenosis in the follow-up period (p = 0,003*).

Mention should be made that the stent's design did not significantly influence the incidence of restenosis in the follow-up period (p = 0,141); however, the patients with restenosis more frequently had coil stents implanted (6/8 cases; 75%, p = 0,198).

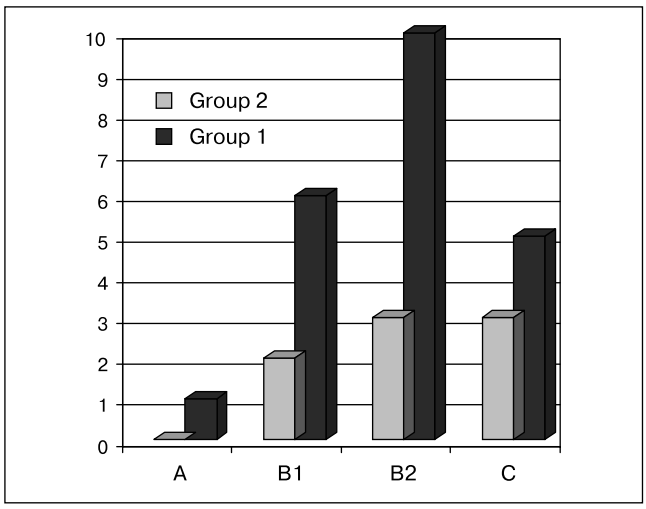


Diagram 14. Type of coronary lesions in patients with restenosis in both groups

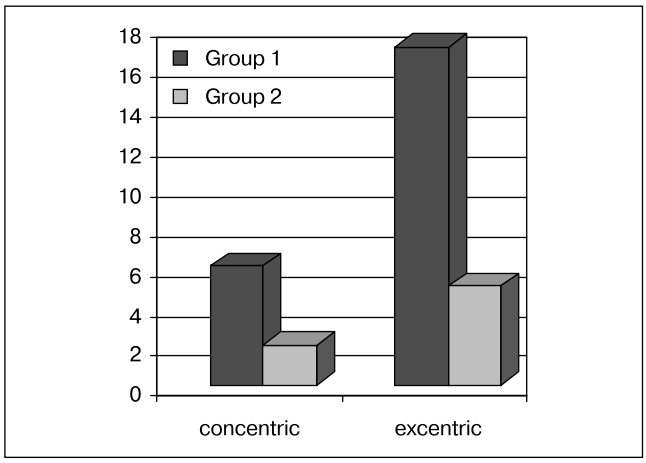


Diagram 15. Prevalence of eccentricity in both groups' patients with restenosis

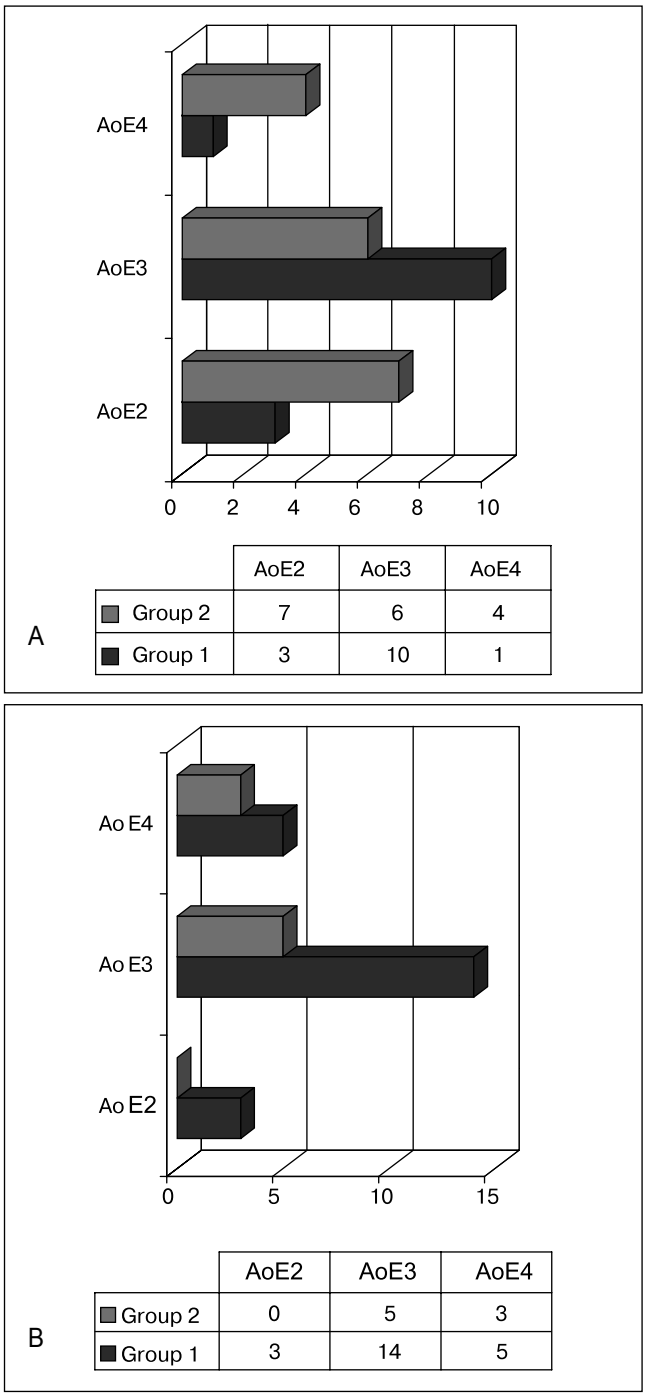
The analysis of the qualitative and quantitative criteria showed that reliable predictors for development of restenosis in the overall cohort of the patients are as follows: pronounced clinical manifestations of CAD at first examination (Spearman's coefficient r = 0,278, p = 0,024*) (Diagram 16) and end-diastolic left ventricular volume (Spearman's coefficient r = 0,330, p = 0,012*). In patients with the initially high functional class of angina of effort, decreased stress test load (Spearman's coefficient r = 0,426, p = 0,005*) and impaired diastolic function of the left ventricle, the probability of restenosis following the second procedure is considerably higher.

Besides, in the group of stented patients, the reliable predictors for coronary arteries restenosois were: hypercholesterolemia (5.5 mmol/l), hypertriglyceridemia, length of lesion ≥ 18 mm, stent length ≥ 20 mm (p = 0,027*, p = 0,015*, p = 0,001*, p = 0,003, respectively

Discussion

Restenosis is the main problem in the follow-up after successful PTCA. The purpose of the present work was to address this problem by comparatively assessing the long-term outcomes of stenting and repeated PTCA in patients with restenosis after primary PTCA.

This work was based on the findings of examination and treatment of two groups of patients with chronic forms of



	AoE2	AoE3	AoE4
Group 2	7	6	4
Group 1	3	10	1

	AoE2	AoE3	AoE4
Group 2	0	5	3
Group 1	3	14	5

Diagram 16. Functional class of angina of effort at baseline examination as a reliable predictor of restenosis in patients of both groups
A – without restenosis, B – with restenosis

CAD: Group 1 comprised 36 patients subjected to repeated balloon dilatation for restenosis; and Group 2 consisted of 30 patients who underwent 30 procedures of coronary stenting.

The patients in Groups 1 and 2 did not differ by age, sex, risk factors of development of CAD and associated morbidity, the number of the previous myocardial infarctions, diagnosis at the time of procedure, drug treatment used, size of coronary lesion, and the type of coronary circulation.

The long-term survival of the patients in both groups amounted to 100%.

According to our data, there was a reliable difference in the number of the patients with angina of effort at the time of the control examination [26 (72,2%) patients in Group 1 and 9 (30%) in Group 2, p = 0,001].

According to the findings of the present study, the form of CAD present at the moment of the primary procedure significantly influenced the clinical state of patients in both groups in the follow-up period (p = 0,024).

We aimed to study the dependence of the patients' clinical state on the completeness of the revascularization, long-term outcomes of the interventional procedures, and progression of atherosclerosis. It was shown that the patients with a good follow-up result of the procedure and without progressive atherosclerosis are in reliably better clinical state.

Our study showed a reliable growth of stress test load in Group 1 - from 70 ± 25 Wt to 82,03 ± 223,96 Wt (p = 0,0001); in Group 2- from 61,7 ± 22,9 Wt to 78,3 ± 26,4 Wt (p = 0,0001). At control examination, the majority of the Group 2 patients having performed the stress test yielded a negative result - 14 (58,3%), as compared with only 10 (31,3%) patients from Group 1 (p = 0,188)]. Increased time and volume of the performed physical exercise in the follow-up period were also observed by D. Rosing et al. and Y. Naim et al. [6, 7].

We evaluated the results of stress test with due regard for the interventional procedures in the follow-up period. Negative results of the stress test were obtained reliably more often in the patients without restenosis and progression of atherosclerosis (p < 0,05).

According to our data, the follow-up period after the interventional procedures is characterized by a reliable increase in the mean values of the LVEF from 57,4 ± 9,8% to 62,6 ± 8,7% in Group 1 (p = 0,0001), and from 56,7 ± 9,0% to 62,7 ± 10,4% in Group 2 (p = 0,0001).

Our study revealed a decreased demand for the main groups of antianginal drugs in both groups in the follow-up period, with the reliably decreased number of the Group 2 patients taking nitrates (p = 0,034). We studied the requirements for antianginal therapy depending on the presence of restenosis in both groups. The patients free from restenosis in the follow-up period received considerably lower amounts of nitrates (p < 0,05).

Coronary angiography performed in follow-up period revealed the preservation of good procedural results in 38,9% of patients after repeated PTCA and in 73,3% of patients after stenting, with the difference being statistically significant (p = 0,005). Restenosis (narrowing of the arterial lumen in the site of procedure by >50%) was revealed in 22 (61,1%) cases in Group 1, and in 8 (26,7%) in Group 2 (p = 0,005); occlusion in 0 (0%) and 2 (6,7%), respectively, p < 0,05). This result is comparable with those obtained in the study of R. Erbel and the studies on the stenting of the native vessels (STRESS; BENESTENT) [8, 9, 10]. In the REST study, the prevalence of restenosis after 6 months in the balloon-angioplasty group reached 32%, while in the group of the stented patients it was only 18% [5]. According to W. Hillegass and R.D. Safian, the incidence of restenosis after re-dilatation varies from 19 to 65% [11, 12].

According to our data, repeated interventional procedures were carried out in 2 patients of Group 1 (5,6%), in 3 patients of Group 2(10%); CABG was performed in 9 (25%)

and 3 (10%) patients, respectively. The Group 2 patients were less frequently subjected to repeat procedures of myocardial revascularization (PTCA, CABG) in the follow-up period [6 (20%) patients] than those from Group 1 [11] (30,6%) patients], (p = 0,0017), the differences are significant. In the study of Erbel R. et al., only 10% of the patients stented for PTCA restenosis required repeat revascularization (10% vs 27%, p < 0,0001) [5].

We also studied the factors prognostically significant for restenosis development in the follow-up period after interventional procedures. According to our data, the age and sex of the patients, a history of type 2 diabetes mellitus and AMI, tobacco smoking did not reliably influenced the overall restenosis development (p > 0,05). However, in the patients stented for restenosis, reliable predictors of coronary vessels restenosis development were hypercholesterolemia (≥ 5,5 mmol/l) and hypertriglyceridemia (p < 0,05). Besides, the form of CAD at the time of the initial procedure did reliably influence the overall level of restenosis in the follow-up period (p = 0,024). The analysis of the literature revealed the lack of common opinion concerning the assessment of the effect of such factors as sex, age, or diabetes mellitus on the level of restenosis. For example, D. Antoniucci et al. reported high incidence of revealing coronary arteries restenosis in elderly and female patients [13], however, the works of Ch. Bauters, J. Carozza and some other authors did not confirm these data [14, 15]. A. Kastrati et al. (1977), J. Carozza et al. (1992), M. Hamasaki et al. (1997) reported a high risk of restenosis development in the patient with diabetes mellitus, while Ch. Bauters et al. (1998) failed to find out such a dependence [14, 15, 16, 17].

Restenosis or occlusion in the site of the procedure were mostly often revealed in the LAD (72,7% in Group 1 and 75% in Group 2), less often - in the RCA and CA, with the differences being statistically not significant (p = 0,615). J. Carozza et al. [15], M. Hamasaki et al. [17] and S.G. Park [18] reported predominantly revealing restenosis in the circumflex artery [14].

In cases of lesion localization in the proximal segment, restenosis was revealed more often in Group 2 patients [6/8 (75%), p = 0,559], on the contrary, in Group 1 restenosis was diagnosed in a larger percentage of cases of lesion localization in the middle segment (14 of 22, 63,6%, p = 0,697).

We also evaluated the effect of the lesion's morphology on the incidence of late restenosis. We saw an insignificant increase in restenosis rate in the patients of Groups 1 and 2 with type C lesions [5 (22,7%) and 3 (37,5%) patients, respectively] as compared with the type A lesions [1 (4,5% and 0 (0%) patients, respectively] (p > 0,05). Type A lesions characterized by the most favorable morphology gave a better long-term angiographic outcome, as compared with type C lesions. Similar dependence of the restenosis development incidence upon the lesion's morphology was shown by D. Antoniucci [13], Ch. Bauters [14], S.G. Park et al. [19], J. Haase [20]; according to their data, the rate of restenosis in the presence of type C lesions was 34 – 43% in stented patients, and 41 - 64% in those after PTCA.

According to our data, the lesion's length reliably influences the long-term restenosis incidence in the stented subjects (p = 0,001). Thus, restenosis was observed reliably more often in patients with the lesion' length ≥ 18 mm (p = 0,001).

We revealed a reliable increase in the restenosis incidence depending on the length of the stent used. Restenosis was revealed more often in the presence of stents ≥ 20 mm of length (p = 0,003). Similar dependence of the restenosis incidence on the length of the stent used was shown by D. Antoniucci [13], Ch. Bauters [14], H. Le Breton [21].

Besides, we analysed the effect of coronary stent design on the incidence of late restenoses. Though we didn't reveal any statistical difference, restenosis was more commonly seen in coil stents (6/8 cases; 75%) (p = 0,198).

Hence, according to the findings of our study, we revealed that the therapeutic effect of the procedures manifested as the lack of clinical signs of angina pectoris, high volume of physical exercise, decreased demand for antianginal therapy was preserved in the follow-up period in the majority of patients after coronary stenting (p < 0,05).

The following factors reliably increased the probability of restenosis after stenting: hypercholesterolemia (≥ 5.5 mmol/l), hypertriglyceridemia, length of lesion ≥ 18 mm, stent's length ≥ 20 mm (p = 0,027*, p = 0,015*, p = 0,001*, p = 0,003*, respectively). Besides, the wire design of the stent, complicated (type B2 and C) morphology of the lesion, carrying out the procedure in the pool of the left anterior descending artery, as well as in the proximal segment of the vessel increased the risk of late restenosis after the repeated procedures (p > 0,05).

On the base of the above-mentioned data, a conclusion can be drawn that the use of coronary stents seems reasonable in order to decrease the rate of secondary restenosis and the need for repeated procedures of myocardial revascularization in the follow-up period.

Stenting in the site of restenoses following PTCA should be recommended for a particular cohort of patients, with the basic criterion for selection of patients for the intervention being the length of the coronary artery lesion. In particular, in cases of a segmental, discrete lesion (up to 18 mm long) the stenting of restenosis can give the most optimal results.

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Comparative study of immediate and long-term results of crimped stent "AngioStent C1" implantation

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Key words
Crimped stent "AngioStent C1", stenting, percutaneous coronary interventions.

Introduction

In the vast majority of cases interventional cardiologists prefer to use premounted stents for coronary artery stenting. On the contrary, application of so-called bare stents [1, 2] is not widely adopted into clinical practice. In contrast to premounted stent, bare stent is not a constituent part of a stent delivery system and has to be manually crimped on the balloon catheter. There is some reluctance among the practitioners to implant bare stents because of concerns regarding the possibility of stent dislocation [3, 4] and the risk of balloon damage and rupture [5]. In addition, this technique is not as simple as that for the premounted stents.

The above-mentioned disadvantages and associated limited acceptance of bare stent implantation resulted in a very scant information concerning this question in scientific publications. The main manuals of interventional cardiology under the editorship of Topol E. [6], Colombo A. [7], Marco J. [8], Safian R.D. [9] don't even mention this stenting technique. In contrast, Russian manuals of percutaneous coronary artery stenting [10, 11] contain detailed descriptions of bare stent crimping on the balloon catheter.

The interest of our interventionalists in this stenting technique is mainly attributable to its economical aspect. The point is that in case of a bare stent it is possible to use only one balloon catheter to perform predilatation and to deliver the stent, because bare stent is crimped on the same balloon catheter. So, crimped stent technique allows to reduce the cost of each procedure by the price of one balloon catheter (from 400 to 600 US $) [2].

We have not find any works concerning the application of "AngioStent C1" as a manually crimped stent.

The object of this study was to evaluate the results of coronary artery stenting with crimped stents "AngioStent C1".

Materials and methods

The analyzed group consisted of 88 patients who underwent stenting procedure with "AngioStent C1" (Angiodynamics), which was manually fixed (crimped) on the balloon catheter of the delivery system. A total of 106 "AngioStent C1" stents were implanted in 88 patients.

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The Tables 1 and 2 summarize the patients' clinical data and angiographic results.

Among the 88 patients of the "AngioStent C1" group there were 57, in whom the lesions presented technical difficulties. 23 patients (26,1%) underwent crimped "AngioStent C1" implantation because of bifurcated lesions. In 34 patients stenting was performed after the recanalization of occlusion (38,6%). One patient presented with bifurcated lesion involving distal portion of the left main coronary artery and proximal segment of the circumflex artery.

For the rest of 33 patients (37,5%) implantations of the crimped stents were performed to treat technically uncomplicated lesions. To define such lesions we used the following criteria: the diameter of diseased coronary artery >3,0 mm; the extent of stenosis < 23 mm, no signs of occlusion

Table 1. Clinical characteristic of the "AngioStent C1" group

Group / The analyzed parameters	"AngioStent C1" group n=88
Age (years)	52,84±9,42
Female	16 (18,2%)
Acute coronary syndrome	30 (34,1%)
Stable angina pectoris	58 (66%)
functional class I-II	34 (38,6%)
functional class III-IV	24 (27,3%)
Previous myocardial infarction	51 (58%)
Ejection fraction, %	59±9,25
Left ventricular aneurysm	10 (11,4%)
Previous CABG	8 (9%)
Hypertension	50 (56,8%)
Diabetes mellitus	3 (3,4%)

Table 2. Coronary angiography results in the "AngioStent C1" group

Group / Coronary angiography data	"AngioStent C1" group n=88
The average severity of stenosis, %	85,92±13,5%
The average diameter of the intact segment of the target artery, mm	3,5±0,45
Number of vessels diseased	
Single-vessel disease	27 (30,7%)
Double-vessel disease	39 (44,3%)
Triple-vessel disease	22 (25%)
Location of the stenosis	
The total number of target stenoses	106
Left anterior descending artery	49 (46,2%)
Circumflex artery	14 (13,3%)
Right coronary artery	42 (39,6%)
Left main coronary artery	1 (0,9%)

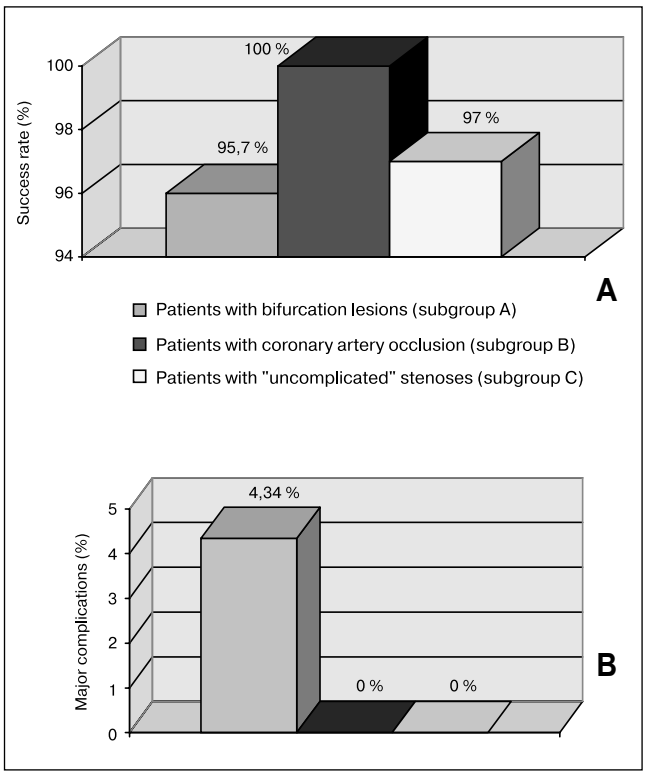

Figure 1. Immediate results of the intervention in the subgroups of the "AngioStent C1" group
A - success rate;
B - major complications

of the target vessel and the absence of the side branches at the site of stenosis.

In order to demonstrate safety and efficacy of crimped stent "AngioStent C1" we have assessed the results both in the whole group and separately in patients with uncomplicated lesions and in patients with lesions, technically difficult to treat. Thus, the whole group was divided into 3 subgroups. The subgroup A consisted of 23 patients with bifurcated lesions. 25 crimped stents were implanted in these patients. The subgroup B included 34 patients presented with coronary artery occlusions. The amount of implanted stents is this subgroup was 36. The subgroup C included 33 patients who underwent implantation of 45 stents as a treatment of "uncomplicated" stenoses.

The essence of the crimping technique consisted in stent fixation on the balloon by manual compression. Advancement of the crimped stent to the target stenosis was executed only after predilatation if proximal region of the target vessel was not too tortuous.

Results

The analysis of immediate results in patients of the "AngioStent C1" has shown that the procedure was successful in 86 patients (success rate 97,7%). One female patient with recurrent myocardial infarction died in the operating room due to stent thrombosis in the infarct-related vessel. In the second patient intervention was not successful because of severe dissection occurring distally off "AngioStent C1" implantation site.

The mean length of crimped stents was 13,95±5,43 mm. Dislocation of the stent was only noted in one case (0,94%). There was no stent embolization and stent was removed by retrieving the whole complex of guidewire balloon catheter and guiding catheter.

The rates of successful interventions and major complications in the subgroups of "AngioStent C1" group are shown in Figure 1.

Analysis of the long-term results in the whole group and in the subgroups is presented in Table 3. 62 patients (70,5% of the initial group) were examined 7,35±3,5 months after the intervention.

Unstable angina attributable to restenosis at the stent implantation site was observed in 4 patients (6,4%). No other adverse events were noted in the patients during the reviewed period. 34 patients (54,8%) of the "AngioStent C1" group had no angina over the long-term follow-up. Percutaneous coronary interventions (PCI) were effective in 75,8% of cases (47 patients). 9 patients (14,5%) underwent repeated revascularization because of restenosis at the stent implantation site.

The analysis of the long-term results in each subgroup of the "AngioStent C1" group revealed generally worse stenting results in patients with bifurcation lesions. So the rate of unstable angina in the subgroup A during the analyzed period was in fact 3 times greater than those in the subgroups B and C (12,5% vs. 4,5% and 4,2% respectively). Analysis of the repeated revascularization rates has shown similar results. CABG or PCI due to in-stent restenosis were performed in 31,3% of subgroup A patients, and only in 9% and 8,4% of those in the subgroups B and C respectively.

Discussion

We could not find in the literature any proof for the custom point of view that stent dislocation is more likely to occur after implantation of bare stent. Eggebrecht H. et al. [13] reported that there was a risk of stent embolization downstream in the coronary circulation as a result of its dislocation. But that risk was evaluated to be 0,27% for the premounted stents and 1,04% for the manually crimped stents. Meanwhile others [2, 14] did not confirm higher probability of dislocation for the crimped stent. According to the study performed by Chevalier B. et al. [1] the stent dislocation rate was even greater in the premounted stent group.

The use of crimped stents for direct stenting, a method associated with a higher risk of dislocation, has been analyzed in the work of Figulla H.R. et al. [4]. 80% of stents were

Table 3. Long-term results of coronary artery stenting in the analyzed group of patients and in the subgroups A, B and C

"AngioStent C1" group and subgroups / Long-term results evaluation criteria	"AngioStent C1" group n=62	Subgroup A n=16	Subgroup B n=22	Subgroup C n=24
The mean follow-up duration (months)	7,5±3,5	7,2±3.4	7,65±4.4	7,65±4.4
Adverse events - death - myocardial infarction - unstable angina	4 (6,4%) 0 (0%) 0 (0%) 4 (6,4%)	2 (12,5%) 0 (0%) 0 (0%) 2 (12,5%)	1 (4,5%) 0 (0%) 0 (0%) 1 (4,5%)	 0 (0%) 0 (0%) 1 (4,2%)
Clinical efficacy	47 (75,8%)	11 (68,7%)	17 (77,3%)	19 (79,2%)
Absence of angina pectoris	34 (54,8%)	9 (56,3%)	15 (68,2%)	10 (41,6%)
Repeated target vessel revascularization	9 (14,5%)	5 (31,25%)	2 (9%)	2 (8,4%)

successfully implanted, 10% of cases required predilatation. The attempts to implant the remaining 10% of stents failed, so in these cases it was necessary to insert premounted stents.

Theoretically, the implantation of bare stents is associated with a higher risk of stent dislocation, nevertheless we did not find any definite confirmation in the literature that this complication influenced the short- and long-term results of the procedure [1, 2, 14, 15]. The only randomized study of Schneider T. I. et al. [15] comparing the results of stenting with premounted and crimped stents did not reveal significant differences between the analyzed groups in the number of successful procedures, the incidence of major complications and the rate of restenosis according to control angiography performed 6 months after the intervention. Furthermore, Chevalier B. et al. [1] in their study of 6314 implanted stents have shown that if the target vessel had no calcification, the rates of stent dislocation and major complications were significantly lower in bare stent group than in premounted stent group.

Safety and efficacy of manually crimped stents has been proved by a number of works concerning the application of this technique in difficult clinical situations and/or in patients with complex anatomy [16, 17, 18, 19, 20]. The study of Urban P. et al. [20] has demonstrated a successful placement of bare stents through the 6F guiding catheter in patients presenting with dissection after previous balloon angioplasty (success rate 96%). Almagor Y. et al. [16] reported 95% success rate of the interventions in a group of patients, the majority of whom presented with unstable angina. Pierli C. et al. [19] effectively performed bare stent placement during emergency interventions in patients with left main coronary artery subocclusion. The other two studies [17,18] indicated the safety and efficacy of this stenting technique for the vessels less than 2,8 mm in diameter (success rate 98% and 100% respectively).

In our study interventions were successful in 97,7% of cases, major complications were noted in just one case (1,1%). The long-term clinical efficacy was maintained in 75,8% patients, 9 patients (14,5%) underwent repeated revascularization. Among the 88 patients of "AngioStent C1" group 57 (64,7%) presented with lesions technically difficult to treat (bifurcation lesion, coronary artery occlusion, left main coronary artery disease). The analysis of short- and long-term outcomes of stenting in those patients has shown that the results were identical to those in the similar subsets of patients according to the published data.

Conclusion

Stenting procedure with the use of manually crimped stents "AngioStent C1" is a safe and effective method of PCI for patients with "uncomplicated" stenoses and also for patients with coronary lesions technically difficult to treat.

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PTCA with and without in-house cardiac surgery standby: Experiences by the same group of operators at two institutions

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Abstract

Since the inventions of PTCA in-house surgical backup was advocated to be mandatory. We and others reported excellent results and low complication rates despite the lack of readily available urgency. Since 1995 cardiac surgery was established in one of our two institutions.

We retrospectively analyzed the outcome of 10,895 PTCAs performed in 1995 and 1996 by the same team of high volume interventional cardiologists at 2 institutions. Reasons for assignment to one center or the other were private insurance and procedural risk did not influence patient assignment to either center. To avoid potential bias, patients with acute MI, cardiogenic shock and PTCAs performed under protection of cardiopulmonary bypass were excluded. Surgical back-up was provided on a "next room available" basis by the same cardiac surgery department, located in-house for one interventional center (Heart Center Frankfurt, HCF) and 1 mile away from the second (Red Cross Hospital, RCH).

Results. Patients at the HCF were slightly older (age > 70 years, 27,2% vs. 24,2%) had more often prior CABG (9,9% vs. 8,7%) and unstable angina (20,1% vs. 8,4%) and, due to the lack of availability of a laser wire at the RCH, a higher proportion of chronic occlusions was treated (26,1% vs. 15,1%). This may explain a slighty lower primary success rate at the HCF (91,5% vs. 94,5%). Death occurred more commonly at the HCF (0,9% vs 0,4%), while no significant difference was seen in the incidence of emergent CABG (0,7% vs 0,5%) and Q-wave MI (0,6% vs. 0,5%).

Conclusions. For experienced cardiologists surgical back-up for interventional procedures at a nearby facility is a safe alternative to on-site cardiac surgery. In-house surgical backup does not improve the result of PTCA.

Keywords. PTCA, surgical stand-by, cardiac surgery, coronary bypass

Introduction

Surgical stand-by has long been considered essential for the safe performance of balloon angioplasty (PTCA). However, whether the presence of stand-by should be required at the same institution or whether backup at a nearby facility is adequate has been controversial. Among the first 50 patients treated by Gruntzig seven patients underwent emergent coronary bypass surgery (CABG) due to acute ischemia secondary to sudden or threatened vessel closure [1]. Similar outcomes were observed at other institutions in the early phase of PTCA. Therefore, readily available in-house surgical back-up appeared mandatory. Throughout the procedure an operating room as well as a surgical team were available. Almost all of the early operators, including Andreas Gruntzig, felt that an acute occlusion due to dissection should not be crossed with a guidewire, since this could result in extension of the dissection and an undue delay of emergent CABG. However subsequent experience has shown that an occlusive dissection can be opened rapidly, with the options of restoring flow by means of further dilatations or sending the patient to emergent CABG with guide wire and/or perfusion catheter in place. Furthermore, improvement of equipment and particularly the introduction of intracoronary stents have led to a markedly reduced incidence of emergent CABG after PTCA. As a result, surgical back-up is now routinely provided on a "next room available" basis. Nevertheless, in-house cardiac surgery stand-by is still a requirement for PTCA in many countries, including the US [2-7]. In other countries, particularly in Germany, interventional institutions without in-house cardiac surgery have been established, with back-up being provided by a cardiac surgery division nearby. Already, in 1993 more than 50% of all PTCAs (approx. 35,000 of 60,000) in Germany were performed at institutions without in-house stand-by [8-10]. Still, the most recent guidelines for the performance of PTCA by the German Society of Cardiology again recommend the presence of in-house surgical stand-by at the same institution. For low-risk patients surgical stand-by with a transport time of maximally 30 minutes is considered acceptable [11]. When comparing results and outcome of procedures performed at institutions with and without in-house surgical stand-by, it becomes apparent that, despite similar rates of success and complication, high-risk patients are preferentially treated at centers with in-house cardiac surgery. Due to this bias, the finding of similar rates of success and complications with both modes of stand-by may be of questionable validity. The goal of the present study was therefore to compare the results of PTCA, performed by the same group of operators, without prior risk stratification of patients at an institution with and a center without in-house cardiac surgical stand-by.

Methods

All patients undergoing percutaneous coronary interventions at our two institutions in 1995 and 1996 were retrospective-

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ly analyzed and compared with respect to procedural success rate and the incidence of a major adverse cardiac event (MACE), i.e. emergent CABG, Q-wave myocardial infarction or death, using a data base, which routinely stores information of all patients undergoing treatment at the respective institution. To put these results in perspective, comparable data from prior years at the same centers were obtained. Statistical comparison of proportions was performed using the χ^2 - test.

Study centers

Figure 1 shows the case load of PTCA procedures at both participating institutions, the Red-Cross Hospital (RCH, since 1985) and the Heart Center (HCF, since 1994), both in Frankfurt, Germany. In 1996 alone, over 5,000 PTCAs and over 6,000 diagnostic coronary angiograms were performed at both centers combined by the same team, consisting of 12 experienced interventional cardiologists with an individual annual case volume of at least 350 PTCAs/year. All 5 catheterization laboratories (3 at the RCH, 2 at the HCF) are equipped with digital imaging technology (Philips DCI, Philips Medical Systems, Best, Netherlands).

A 24 hour interventional coverage by two cardiologists (one in-house, one as back-up) is provided 7 days a week. Cardiac surgery back-up for both interventional institutions is available at all times in the next available operating room at the HCF, which is located about 1 mile from the RCH. Thus, cardiac surgery backup was provided by the same large surgical facility (approximately 1,700 open heart procedures/year) for both interventional institutions.

Patient population

In 1995 and 1996, of all patients undergoing coronary angiography at our institutions, 21% were referred to elective CABG, 53% had a percutaneous coronary intervention, while the remaining 26% were treated medically. Figure 2 shows the proportion of the different interventional techniques used at both centers in 1995 and 1996. The overwhelming majority of procedures consisted of balloon angioplasty with and without stent placement.

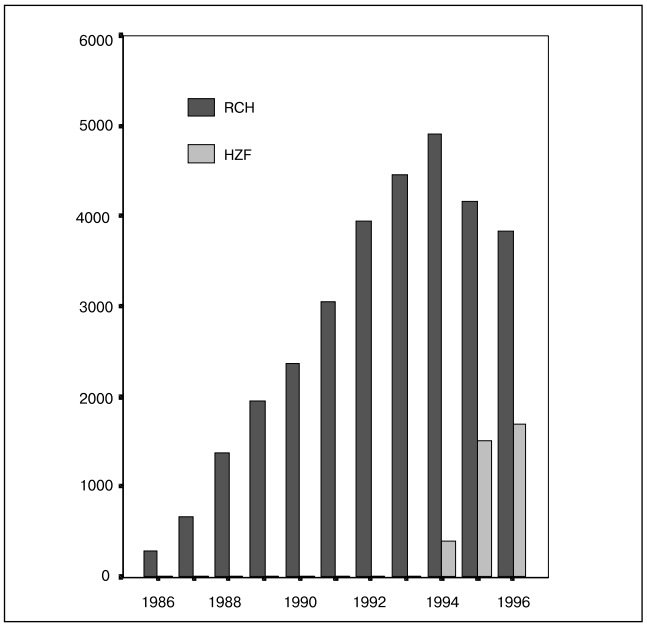

Figure 1. Number of annual interventional procedures at the Red Cross Hospital (RCH, since 1985) and at the Heart Center

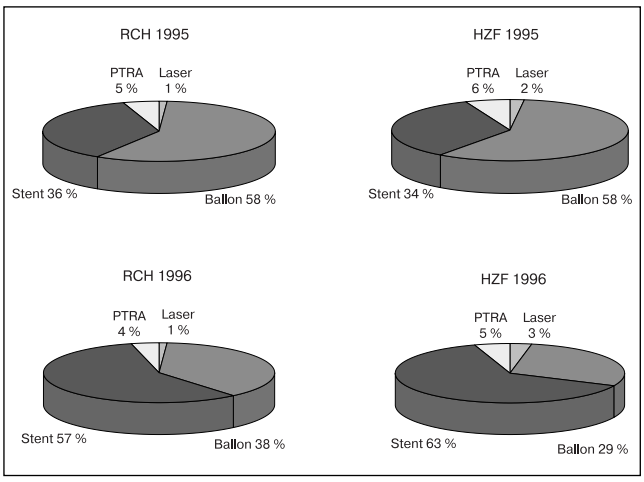

Figure 2. Proportions of interventional techniques applied at the Red Cross Hospital (RCH) and the Heart Center Frankfurt (HCF) in 1995 and 1996

A total of 11,177 patients underwent PTCA at our institutions (71,4% at the RCH, 28,6% at the HCF) in 1995/6. 40-50% of these patients were referred from other institutions after coronary angiography. 18% of patients were referred because interventional therapy was considered not feasible at another center, due to high risk, high degree of technical difficulty, or multi-vessel disease. For health insurance related reasons, more patients with acute coronary syndromes (acute myocardial infarction and unstable angina) were treated at the HCF (20,9%) than at the RCH (8,4%). To avoid a potential bias due to differences in procedural risk between patients treated at the two institutions, patients with acute myocardial infarction (RCH : n=119; HCF: n=133), cardiogenic shock (RCH: n=9; HCF: n=37), and interventions under CPS protection (HCF: n=75) were excluded.

Procedural technique

Patients are admitted the day prior to the procedure. β-blockers are discontinued and an oral calcium channel blocker (Verapamil or Diltiazem) or nitrates are given in addition to aspirin (300 mg) that day, as well as in the morning of the procedure.

PTCA is perfomed using 6F or 8F guiding catheters and mono-rail balloon catheter systems after administration of 10,000 - 15,000 U Heparin intravenously.

Other interventional techniques are used according to the following guidelines:

Stent implantation: acute or threatened closure due to dissection, residual stenosis > 30% after PTCA, chronic occlusions, lesions in vein grafts > 3 years old, recurrent restenosis after PTCA.

Rotational atherectomy: heavily calcified lesions, incomplete balloon expansion at inflation pressures >15 atm or diffuse atherosclerosis with long, calcified lesions.

Excimer laser angioplasty: chronic occlusions if crossed by a guidewire but not by a balloon, diffuse in-stent restenosis; laser wire in chronic occlusions, if a conventional guide wire could not cross the lesion.

Directional atherectomy: in rare cases of eccentric ostial stenosis.

Patients were referred for emergent CABG if a significant area of myocardium was at risk due to acute or threatened closure, despite repeated dilations and/or stent placement. Patients at the RCF were brought to the HCF by ambulance, which is located about 1 mile away.

Data collection

Data of all patients treated at either center are entered into a central data base, including QCA data, information regarding lesion morphology as well as clinical data, such as ECGs obtained prior to, immediately after, and 12 hrs following PTCA and whenever clinically indicated, creatine-phospho-kinase (CPK) and MB-fraction prior to, 6 and 24 hrs after the procedure, and any clinical events during hospitalization. Specially trained physicians on the ward as well as in the catheterization laboratory obtain data. Completeness of all relevant information is assured for each patient 4 to 8 weeks after the procedure.

Definitions

Unstable angina: typical anginal symptoms at rest despite maximal antianginal therapy (Braunwald classification IIIb).

Chronic occlusion: complete vessel occlusion of >12 weeks duration.

Primary procedural success: residual stenosis <50% without major adverse cardiac event (MACE) during hospitalization (Q-wave myocardial infarction, emergent CABG, death).

Non-Q-wave myocardial infarction: Increase of serum CPK level to >2,5x of the upper normal limit with >10% MB-fraction.

Emergent CABG: Operation within 24 hrs after PTCA due to angina, ischemia or angiographically documented vessel closure.

Results

Table 1 shows the change of patient characteristics from 1986 to 1996. Over time, older patients and more patients with higher risk features such as multi-vessel disease, prior CABG, and chronic occlusions were treated.

Table 2 compares baseline patient characteristics at the RCH and the HCF. Age >70 years, unstable angina, and prior CABG were slightly, but statistically significantly more common in patients treated at the HCF. Since the laser wire system is available at the HCF only, chronic occlusions were more common at that institution. No difference was found with respect to predictors of increased risk, such as the presence of multi-vessel disease and ejection fraction.

Emergent CABG was necessary in 65 of 10,895 patients (0,6%) treated at both institutions in 1995 and 1996. No significant difference was found between the two institutions (0,5% vs. 0,7%, table 3). Compared to the years prior to establishing our own cardiac surgery back-up at the HCF (starting in 1994), the need for emergent CABG increased (from 0,3% to 0,6%), despite the introduction of intracoronary stenting in the interim.

Table 1. Change of baseline characteristics of patients undergoing PTCA at the study centers from 1986 to 1996

Parametrs	1986-1990	1991-1993	1994-1996
patients, n	6458	8777	16200
age >70 years, %	9,8	16,4	25,2
multivessel disease, %	50,2	60,4	73,1
EF <50%, %	50,5	54,7	55,1
prior CABG, %	4,6	8,4	9,1
chronic occlusion, %	8,7	12,9	16,4

Discussion

The requirement for in-house cardiac surgery stand-by is based on very early experiences when PTCA as a novel technique was accompanied by relatively frequent life-threatening complications, with CABG as the only possible means of emergent revascularisation. Hereby, an operating room was kept available while PTCA was performed, with a surgical team, including a cardiac surgeon, a perfusionist and an anestesiologist standing by, resulting in a substantial allocation of resources. The subsequent development and maturation of PTCA, with increased operator experience, improved equipment, as well as the introduction of intracoronary stents [12, 13] has demonstrated the effectiveness of the concept of percutaneous revascularisation and has led to a reduction of severe complications by an order of magnitude [14, 15]. Therefore, and in response to increasing cost pressure, most institutions worldwide have reorganized surgical stand-by on a "next room available" basis. Now, the typical time required from making the decision to proceed

Table 2. Comparison of patient characteristics at Red Cross Hospital

Parametrs	RCH	HCF	p-value
Patients, n	7986	3191	—
Age >70 years, %	24,2	27,2	<0,001
Multivessel disease, %	75,9	74,5	NS
EF <50%, %	62,1	63,5	NS
Prior CABG, %	8,7	9,9	<0,05
Chronic occlusion, %	15,1	26,1	<0,001
Type B/C stenosis, %	87,8	88,3	NS
Unstable angina, %	8,4	20,9	<0,001

Table 3. Comparison of outcome after PTCA at Red Cross Hospital (RCH) and Heart Center Frankfurt (HCF)

Parametrs	RCH	HCF	p-value
Patients, n	7867	3028	—
Primary success, %	94,5	91,5	<0,001
Q-wave MI, %	0,5	0,6	NS
emergent CABG, %	0,5	0,7	NS
death, %	0,4	0,9	<0,001

with emergent CABG to establishing cardio-pulmonary bypass is 90-120 minutes [17-19]. It becomes obvious, that logistical issues involving operating room availability by far outweigh the time required to actually transfer the patient, as long as the transport can be completed within 30 minutes. The outcome after PTCA is highly dependent on experience of operator and interventional team, irrespective of whether cardiac surgical back-up is provided in-house or at another institution close by [20, 21]. Similar results with comparable rates of success and complications were found by the German working group of hospitalists in cardiology in a comparison of institutions with and without a cardiac surgery department [22-24]. However, these comparisons are limited by potential bias introduced by differences in operator experience and patient selection. For example, high-risk patients are more commonly treated at centers where in-house cardiac surgery is available. This has led to the widespread belief, that given the higher risk population, the finding of similar results with both modes of backup may actually indicate superior outcome at centers with cardiac surgery.

The present investigation, for the first time, compared outcome after PTCA in a large patient population with surgical back-up in-house vs. back-up at a nearby institution, while eliminating any influence related to operator and equipment. Great care was taken to avoid bias due to patient selection. Elective interventions were performed at either center independent of patient risk. Comparing the baseline characteristics of patients treated at the 2 study centers, a higher proportion of patients with acute MI (7,5% vs. 3,1%), unstable angina (20,9% vs. 8,4%), and patients who where not felt to be candidates for PTCA elsewhere are notable at the HCF. These differences are largely attributable to health insurances related issues, which restrict treatment of patients with public health insurance at the HCF to emergencies. To avoid any bias introduced by this overrepresentation of high risk patients with acute coronary syndromes at the HCF, we excluded patients with acute MI and cardiogenic shock from our analysis, as well as patients who underwent PTCA under the protection of cardio-pulmonary bypass. Since in our experience, in the age of coronary stenting, patients with unstable angina no longer have an increased risk of complications, these patients were not excluded, despite an uneven distribution between the two centers. Indeed, analysis of data excluding patients with unstable angina did not change our findings: primary success rate remained slightly lower and death slightly higher at the HCF, without significant differences in the incidence of emergent CABG and Q-wave-MI (data not shown). The present study also excludes any influence of the quality of the cardiac surgeon or the surgical institution on outcome after PTCA, since an identical team of cardiac surgeons at the same surgical facility provided backup for both interventional centers.

In our large patient population, we did not find superior outcome after PTCA with in-house surgical backup. Several reasons may account for this finding. The availability of a cardiac surgery team in-house may lead to referral for emergent CABG more frequently than absolutely necessary. This may explain the trend toward more frequent emergent CABG at the institution with in-house cardiac surgery observed in our study. Potentially, this could result in an increase of overall complications, since emergent CABG in the setting of transmural ischemia is associated with a markedly increased risk of serious complications [25, 26]. In selected instances acute myocardial infarction without emergent CABG may even represent a smaller risk. As already mentioned, patient selection may be affected. A false sense of security based on the presence of in-house cardiac surgery may cause the interventionalist to accept patients for PTCA, who would have otherwise been referred for elective CABG. This was not the case in our comparison, since the proportion of our patients treated by PTCA has not changed compared to the years prior to 1995, when in-house surgical backup was not available to us. At that time 52% of patients underwent PTCA (53% in 1995 and 1996), 20% were referred to CABG (21%), while 28% (26%) were treated medically. Outcome and complication rate in the present study were comparable to the results from the earlier period [27]. Nevertheless, it seems likely that today complex lesions are treated percutaneously, that would have been treated conservatively or by CABG in the past. This notion is supported by the stronger representation of patients age >70 yrs., presence of multivessel disease, chronic occlusions and prior CABG at both institutions (table 1). The growing number of complex interventions may contribute to the slight increase of complications over time at our centers, despite the use of coronary stents (emergent CABG from 0,3% before 1994 to 0,6% presently).

Every retrospective study is hampered by incomplete data or missing documentation. In our study, this influence was minimized by routine paperless documentation of all relevant data at our institution, which does not allow generation of the mandatory letter to the referring physician at the end of the patient's hospitalization if any data are missing.

The present as well as previous studies do not support a requirement for in-house surgical backup for PTCA, since there appears to be no beneficial influence on outcome parameters. The annual number of procedures performed by the operator and the institution seems to be of much greater importance, as well as external quality control, already in place at several centers [28,29]. Furthermore, establishing a larger number of cardiac surgery departments to provide in-house backup would not only represent an unnecessary financial burden, but may also be detrimental to patient care, since emergent CABG in the setting of transmural ischemia is a high risk procedure, that requires a highly experienced surgical team.

Conclusion

Based on the present study, which excludes bias due to patient selection, operator experience and equipment, there appears to be no benefit of in-house cardiac surgical back-up over stand-by on a "next room available" basis at a nearby facility. If patient transport can be done within 30 min. under safe conditions, no undue delay of emergent revascularization will occur. here was no clinically relevant difference in primary success rate or MACE between the two modes of back-up.

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Uterine artery embolisation

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Introduction

Percutaneous transcatheter embolisation has been practised by radiologists for well over 20 years. In many different clinical situations a great variety of embolisation materials or agents has been used in all parts of the body, but generally these procedures have been performed rarely. An important indication is severe bleeding not responding to conservative measures, where the alternative treatment would involve major surgery. Embolisation has also been used in tumours, particularly where they are hypervascular, when the role has often been to debulk and devascularise immediately prior to surgery. The third main indication is in arteriovenous malformations and fistulae. Thus, it is somewhat surprising that it was not until 1995 that uterine artery embolisation (UAE) was first advocated as a treatment for uterine fibroid disease [1].

First described in 1979, embolisation of the uterus has been reported in a variety of conditions including postpartum haemorrhage and bleeding following caesarean section or gynaecological surgery, haemorrhage after ectopic pregnancy, arteriovenous malformations and in gynaecological cancer [2-4]. In 1995, Ravina, a gynaecologist in Paris, described embolisation as a pre-operative adjunct to surgery in 31 patients [1]. One year later, the same group reported on 16 patients in whom uterine artery embolisation was used as the primary treatment [5]. They selectively catheterised both uterine arteries, which they then embolised with polyvinyl alcohol particles to the point of complete occlusion. At a mean follow-up of 20 months, 11 of their patients had a good clinical result, with 3 partial improvements and only 2 failures that progressed to surgery. Since this report, there has been great interest in this procedure, particularly from interventional radiologists. The literature on this procedure is not large and though good long-term data are still not available it is being increasingly accepted and it is estimated that over 15000 women have now been treated.

Indications

The indications for uterine artery embolisation for uterine fibroid disease are the same as for hysterectomy or myomectomy. One important difference between UAE and surgical procedures is that pathological confirmation of uterine fibroid disease is not obtained in UAE and the spectre is always raised that a uterine sarcoma could be missed [6, 7]. Uterine sarcomas are, however, extremely rare and their clinical presentation should be different. If there is any suggestion that a sarcoma could be present then further investigation with magnetic resonance imaging (MRI) is indicated [8]. It is also important to recognise that adenomyosis, may present with symptoms similar to those of uterine fibroid disease. Though embolisation has been advocated there are no data to suggest that embolisation is effective in this condition.

Many women, for a variety of reasons, choose not to undergo, or are reluctant to submit to a hysterectomy. In addition to seeking a uterus-conserving treatment, the morbidity of surgery and the time lost from work following surgery, has led many women to seek less invasive options. Myomectomy as a surgical alternative is only suitable for certain patients and involves the risk of severe bleeding and hysterectomy. Thus, many women will self-select for uterine artery embolisation and there is now a widespread awareness of the procedure as the result of publicity and information carried on the Internet. Indeed, many women will now approach their gynaecologist with a fair degree of knowledge about fibroid embolisation.

At present, all types of fibroid disease are considered suitable for uterine artery embolisation with the exception of the pedunculated subserous fibroids. Cases have been reported where necrotic subserous fibroids have resulted in bowel adhesions. The only other contraindication to the procedure is the presence of pelvic inflammatory disease, which should be excluded clinically. Women who would not consider a hysterectomy in any circumstances should also not be considered.

It is essential that all patients are recently assessed by a gynaecologist to confirm the clinical diagnosis and to assess whether the fibroids are the cause of significant symptoms. Just as it is important for women to be seen and assessed prior to uterine artery embolisation, it is equally important that they are followed up by the same gynaecologist who can be readily consulted in the event of any complications. There is a tendency now for women to be noted on routine ultrasound or computed tomography as having asymptomatic fibroid disease and to then assume that some treatment is necessary. These women need to be reassured that no treatment is necessary.

Establishing a Fibroid Embolisation programme

It is essential if a fibroid embolisation programme is to be established that radiologists and gynaecologists work in close co-operation [9]. Women should always have been recently seen and assessed by a gynaecologist who is both happy with the clinical diagnosis and that the fibroids are the cause of significant symptoms. Sometimes a woman will directly approach a radiologist known to be active in fibroid embolisation requesting the procedure. Even though a majority of women are suitable for fibroid embolisation it is important that they be advised to see a gynaecologist who,

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in addition to assessing them, can discuss alternative uterus conserving therapies such as myomectomy. A radiologist can only present a woman with details of the embolisation process and what the current experience is in terms of results and complications.

It is equally important that a woman has a responsible gynaecologist in the post-embolisation period. Though complications are relatively rare they do occur. Even though a radiologist can field post-procedure concerns particularly soon after the procedure, if a clinical assessment is considered necessary then a gynaecologist must be involved. This shared responsibility may vary between different groups of radiologists and gynaecologists but it is vital that it is clearly defined. It makes sense for the radiologist to be responsible for the woman's care whilst in hospital in the post-embolisation period but it is not essential. It is important that when a woman is discharged from hospital that she knows who to call in the event of any problems.

Assessment prior to the procedure

In addition to a recent gynaecological assessment, some form of routine imaging [9], usually ultrasound, is usually obtained. MRI will demonstrate fibroid disease in greater detail but the cost considerations will often restrict its use [8].

It is important to exclude the presence of any pelvic inflammatory disease that would be a contraindication to uterine artery embolisation. It has been suggested that a cervical swab should be routinely used but our approach is to exclude infection by the clinical history [9]. A pregnancy test should be routinely performed.

One of the concerns following uterine artery embolisation is that amenorrhoea has rarely been reported. It is particularly important in younger women. It is advisable to obtain follicle-stimulating hormone (FSH) levels on all women under the age of 45 years on day three of their cycle as this will give a pointer if early menopause is occurring.

Embolization Technique

All women, before they consent to uterine artery embolisation must be given a clear account of what the realistic expectations of the procedure are. It is important to explain exactly what embolisation entails and this is best achieved with a patient information leaflet [9]. The radiologist then must be available to deal with any questions or concerns. It is particularly important to explain that severe pain often results immediately following the procedure and to detail how this will be managed. It has been suggested, mainly in the USA, that uterine artery embolisation can be performed as a day-case procedure but we feel that the pain felt after the procedure requires an overnight admission. Radiologists should only attempt these procedures when they are well experienced with arteriography and embolisation techniques. It is also important that the procedures are carried out using state-of-the-art angiographic equipment that will enable the X-ray dose to be kept to a minimum.

The technique, using a standard arteriographic approach, involves selectively catheterising both uterine arteries and embolising them to the point of complete or near-total occlusion (Fig. 1). No attempt is made to selectively catheterise and embolise the fibroids as opposed to the remainder of the uterus. Some have advocated a coaxial embolisation (double-catheter) technique but this increases the complexity of the procedure, the time taken, the radiation dose, and also increases the cost [10, 11]. Other radiologists have found it difficult to catheterise both uterine arteries from the one femoral artery approach and prefer a bilateral femoral arterial access [12]. The aim is to safely position the tip of the catheter into both uterine arteries and filming is only necessary to confirm this and to demonstrate the vascularity of the uterine artery and the fibroid uterus. The uterine arteries have a characteristically tortuous course, usually being fairly low in the pelvis and coursing medially and anteriorly (Fig. 2). Usually a small (4F) catheter and steerable guide wire combination, this is fairly achievable by the experienced angiographer. However, this can sometimes prove difficult and technical failure occurs rarely.

The uterus is supplied by paired uterine arteries and, with rare exceptions, no other arteries need to be considered. They are usually of equal size but there may be some asymmetry [13, 14]. In fibroid disease, they give rise to abnormal vessels surrounding the fibroid which have a corkscrew-like appearance with marked vascularity and often the shape of fibroids is outlined by the abnormal vascularity. The aim of the embolisation is to occlude the vascular bed and the main artery to the point of complete occlusion. This is achieved by injecting particulate emboli mixed with contrast medium until the forward flow in the artery has been abolished and there is a tendency to reflux into the

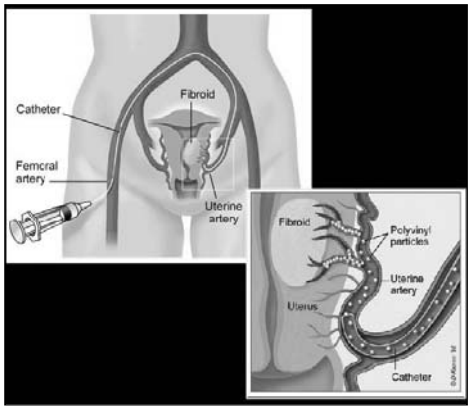

Figure 1.
Scheme of UAE operation. Selective catheterization of the left uterine artery through femoral artery, emboli delivery through the catheter

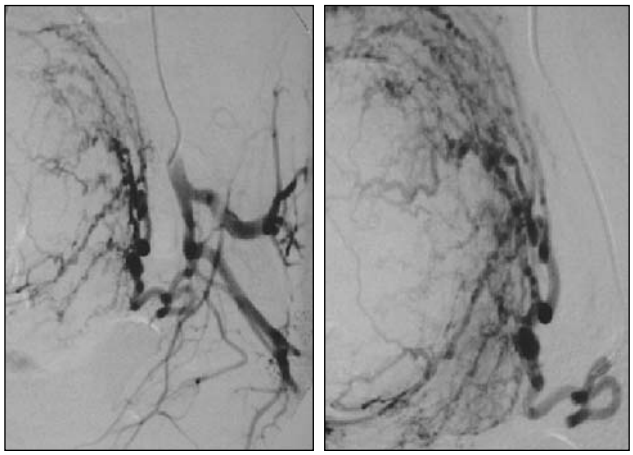

Figure 2.
Left - selective angiography of the left internal iliac artery;
Right - selective angiography of the left uterine artery

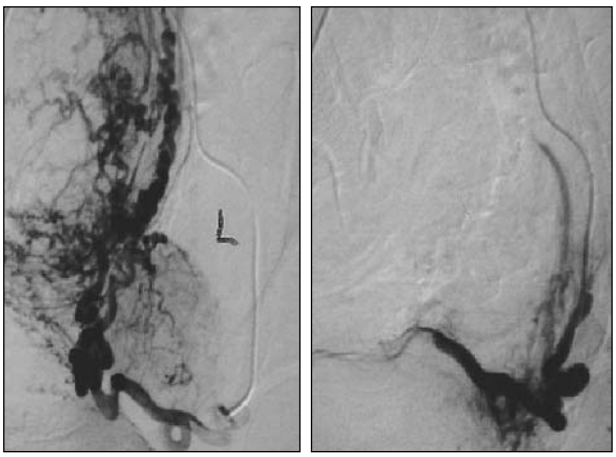

Figure 3.
Left - selective angiography of the left uterine artery before the embolisation; Right - after the embolisation

main internal iliac artery (Fig. 3). Polyvinyl alcohol (PVA) particles, which have been used in embolisation for over 20 years, are most commonly used [15]. These come in a range of particle sizes and the most commonly used size is 500 µ. Quite large quantities may be needed to effect occlusion in large fibroid uteruses and the polyvinyl alcohol particles are often supplemented by the injection of a suspension of Gelfoam. It has been suggested that Gelfoam, which is much less expensive than PVA, achieves the same result but it is biodegradable and the particle size is less controllable.

Though PVA is well established as a particulate embolisation agent its sized particles can be quite irregular in shape and there is a tendency for it to clump in suspension resulting in an embolisation procedure that is not uniform. Embosphere microspheres which are spherical microbeads specifically designed for embolisation have been advocated particularly for UAE [16]. It is suggested that they give a more uniform embolisation and that there is less post-embolisation syndrome but there is no good data to support this.

There is a real concern about uterine artery embolisation, particularly in younger women, as the ovaries are directly in the X-ray beam for much of the examination [17]. It is important that every possible measure to decrease the amount of radiation is used. State-of-the-art angiographic equipment with dose-reduction features including pulsed fluoroscopy are important. The skill of the angiographer should enable fluoroscopy times to be kept to a reasonable level. Limited filming should be obtained and it is only necessary to demonstrate selective catheterisation of the uterine artery if attention to these measures is not given, high X-ray doses can result which are equivalent to several barium enema studies [10]. This is particularly important in younger women who may possibly want to become pregnant at some future date.

Prior to starting up a uterine artery embolisation programme, it is essential to establish a pain relief protocol and anaesthetists and pain relief specialists should be consulted. Women should be monitored throughout the procedure. The approach at Guy's & St Thomas' Hospital is to give intravenous sedation at the beginning of the procedure. Pain does not occur until the second uterine artery is embolised and it is important to give strong analgesics just prior to this stage. We give an intramuscular injection of 10mg morphine and, at the end of the procedure, we establish an intravenous patient-controlled analgesia (PCA) pump set to give 1-mg boluses of morphine with six-minute lock-out periods. We find that non-steroidal anti-inflammatory such as Diclophenac 100mg given as a suppository either alone or combined with the PCA are effective following the procedure and these drugs can be repeated once after 12 hours. The postembolisation syndrome, as well as the morphine, is likely to result in some nausea and vomiting and it is important to prescribe anti-emetics. With rare exceptions, women are able to go home the next day but it is important that they are given a supply of analgesics as some less severe pain may persist for two to three weeks. They are advised to take about two weeks off work but some women are able to go back to work sooner.

There are real concerns regarding the risk of infection following UAE and it is important to realise that this can occur several months later with necrotic fibroids. Many radiologists will routinely give prophylactic antibiotics at the time of the procedure even though there are no good data to support this approach. Based on the gynaecological surgical experience and the knowledge that anaerobic infections may occur, giving a single dose of metronidazole with a cephalosporin or quinalone drug has been recommended [9].

Complications

Early complications

The postembolisation syndrome, of which pain is the most important component, occurs in the majority of women following UAE. Nausea and vomiting and a feeling of general malaises are also features of this syndrome which may last for up to two weeks. Potentially, local femoral artery complications can occur following arteriography but with the use of small catheters and in non-atheromatous patients, these should be extremely rare. Some moderate haematoma can occur as in any arteriographic procedure. Constrast reactions are now extremely rare. There is a possibility that other arteries can be embolised (non-target embolisation) but this should be wholly preventable by embolization technique and careful fluoroscopy during the embolisation procedure. Any reflux from the uterine artery would only embolise other branches of the internal iliac and, unless significant reflux occurred, this would have no clinical sequelae. Our experience suggests that technical failure occurs in about 2,5% of patients. This includes inability to selectively catheterise a very tortuous uterine artery and also anomalies where a small or non-existent uterine artery is rarely present on one side.

It is quite common for some discharge to occur, starting a few days after the procedure and lasting several weeks. This is usually an intermittent non-purulent discharge and sometimes fragments of fibroids may be passed. If the discharge becomes offensive and if later this is associated with pain or fever, infection should be suspected and the patient urgently assessed with a view to treatment. The early experience of uterine artery embolisation did not pay much attention to complications. Whereas the results of uterine artery embolisation are limited by the short term of the follow-up, it

is possible to address complications as they should be apparently within approximately three months. The following assessment is based on our initial experience of 300 women and, in particular, of 212 in whom there was a greater than 3 month follow-up period. The women were notable in that they had relatively large fibroid disease with a mean fundal height of 17 weeks and included a high proportion of Afro-Caribbeans.

Late complications

Fibroid expulsion occurred in 8% of patients and occurred at any time from 1 week to 4 months. Others have reported a lower incidence and an even later occurrence. Fibroid expulsion was more common with large fibroid uteruses particularly when submucous fibroids were present and, in a few cases, adjunctive gynaecological procedures were needed for the fibroid removal. Apart from one patient, who had a hysterectomy associated with infection, all the patients recovered well, and this would appear to be a good outcome.

Occasionally cervical fibroids present as a particular problem when they are not accessible to a hysteroscopic approach. These cases would appear to respond well to UAE with the likelihood that the fibroid will shrink and subsequently be passed vaginally. These patients need careful follow-up as they will usually require some gynaecological assistance.

Chronic vaginal discharges occurred in 7% of patients. This usually necessitated antibiotic treatment and could be quite persistent. Gynaecological ancillary procedures with either suction evacuation or fibroid removal were necessary in about half of these patients. Again, this was associated with larger fibroid disease.

Amenorrhoea occurred in three women. One, aged 38 years, had normal FSH levels and cyclical symptoms and was thought to have endometrial atrophy. A woman aged 41 years developed amenorrhoea with an elevated FSH (no pre-uterine artery embolisation FSH). The third woman was 47 years old and FSH levels were not obtained. Others have reported a higher incidence of amenorrhoea but most have occurred in women who are perimenopausal.

The most significant complication of UAE is the presence of infection necessitating hysterectomy. This initially occurred in 4/212 women and subsequently in 5/300 women. All the women were Afro-Caribbean with a fundal height between 20 and 34 weeks. One occurred 1 week postembolisation but the others occurred at 18,20 and 13 weeks. The hysterectomies were difficult procedures and necrotic fibroids were present in all except one woman who had a pyosalpinx. It is likely that an increasing awareness and earlier diagnosis and treatment of this late complication will improve the overall outlook in these patients. It is important to detail this risk to women agreeing to UAE with 1% being a realistic overall figure for hysterectomy.

Two deaths have been reported following uterine artery embolisation. In one, a woman re-presented 11 days post-uterine artery embolisation with septic shock (18). Blood cultures grew Escherichia coli and, despite a hysterectomy, she never recovered. The second case, with only limited data available, was reported from Italy, where a woman of 60 years of age known to have breast cancer died of a massive pulmonary embolism one day later.

Results

There are only limited and less satisfactory data available on results following uterine artery embolisation. No randomised control data are as yet available and there are no long-term results. In the limited literature of about 1000 women a variety of methods have been used to assess the clinical results, all of them short-term evaluations [19-24].

Furthermore these assessments are made more difficult as it seems to be generally accepted that these are difficult women to assess and many of them present with high expectations of this uterus conserving procedure. Notwithstanding the limitations of these assessments, the overall results suggest that 80-90% of the patients are happy with their clinical result. In addition to the symptomatic assessment of patients, objective assessments have been made of the degree of fibroid shrinkage and overall uterine size reduction. Both ultrasound and MRI evaluations have been used, with MRI being the more sensitive and precise technique for measurement. An overall fibroid size reduction of around 50% has been reported, which may take up to six months and more before it is complete [8, 25].

After the initial enthusiasm for uterine artery embolisation, many workers are now establishing better health-related quality-of-life assessment protocols and [26, 27], in a number of countries, registries are being established and all this should allow better data to be obtained on this new procedure. Ideally, a randomised controlled study should be established with uterine artery embolisation compared with surgery. Whereas there is a general acceptance of this methodology, there are real concerns that recruitment of women to such a trial is going to prove difficult.

Fibroids and fertility

Though fibroids are commonly associated with infertility and miscarriages it is not currently recommended that embolisation is indicated unless the fibroids are also associated with significant symptoms. There are innate concerns regarding uterine artery embolisation in women who may want to become pregnant in the future. Some have suggested that it should not be advocated in such women due to the lack of research into the long-term effects of UAE on both fertility and the child. However this must be balanced against the view that says that there are no easy choices for infertile women with large fibroids. The reality is that there are only two reasonable uterus-conserving options, myomectomy and embolisation. The data for fertility following myomectomy has been better than the uterine artery embolisation. There are however a number of papers attesting to normal pregnancies occurring following embolisation as the experience of this procedure increases [28-31]. In a recent paper 139 women out of 400 who underwent UAE stated a desire for fertility after the embolisation. Of these only 52 were under the age of 40 and their progress was closely followed. 17 pregnancies occurred in 14 women. The course of their pregnancies and their deliveries were unremarkable suggesting that the risk compared favourably with that of patients undergoing myomectomy [32]. In such younger

women who are concerned about future fertility, myomectomy should be weighed up against UAE. Factors affecting the choice include gynaecological experience of myomectomy, number and size of fibroids and the woman's own preferences having been given all the information. More data is required as in UAE in general.

Conclusion

Uterine artery embolisation is a relatively new technique applicable to the majority of women with fibroids. Early results are very encouraging with the majority of the women being happy with the procedure with a low risk of complications. At present the data are short term and longer term data with controlled studies are really required before its place can be established.

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Angiographic diagnosis of the injury of the thoracic aorta and its branches

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Since 1990 through 2002 angiography for suspected injury of thoracic aorta (TA) or its branches was performed in 36 patients. Twenty-four patients presented with blunt chest trauma (most commonly due to car accident), 12 patients had penetrating wounds of the chest (gunshot wounds in half of the cases). Aortic injury was diagnosed in 6 patients and the injury of aortic branches - in 14 patients. Injury of TA or its branches was revealed by angiography in all patients without any false-positive or false-negative results. Despite the implementation of novel diagnostic methods, angiography remains the major diagnostic option for this condition.

Key words Injury of thoracic aorta and its branches, angiography.

Introduction

Injury of the thoracic aorta (TA) and its branches is a life-threatening consequence of blunt trauma or penetrating wound of chest. It has been established that in industrially developed counries TA rupture occur in 20-30 people per 1 million of population [1] and results in instantaneous death in 80-90% of cases [1-7]. Despite the advances in emergency medicine, for the last decades this mortality level has changed only slightly [7]. Vascular injuries sometimes remain undiagnosed due to severe combined damage of musculoskeletal system and the viscera.

Prior to surgery most surgeons prefer angiography (AG), as a diagnostic tool, rather than other diagnostic methods [7-10]. The purpose of the study was to analyze our AG experience in patients with blunt injury of TA and its branches.

Materials and methods

Since 1990 through 2002 thirty-six patients were referred to angiography department with suspected injury of TA or its branches, suggested by the nature of injury, clinical manifestations and radiological study. Among the patients there were 32 men and 4 women aged 14 to 69 (mean age 35.3). AG was performed on the following systems: "Advantex DLX" (General Electric), "Angioscop C" (Siemens) and "Cardiomax CP" (Shimadzu), most commonly through right femoral artery approach; angiography with multiple projections was attempted in patients with normal general state.

Results

Twenty patients were directly referred to our hospital from the site of accident, whereas 16 patients were referred from other hospitals. Twenty-four patients presented with blunt injury and 12 patients - with wounds. TA injury was suspected in 21 patients (subsequently confirmed in 6 patients) and the injury of aortic arch branches – in 15 patients (subsequently confirmed in 14 patients). The nature and location of injury are summarized in table 1.

Aortic injury was detected by AG as an additional cavity with irregular and fuzzy borders in 5 patients (Fig. 1 a, b), local aortic dilation with an additional structure (intimal dissection) in 1 patient (Fig. 2). Injury of the aortic arch branches was seen in 8 patients as a contrast depot or a cavity, in 3 patients – as an occlusion, in 1 patient – as a giant aneurysm with occlusion of the distal arterial segment,

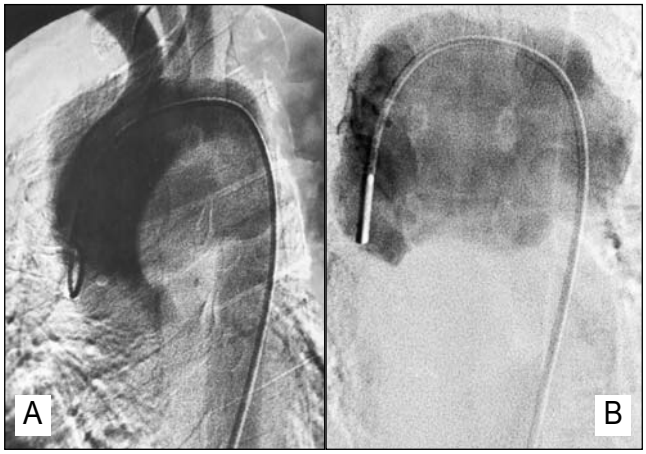

Figure 1.
A - Angiogram. Woman (aged 25) with TA rupture involving the isthmus (occupied the passenger's seat)
B - Opacification of a cavity, originating from the aortic rupture, with irregular and vague borders

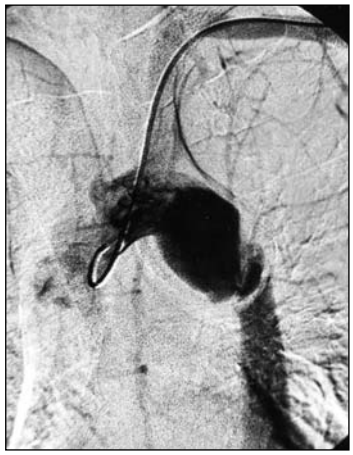

Figure 2. Angiogram. Rupture of TA isthmus with intimal dissection found in a driver (aged 29) injured by the steering wheel

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combination of cavity with arteriovenous shunt was found in 2 patients.

Severe combined trauma of musculoskeletal system and viscera were seen at admission in all patients, particularly those with TA injury.

The analysis showed that the injury of TA and its branches was revealed in all cases without any false-positive or false-negative results. At the same time, in 2 cases the obtained results proved to be incomplete. In one patient with diagnosed rupture of the descending TA during the operation it was revealed, that the main damage was indeed located in the descending portion, but the rupture of lesser degree advanced to the aortic arch as well. In other patient an extravasate was found between the origins of brachiocephalic trunk and left common carotid artery in close proximity to the aorta. Aortic arch rupture was diagnosed, whereas autopsy showed aortic arch rupture involving the brachiocephalic trunk. AG was preformed repeatedly in one patient, as the first procedure didn't exclude partial rupture of the aortic arch, and the results of computer tomography (CT) and ultrasound study were unequivocal. Repeated AG denied the suspected aortic defect.

Discussion

Chest X-ray, [11-14], aortic angiography [8, 15-19], computed tomography (CT) [9, 10, 16, 18, 20-22], ultrasound study [16, 18, 23-26] are used to diagnose injury of TA and its branches.

Review of publications [11-14] suggests that this injury can be associated with up to 15 different radiographic symptoms, either alone or in combinations: widening of mediastinal shadow on X-ray, mediastinal/thoracic ratio exceeding 0.25, displacement of trachea to the right, flatness and fuzziness of aortic borders, compression of left principal bronchus, fractures of ribs and clavicle, displacement of nasogastric tube to the right, etc. No such symptom, either alone or in combination, is specific, it can merely be the basis for the diagnosis of suspected aortic injury.

Angiography is a conventional diagnostic option, commonly named "the gold standard"[8, 15, 17, 19]. However, this is an invasive and expensive method, which isn't completely bereaved of mistakes: its sensitivity can be as low as 91%, specificity – 94.6%, true-positive results – 92.2%, true-negative results – 93.7% [18]. At the same time, in the group of patients, assigned to AG after screening studies, these parameters reach 100% [9]. Therefore, other radiological methods were introduced, both for screening and basic examination.

Spiral computer tomography with contrast enhancement is noninvasive, substantially cheaper and requires less time [9, 10, 16, 18, 20-22]. Its sensitivity can be as high as 97-100%, specificity – 99,3-99,8% [18, 22], i.e. exceed that of AG. The problem of CT is that it commonly reveals the mediastinal haematoma without showing its cause [16]. CT is a screening study, useful to exclude aortic injury, as it almost gives no false-negative results, but requires AG due to the low rate of true-positive results - 43,9% [18]. CT doesn't reveal any specific signs of injury of aortic arch branches [8].

Transesophageal echocardiography is used to diagnose TA injury [16, 23-25]. Sensitivity of the method can reach 100%, and the specificity – 98% [25]. However, this method has intraobserver variability and requires high skill for accurate and effective diagnosis [25]; visualization of distal portion of the ascending TA and proximal portion of the descending TA, aortic arch branches is often difficult [23, 25]; combined injury of TA and aortic arch branches can remain undiagnosed [15]. All such cases, again, necessitate AG.

A new method is the intravascular ultrasound [18, 26], which has demonstrated its high performance. Thus, its

Table 1. Nature and location of injury in patients, referred for AG

Nature of injury	Number of patients, referred to AG	Number of patients with vascular injury	Injury location
Aorta			
1. Road accident	9	4	aortic arch - 1 descending aorta - 3
2. Compression by vehicle side	4	1	aortic arch and brachiocephalic trunk - 1
3. Automobile-pedestrian accident	5	1	aortic arch and descending aorta - 1
4. Fall from a height	3	-	
Aortic arch branches			
1. Gunshot wound	6	5	right subclavian artery - 3 right vertebral artery - 1 left vertebral artery - 1
2. Punctured and incised wound	5	5	left subclavian artery - 2 right subclavian artery - 1 injury of left subclavian artery and vein causing shunt formation - 2
3. Car accident	2	2	right subclavian artery - 1 left subclavian artery - 1
4. Train accident	1	1	left subclavian artery - 1
5. Iatrogenic injury	1	1	right subclavian artery - 1
Total	36	20	

specificity, sensitivity, true-negative and true-positive results for the detection of "minimal" aortic damage (intimal dissection less than 1 cm in length with no or minimal para-aortic haematoma) was 100% [18]. However, this is an invasive, expensive and currently poorly adopted diagnostic option, besides, it is not always able to give an overview of the injury.

Development of novel technologies resulted in the occurrence of the two approaches to the diagnosis of injury of TA and its branches: 1) angiography as the basic method, any other methods merely delay the diagnosis [8]; 2) screening study is performed at baseline, most commonly by CT and only when appropriate, angiography is indicated in ambiguous cases [9].

But even those who support the second approach admit, that AG reserved its role in the following cases [18]: 1) intimal injury; 2) false aneurysm formation; 3) large para-aortic hematomas of the mediastinum, the origin of which cannot be ascribed to any other kind of trauma; 4) ambiguous and uncertainty of CT findings.

Therefore, angiography remained the main diagnostic option, and, in some cases, a "judge"; at the same time, screening studies (particularly CT) can reduce the number of "unnecessary" angiographic studies, when there's no aortic injury, thus making AG exclusively fine and definitive method. Some sorts of TA injuries ("minimal" ruptures) require combined use of different radiological methods.

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Leading Russian Centers of Interventional Cardioangiology

Moscow City Center of Interventional Cardioangiology (MCCIC)

Moscow City Center of Interventional Cardioangiology (MCCIC) was founded in 1996 as a result of joining up of two clinical departments:

1. Urgent and Interventional Cardiology Department of Bakoulev Scientific Center for Cardiovascular Surgery (RAMS), led by a world-known cardiac surgeon V.I. Bourakovsky. Among the staff of the Scientific Center there were well-known cardiovascular surgeons A. Pokrovsky, G. Tsukerman, V. Podzolkov, V. Alexi-Meskishvili, V. Rabotnikov and interventional cardiologists Yu. Petrosian, L. Zingerman, A. Ivanitsky.
2. Cardiology Department №6 of Moscow City Clinical Hospital №15.

For many years both those departments were headed by professor D.G. Iosseliani, who initiated the creation of a new center of interventional cardioangiology. Now he is the Director of the Center of Interventional Cardioangiology. Great assistance in the organization of the Center was rendered by Moscow Mayor Yuri Luzhkov.

The support of Moscow Government allowed to create state of the art medical institution satisfying all up-to-date requirements, to solve the problem of capital repairs of the hospital buildings, and to supply MCCIC with the most modern medical equipment.

Today MCCIC has three main buildings, one of which (the clinic) is located in downtown Moscow, the other (the ambulatory) is located in one of the new districts, and the third (rehabilitation service) is situated in beautiful green area near Moscow, in the village Bykovo.

At present MCCIC provides a wide range of diagnostic and therapeutic services for Moscow residents, including endovascular procedures and surgical treatment. However, the main priority of MCCIC is a treatment of CAD patients.

MCCIC possesses unique experience for Russia in endovascular restoring of the impaired cardiac circulation in patients with acute myocardial infarction and unstable angina pectoris.

Currently Moscow City Center of Interventional Cardioangiology is the head medical institution of Moscow City Health Department dealing with cardiovascular diseases in adults. Over the last several years the director of MCCIC Professor D.G. Iosseliani has been occupying the position of the Chief Cardiologist of Moscow.

MCCIC collaborates with cardiological clinics in different countries. Staff members involved in therapeutic procedures were trained in leading medical institutions of Europe and USA. Close working relations are maintained with St. Luke's Hospital (Milwaukee, Wisconsin, USA).

Since 2001 MCCIC has been collaborating with the Clinique Saint-Augustin (Bordeaux, France). The staff members of MCCIC routinely perform surgical myocardial revascularizations in co-operation with the surgeons of Clinique Saint-Augustin led by Jean-Charles Vernet. The collaboration is carried out according to the long-term agreement approved by Moscow City Government and Moscow City Health Department. Earlier the director of MCCIC D.G. Iosseliani was awarded the State Prize of Russian Federation for putting direct myocardial revascularization into clinical practice.

A close interaction between MCCIC and Moscow's Ambulance and Emergency Care Service allowed to develop and put into practice the Program of complex gradual myocardial reperfusion for patients with acute myocardial infarction. The results of this joint scientific and practical work, evaluated in 2002, showed reduction of in-hospital mortality rate to 4,2% in patients with acute transmural myocardial infarction. The authors of the Program were awarded the Moscow Government's Prize in the field of medicine.

MCCIC consists of the following Units:

1. Cardiac Intensive Care Unit for patients with emergent conditions - 12 beds*.
2. Intensive Care Unit for patients following cardiac surgery and major vessel surgery - 4 beds.
3. Cardiological Department for patients with acute myocardial infarction and unstable angina pectoris - 40 beds.
4. Cardiological Department for patients with different cardiac diseases - 40 beds.
5. Cardiovascular Surgery Department - 20 beds (2 operating rooms and 2 artificial blood circulation apparatus, one of these operating rooms is equipped with mobile X-ray unit "Powermobil" (Siemens)).
6. Rehabilitation Department for patients with cardiovascular diseases - 90 beds - located outside Moscow in a nice quiet green area (village Bykovo). The department consists of Rehabilitation Unit for patients with acute myocardial infarction (45 beds) and Rehabilitation Unit for patients following cardiovascular surgery or endovascular interventions (45 beds).
7. Radiological Department focused on diagnostics and endovascular treatment of cardiovascular diseases. Till the middle of 2003 there was only one operating room equipped with X-ray system Coroscop Hicor Classic (1996, Siemens). At present MCCIC is outfitted with two more operating rooms equipped with angiographic systems Axiom Artis FC and ANGIO CT MIYABI (a combination of AXIOM Multistar and SOMATOM CT). Actually, endovascular diagnostic and therapeutic procedures are performed by 12 surgeons, six of them can execute all procedures in patients with CAD and major vessels

* The Center is permanently open for urgent cases brought by emergency care teams.

diseases. MCCIC provides a full array of interventional services, except for carotid artery manipulations.

8. Functional Diagnostic Department.

9. Biochemical Lab.

10. X-Ray Department (Radiography and Computed Tomography (Volume Zoom)).

11. Consultative Diagnostic Outpatient Clinic consisting of two outpatient departments: the first is located within MCCIC, the second - in another district of Moscow. These outpatient departments are focused both on selection of patients to be referred to MCCIC and on the rehabilitation services for discharged patients with cardiovascular diseases.

The Outpatient Clinic has a Medical Labor Expert Commission for patients following acute myocardial infarction and endovascular or surgical interventions.

Clinical activity of MCCIC: from 1996 to 2003, MCCIC served 23650 patients, of which 18872 were treated conservatively, 3942 underwent endovascular procedures (all endovascular interventions were performed in the only available operating room), and 855 patients received surgical treatment. Among all those patients 3784 (16%) presented with AMI, 3547 (15%) presented with unstable angina pectoris, 10406 (44%) had chronic CAD, 3074 (13%) presented with valvular heart diseases, cardiomyopathy or heart rhythm disturbances and 2839 (12%) patients had vessel diseases. Overall mortality rate was 0,65%.

During the reviewed period 10135 cardiac and major vessel catheterization procedures were performed. In the vast majority of cases there were selective coronary angiography and left ventriculography procedures. 810 angiographic examinations of major vessels were performed.

Selective coronary angiography and left ventriculography was performed in 976 patients with AMI. 750 patients underwent balloon angioplasty of infarct-related artery, stents were implanted in 190 patients. In 9159 cases selective coronary angiography and left ventriculography were executed in patients with other forms of CAD, 2700 patients underwent transluminal coronary balloon angioplasty and 1052 – coronary artery stenting. Overall mortality rate after PTCA and stenting procedures was 0,14%, in patients with AMI it was 0,2% and in patients with other forms of CAD – 0,07%.

It's worth mentioning that over the last two years there was a dramatic increase in the number of endovascular diagnostic and therapeutic procedures.

During 2002-2003, 4084 contrast examinations were performed in MCCIC, among them 3761 were selective coronary angiography and left ventriculography and 323 - angiography of the major vessels. 1194 coronary artery balloon angioplasties were performed in 970 patients and 489 coronary artery stenting procedures were accomplished in 396 patients. 448 patients presented with AMI underwent selective coronary angiography and left ventriculography, 320 of them received balloon angioplasty of the infarct-related artery and 44 underwent stenting procedure. Mortality rate was 0,28%. 3132 procedures of selective coronary angiography and left ventriculography were performed in patients with chronic forms of CAD. 763 patients underwent coronary artery balloon angioplasty and 338 – coronary artery stenting. Mortality rate was 0,08%.

Angiography of the major vessels was performed in 315 patients. 28 of them underwent balloon angioplasty and 30 underwent stenting procedure. Mortality rate was 0%.

During the reviewed period 855 cardiovascular operations were carried out, 179 of which were direct myocardial revascularizations. Mortality rate was 1,5%.

The main scientific interests of MCCIC are the following:

— Development of a method for gradual myocardial revascularization using pre-hospital thrombolysis with subsequent in-hospital coronary artery angiography and PTCA / or stenting in patients with acute myocardial infarction.

— Study of long-term outcomes of PTCA for in-stent stenoses.

— Analysis of short- and long-term results of coronary artery stenting with new generations of stents.

— Total endovascular myocardial revascularization: whether it is good alternative for direct myocardial revascularization or no?

— Automated systems in the interventional cardiology.

— Endovascular interventions on coronary arteries following direct myocardial revascularization.

— Comparative analysis of PTCA and stenting for the treatment of brachiocephalic, renal and lower extremity vessel lesions.

As soon as new operating rooms are ready, the procedures of endovascular closure of patent foramen ovale, endovascular aortic stenting and implantation of pacemakers and cardioverters will be put into clinical practice of MCCIC.