Original article

Different reactivity of the proximal and distal segments of the radial artery to vasoconstrictors in patients undergoing coronary artery bypass grafting

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Abstract

Background: Complete arterial revascularisation using the radial artery (RA) is an attractive alternative to venous graft implantion for the coronary artery bypass grafting (CABG). In spite of the favourable long-term results of this approach, the sensitivity of RA to vasoconstriction and spasm is still limiting its use. It has been suggested that vasospastic properties of the artery may differ depending on the location (proximal or distal).

Aim: To compare the vasoreactive properties of proximal and distal sections of RA grafts.

Methods: Proximal and distal segments of RA were obtained from 27 patients undergoing CABG and isometric recordings of changes in smooth muscle force were performed mounted in the organ bath. Responses to cumulatively increasing concentrations of phenylephrine (PE), angiotensin II (AT-II), prostaglandin F2α (PGF2α) and endothelin-3 (ET-3) were evaluated.

Results: Both proximal and distal segments of RA constricted in response to KCl, PE, AT-II, PGF2α and ET-3. Proximal segments demonstrate significantly greater spastic response to KCl, as well as to receptor-mediated agonists PE and more importantly vasoactive peptide AT-II. These differences remained statistically significant after correcting for vessel size and weight. In contrast, reactivity of both segments of RA to increasing cumulative doses of PGF2α and ET-3 was similar.

Conclusion: Proximal segments of the radial artery are more susceptible to vasoconstriction induced by PE and AT-II, which should be taken into consideration in the clinical setting of CABG surgery. Increased muscle content in this segment does not fully explain this difference, which may result from varying receptor density and properties.

Key words: radial artery, CABG, proximal, distal, angiotensin II, total arterial revascularisation

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Introduction

Complete arterial revascularisation using the radial arteries is a promising method that may replace the saphenous veins as aorto-coronary grafts because of decreased rate of restenosis associated with arterial grafts. There are observations suggesting that the use of the radial artery (RA) reduces early and late mortality and morbidity [1], leading to prolonged survival [2] in comparison with saphenous vein grafts. There is still an increasing number of arterial coronary artery bypass grafting (CABG) procedures in Poland and worldwide because of promising long-term outcomes. More interestingly, any attempts to apply other arterial grafts, including gastroepiploic or epigastric ones, have failed due to several contraindications and postoperative complications [3-7].

Advantages of RA are also associated with its anatomy. Benefits include its length of >20 cm that allows it to be implanted into a number of sites; inner diameter of 2-3 mm that enables an optimal anatomical as well as functional match to the recipient coronary arteries; and a thick muscular layer that makes anastomosis technically easier. Moreover, clinical

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conditions such as obesity, diabetes and previous laparotomy do not exclude RA use [8]. For all these reasons, increased clinical interest in the use of RA for arterial CABG has been observed.

A significant limitation of the extensive use of RA as an aorto-coronary graft is its susceptibility to vasoconstrictors that can induce arterial spasm manifested clinically. Currently, three approaches to minimise or abort undesired artery spasm are applied: the 'no-touch' technique of graft harvesting [9, 10], flushing of harvested artery with papaverine (phosphodiesterase III inhibitor) instead of using mechanical artery dilatation leading to endothelial damage, and postoperative vasodilatation with calcium channel blockers or nitrates [8, 11].

It has been suggested that RA spasm may result from excessively traumatic surgical intervention, local tissue acidosis or receptor-mediated mechanisms of reaction to circulating catecholamines and platelet-derived factors or higher number of smooth muscle cells within RA media compared to other arterial vessels [8].

Recently it has been suggested that individual RA segments may present with different vasoconstrictive sensitivity, including susceptibility to vessel spasm. Thus, during CABG the use of an RA segment less prone to vasoconstriction may have important clinical implications and may reduce myocardial hypoperfusion following surgery.

In the present study vasoconstrictive activity of distal vs. proximal RA segments was compared in response to several vasoconstrictors.

Table I. Clinical characteristics of the examined group of patients

Characteristics of examined patients	Value
Age [years]	63.1±1.5
Male gender	18
Risk factors of atherosclerosis:	
• smoking	9 (33%)
• arterial hypertension	27 (100%)
• diabetes mellitus	8 (29%)
• hypercholesterolaemia	21 (78%)
• myocardial infarction	13 (48%)
• mean blood pressure [mmHg]	132±2.1/80±1.3
• max systolic blood pressure [mmHg]	169±4.3/93.9±2.3
• body mass index [kg/m^2]	28.9±0.9
Administered medications:	
• beta-blockers	21 (78%)
• aspirin	21 (78%)
• nitrates	16 (59%)
• reductase HMG-CoA inhibitors	22 (81%)
• Ca-blockers	6 (22%)
• ACE-I	18 (67%)
• insulin	3 (11%)
• oral hypoglycaemic drugs	5 (19%)
• diuretics	8 (30%)

Methods

Clinical characteristics of patients

Specimens of blood vessels were harvested from 27 patients (18 men and 9 women) undergoing CABG with radial arteries. Table I outlines characteristics of patients and medication. The following risk factors of atherosclerosis were selected: hypertension (patients on chronic antihypertensive medications or blood pressure >140/90 mmHg in at least 3 separate measurements); diabetes mellitus (fasting serum glucose level ≥7.0 mmol/l or ≥6.1 mmol/l when measured in the whole venous blood or therapy with insulin or oral anti-diabetic medications), hypercholesterolaemia (total serum cholesterol concentration >4.8 mmol/l or the use of lipid lowering drugs), smoking (current or within the last 6 months). All examined patients had a history of hypertension. Patients operated on were usually receiving chronic medications and medical therapy was not interrupted for the time of operation.

The study protocol was approved by the Ethical Committee and according to its requirements written informed consent to participate in the study was obtained from all patients.

Examined vessel segments

Short distal and proximal segments of RA were harvested during CABG. These vessel segments were taken from a given patient in the paired manner. All vessels were harvested using the 'no-touch' technique and placed in cooled Krebs-HEPES buffer [12], then immediately in ice and finally transported to the laboratory according to the procedure developed by us and published previously [11, 12]. Vessels were dissected free meticulously from the adjacent tissues and divided into smaller segments using microinstruments under inverse microscope guidance. The experiment was started within 30 to 45 minutes from harvesting.

Physiological study of isolated vessel rings

Blood vessel reactivity in vitro was assessed using an organ bath chamber according to the methodology that was developed and described previously [12, 13]. The arterial segments after division into rings of 2 to 3 mm in length were placed in 5 ml organ chambers and hung between two hooks. Proximal and distal RA segments harvested from a given patient were examined simultaneously. The bath chambers were filled with warmed (37°C) Krebs-Henseleit buffer (KHB) (120 mN NaCl; 4.7 mM KCl; 1.2 mM $MgSO_4$; 1.2 mM KH_2PO_4;

2.5 mM $CaCl_2$; 25 mM $NaHCO_3$ and 5.5 mM glucose). The vessel rings spread between two steel hooks of the device were equilibrated for 60 to 80 minutes then strained passively to the baseline value of 20 mN. The vessel rings were contracted a few times with equal concentrations of potassium chloride (KCl) (60 mM). After repetitive responses to KCl were achieved, cumulative increasing doses of phenylephrine (PE) (from 10^{-9} to 10^{-2} M) then of angiotensin II (AT-II) (from 10^{-12} to 10^{-6} M), prostaglandin F2α (PGF2α) (from 10^{-9} to 10^{-5} M) and endothelin-3 (ET-3) (from 10^{-9} to 10^{-7} M) were added one by one. Examined substances including KCl, PE and PGF2α were used in the concentration range presented in the previous reports and added to the organ bath chamber model during study of RA segment physiology [11], while in the case of AT-II the concentration range was extended (by one order of magnitude higher and two orders lower) [11, 14]. Dose of administered ET-3 was suggested by published data where concentration range was $6 \times 10^{-9} - 95 \times 10^{-9}$ M [15]. Each vascular ring was exposed to three tested chemicals at all aforementioned doses, but order of substances differed each time to avoid any disturbances of the observed effect possibly related to the sequence of the added vasoconstrictors. Agonist agents used were rinsed before administration of the subsequent one for approximately 45 minutes. Responses to vasoconstrictors presented below are mean values for the given concentrations to minimise any possible effect of substance property changes. Contraction was expressed as an absolute value in mN (after subtraction of baseline tension) and in the case of a number of experiments (n=8) the findings were presented as mN/mg of vessel weight (wet vessel weight). All experiments were performed in the presence of indomethacin (at a dose of 10 µmol/L) to inhibit vascular prostaglandin synthesis [12], which was found in the preliminary experiments to lead to marked instability of vascular stress in vitro.

Statistical analysis

Results are expressed as the mean value with standard error of mean (± SEM). For comparison of two groups of vascular rings (proximal vs. distal segments) tests such as Student's t-test, Wilcoxon or Mann-Whitney U test were used depending on variable distribution and probe character. In order to calculate EC_{50} (dose of agent causing 50% of maximum contraction) a non-linear regression model was applied. The value of $p < 0.05$ was considered statistically significant.

Results

Receptor-independent contractile responses

First, contraction of the vascular segments in response to KCl as independent from receptor-mediated mechanisms but related to direct change of smooth muscle cell membrane polarisation was evaluated.

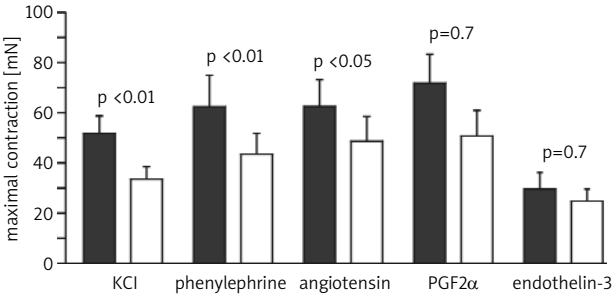

Figure 1. Comparison of maximal vasocontractile response of the distal (black bars) and proximal (white bars) radial artery segments after KCl (60 mM), phenylephrine (3×10^{-3} M), angiotensin II (1×10^{-8} M), PGF2α (1×10^{-6} mol/l) and endothelin-3 (1×10^{-7} M) administration. Measurements were performed in vitro in the organ bath chamber. Absolute value of contraction was expressed in mN. The bars present arithmetical mean ± SEM (n=13)

Table II. Comparison of maximal vasocontractile responses of the proximal and distal radial artery segments (doses of vasoconstrictors as in Figure 1). Contraction is presented in mN/mg of vessel and expressed as arithmetic mean ± SEM (n=8)

Substances	Proximal arterial segment [mN/mg]	Distal arterial segment [mN/mg]
KCl	4.1±1*	2.7±0.8
Phenylephrine	6.2±1.5*	4.2±1.3
Angiotensin II	2.6±1.3*	1.2±0.7
PGF2α	5.7±1.1	5.1±0.9
Endothelin-3	2.8±1.1	2.8±0.8

*$p < 0.05$

Contractile responses after KCl administration (60 mN) were significantly more pronounced in the proximal RA segments than distal parts expressed as either mN (Figure 1) or mN/mg of the vessel (Table II).

Receptor-activated contractile responses

Response to PE. Proximal RA segments revealed significantly higher maximal contractile responses to increasing PE concentrations (Figure 1). This difference was observed starting at PE concentration of 3×10^{-5} M (41.7±8.7 vs. 25.9±6.5 mN for proximal and distal segment, respectively; $p < 0.02$) and then gradually increased together with higher PE concentration up to 1×10^{-2} M (58.7±11.4 vs. 41.8±8.6 for proximal and distal segment, respectively $p < 0.04$) while maximal difference in contractile response was noted for concentration of 3×10^{-3} M (Figure 1). Response to lower PE concentrations (from 3×10^{-9} to 1×10^{-5} M) did not differ significantly

Table III. The EC_{50} and E_{max} values of responses of the proximal and distal radial artery segments to stimulation with phenylephrine, angiotensin II, PGF2α and endothelin-3

Substances	Proximal arterial segment		Distal arterial segment	
	EC_{50} [mol/L]	E_{max} [mN]	EC_{50} [mol/L]	E_{max} [mN]
Phenylephrine	$5.8\pm1.1 \times 10^{-6}$*	62.1±11.9*	$1.6\pm0.5 \times 10^{-6}$	43.3±9.1
Angiotensin II	$7.5\pm1.3 \times 10^{-8}$	61.7±11.7*	$8.5\pm1.3 \times 10^{-8}$	49.2±9.6
PGF2α	$1.1\pm1.2 \times 10^{-5}$	71.8±12.0	$6.7\pm1.5 \times 10^{-6}$	51.5±8.6
Endothelin-3	$4.2\pm1.1 \times 10^{-8}$	29.3±6.7	$4.3\pm3.3 \times 10^{-8}$	24.3±4.7

**p <0.05 for a comparison of the contractile response (EC_{50} or E_{max}, respectively) to phenylephrine, angiotensin II, PGF2α and endothelin-3 of the proximal vs. distal arterial segment*
EC_{50} – dose of substance causing 50% of maximal vessel ring contraction, E_{max} – maximal contractile response

between compared vascular segments. At the same range of concentrations, a statistically significant difference of vasocontractile response expressed in mN/mg of vessel was observed (Table II).

Response to AT-II. Similarly to PE, increased cumulative concentrations of AT-II caused significantly higher contractile response of proximal RA segments. This difference was observed for concentrations ranging from 1×10^{-8} to 1×10^{-6} M (an example for concentration of 1×10^{-6} M is shown on Figure 1). Meanwhile, the absolute contractile response to AT-II concentrations between 1×10^{-12} and 3×10^{-9} did not differ significantly. Similarly, vasocontractile response of RA segments expressed as mN/mg did not differ significantly in concentrations ranging from 3×10^{-9} to 1×10^{-6} M (Table II).

Responses to PGF2α and ET-3. Contractile response to PGF2α within the analysed concentration range, i.e. from 1×10^{-9} to 1×10^{-5} M, did not differ significantly between the proximal and distal RA segment (an example for PGF2α concentration of 1×10^{-5} M is presented as Figure 1).

Administration of ET-3 in increasing concentrations from 1×10^{-9} to 1×10^{-7} M provoked similar contractile responses in the examined vascular segments (an example for ET-3 concentration of 1×10^{-7} M is presented in Figure 1).

After PGF2α and ET-3 administration in the applied concentration range no statistically significant difference in vasocontractile responses expressed in mN/mg of vessel was observed (Table II).

Maximal contractile responses. E_{max} and EC_{50}. Maximal contractile reactions of the examined vascular segments in response to administration of the bath organ chamber increasing cumulative PE (from 1×10^{-9} to 1×10^{-2} M) and AT-II (from 1×10^{-12} to 1×10^{-6} M) concentrations were significantly higher in the proximal than distal vascular segments. Such a difference was not observed for increasing concentrations of either PGF2α (from 1×10^{-9} to 1×10^{-5} M) or ET-3 (from 1×10^{-9} to 1×10^{-7} M) (Table III).

Meanwhile, a comparison of EC_{50}, defined as the concentration of a given vasoconstrictor that induces 50% of maximal contractile response, for the examined arterial segments did not reveal any significant differences after AT-II, ET-3 or PGF2α administration (Table III).

Discussion

In this study, an analysis of the clinically important problem of the use of the proximal and distal RA segments during CABG was attempted. The sensitivity of both proximal and distal arterial segments to several vasoconstrictors has been studied. The use of KCl in experiments on the vascular rings enabled us to evaluate receptor-independent smooth muscle cell contractility. Enhanced contractility of the proximal segments in response to KCl administration is consistent with published data and suggests higher smooth muscle representation within the proximal segment [16]. Thus, vasoconstrictor response of RA segments was expressed in absolute mN values despite the fact that it depends on contractile power of several myocytes and their mass in a given specimen. The histological study was abandoned due to the earlier reports indicating that contents of smooth muscle in the proximal segment are higher than in the distal one. Moreover, all examined vascular segments had the same length. Presentation of the results as absolute values is a commonly accepted method for experimental studies performed in the organ bath chamber model [12].

In some experiments, vasoconstrictor response was expressed in mN/mg of wet vessel mass. Calculation of vascular ring mass is consistent with the measurements of media containing myocytes (medial volume) and the former method of presentation has been used previously [17]. In the experiments described herein, compliance of these measurements was also observed. Only responses to AT-II, a concentration range with a revealed significant difference between the proximal and distal segment, was widened by one order of magnitude when the results were presented as absolute values in mN.

The aforementioned findings suggest that sensitivity to receptor-dependent vasoconstrictors is at least partially distinct in the compared vascular segments. This is especially true for the responses to PE (mediated through alpha1-adrenergic receptor) and AT-II (predominantly via

AT1 receptor). It may also be a result of differences regarding the number and activity of available receptors in the examined vascular segments. A predominant role of the alpha-adrenergic (alpha1 and alpha2) receptor rather than the beta one in vasoconstrictor response of RA was reported [18]. Our results suggest that more alpha1-receptors are available in the proximal segment of the examined vessel.

The experiments performed previously in the organ bath model showed comparable vasoconstrictor activity of proximal and distal RA segments in response to endogenous vasopressors such as norepinephrine and epinephrine, which cause alpha1- and alpha2-receptor--mediated contraction. Different representation of smooth muscle along RA course suggests the presence of a distinct profile of available receptors in the compared vascular segments [16].

Angiotensin II, formed from angiotensin I in a process catalysed by endothelial ACE, provokes direct receptor--dependent (AT1 receptor) vascular smooth muscle contraction and indirect contraction through increased release of norepinephrine from the sympathetic nerve endings [19]. Our experiments suggest better AT1 receptor availability in the proximal RA segment or increased norepinephrine release from the intramural nerve endings.

No differences regarding vasoconstricting activity of the examined segments were shown in the case of PGF2α and ET-3 stimulation. An experimentally proven higher number of smooth muscle cells within the proximal RA segments shows distinct profiles of PGF2α and ET-3 receptors in the compared vascular segments. The response of the vascular rings to endothelin-1 is still being questioned. Endothelin-1 acts mainly via ETA receptors found on the smooth muscle cells. Contrary to endothelin-1, ET-3 acts not only via ETA receptors but also ETB located on the endothelial cells, and through release of NO and PGI2, which may promote vessel relaxation [19].

Most likely, variant sensitivity of the examined vascular segments to contraction is not only a result of higher muscular content, but also distinct receptor-mediated specific reactions. Our results showing that vasoconstrictor response does not differ only for some examined agonists confirm this opinion. If it was associated only with smooth muscle contents within proximal RA segments, they would contract stronger in response to all administered substances. Moreover, the differences in reaction to KCl, PE and AT-II were still noted if vasoconstrictor responses were expressed in mN/mg of vessel (used for correction of segment differences particularly with respect to medial volume).

In a series of our own experiments (not presented in this paper), no statistically significant differences were found in endothelial function based on NO bioavailability (response to acetylcholine). This suggests no differences regarding a correlation between endothelial dysfunction and contractile activity of the examined vascular segments. Data from literature indicate that RA presented lower NO and EDHF bioavailability in comparison with IMA, which may be one of the factors responsible for RA increased contractile susceptibility [20].

Several clinical observations of RA application during CABG procedures indicate that its distal segment is more prone to contraction so its proximal part should be used preferably. However, the experimentally proven higher contents of the smooth muscle cells within the proximal segments indicate the possibility of a pronounced impact of local pathophysiological factors on the regulation of vascular stress and contraction, including receptor--mediated reactions.

In conclusion, the present study documented that the distal RA segment was significantly more prone to vasoconstrictors such as KCl, PE and AT-II. Interestingly, not all tested substances revealed significant differences regarding an influence on the proximal and distal RA segments. Vascular responses to PGF2α or ET-3 were not found to be of statistical significance between the proximal and distal RA segments. Increased susceptibility of the proximal RA segment to contraction is most likely not a result of higher contents of the smooth muscle within arterial media, but rather a pronounced and modulating impact of the systemic pathophysiological and pharmacologic determinants. Thus, contractile response is regulated by number, type and activity of the receptors and the difference in vasocontractile response revealed in this study seems not to be related to endothelium influence [16].

References

1. Cohen G, Tamariz MG, Sever JY, et al. The radial artery versus the saphenous vein graft in contemporary CABG: a case-matched study. *Ann Thorac Surg* 2001; 71: 180-5.
2. Hata M, Seevanayagam S, Manson M, et al. Radial artery 2000 – risk analysis of mortality for coronary bypass surgery with radial artery. *Ann Thorac Cardiovasc Surg* 2002; 8: 354-7.
3. Suma H, Wanibuchi Y, Terada Y, et al. The right gastroepiploic artery graft. Clinical and angiographic midterm results in 200 patients. *J Thorac Cardiovasc Surg* 1993; 105: 615-22.
4. Bergsma TM, Grandjean JG, Voors, et al. Low recurrence of angina pectoris after coronary artery bypass graft surgery with bilateral internal thoracic and right gastroepiploic arteries. *Circulation* 1998; 97: 2402-5.
5. Puig LB, Ciongolli W, Cividanes GV, et al. Inferior epigastric artery as a free graft for myocardial revascularization. *J Thorac Cardiovasc Surg* 1990; 99: 251-5.
6. Barner HB, Naunheim KS, Fiore AC, et al. Use of the inferior epigastric artery as a free graft for myocardial revascularization. *Ann Thorac Surg* 1991; 52: 429-36.
7. Calafiore AM, Di Giammarco G, Teodori G, et al. Radial artery and inferior epigastric artery in composite grafts: improved midterm angiographic results. *Ann Thorac Surg* 1995; 60: 517-23.
8. Verma S, Szmitko PE, Weisel RD, et al. Should radial arteries be used routinely for coronary artery bypass grafting? *Circulation* 2004; 110: e40-6.

9. Reyes A.T, Frame R, Brodman RF. Technique for harvesting the radial artery as a coronary artery bypass graft. *Ann Thorac Surg* 1995; 59: 118-26.
10. Fremes SE, Christakis GT, Del Rizzo DF, et al. The technique of radial artery bypass grafting and early clinical results. *J Card Surg* 1995; 10: 537-44.
11. Mussa S, Guzik TJ, Black E, et al. Comparative efficacies and durations of action of phenoxybenzamine, verapamil/nitroglycerin solution, and papaverine as topical antispasmodics for radial artery coronary bypass grafting. *J Thorac Cardiovasc Surg* 2003; 126: 1798-805.
12. Guzik TJ, West NE, Pillai R, et al. Nitric oxide modulates superoxide release and peroxynitrite formation in human blood vessels. *Hypertension* 2002; 39: 1088-94.
13. Shapira OM, XU A, Aldea GS, et al. Enhanced nitric oxide--mediated vascular relaxation in radial artery compared with internal mammary artery or saphenous vein. *Circulation* 1999; 100 (19 Suppl): II322-7.
14. Chester AH, Marchbank AJ, Borland JA, et al. Comparison of the morphologic and vascular reactivity of the proximal and distal radial artery. *Ann Thorac Surg* 1998; 66: 1972-6.
15. Chardigny C, Jebara VA, Acar C, et al. Vasoreactivity of the radial artery. Comparison with the internal mammary and gastroepiploic arteries with implications for coronary artery surgery. *Circulation* 1993; 88 (5 Pt 2): II115-27.
16. van Son JA, Smedts F, Vincent JG, et al. Comparative anatomic studies of various arterial conduits for myocardial revascularization. *J Thorac Cardiovasc Surg* 1990; 99: 703-7.
17. He GW, Yang CQ. Characteristics of adrenoceptors in the human radial artery: clinical implications. *J Thorac Cardiovasc Surg* 1998; 115: 1136-41.
18. Rang HP, Dale MM, Ritter JM (eds.). Farmakologia kliniczna. *Wydawnictwo Czelej*, Lublin 2003: 290-2.
19. He GW, Liu ZG. Comparison of nitric oxide release and endothelium-derived hyperpolarizing factor-mediated hyperpolarization between human radial and internal mammary arteries. *Circulation* 2001; 104 (12 Suppl 1): I344-9.
20. Gaudino M, Nasso G, Canosa C, et al. Midterm angiographic patency and vasoreactive profile of proximal versus distal radial artery grafts. *Ann Thorac Surg* 2005; 79: 1987-9.

Odmienna wrażliwość na czynniki naczyniokurczące proksymalnego i dystalnego segmentu tętnicy promieniowej u chorych poddawanych pomostowaniu aortalno-wieńcowemu

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Streszczenie

Wstęp: Całkowita tętnicza rewaskularyzacja z zastosowaniem tętnic promieniowych (RA) jest obiecującą klinicznie techniką leczenia choroby niedokrwiennej serca. Pomimo korzystnych obserwacji odległych, istotnym czynnikiem ograniczającym stosowanie RA jest jej wyjątkowa wrażliwość na czynniki naczyniokurczące. W ostatnich latach pojawiły się przypuszczenia, iż poszczególne segmenty RA mogą się różnić wrażliwością na działanie skurczowe, w tym podatnością na kurcz naczyniowy. Zatem zastosowanie w trakcie pomostowania aortalno-wieńcowego (CABG) mniej podatnego na czynniki kurczące segmentu może mieć istotne implikacje kliniczne.

Cel: Porównanie aktywności naczynioskurczowej pomiędzy dystalnym a proksymalnym odcinkiem RA.

Metodyka: Uzyskiwano krótkie końcowe odcinki segmentu dystalnego i proksymalnego RA od 27 badanych chorych poddanych rewaskularyzacji tętniczej metodą CABG. Reaktywność naczyń na czynniki skurczowe oceniano *in vitro* za pomocą łaźni narządowej. Naczynia tętnicze po podzieleniu na pierścienie o szerokości ok. 2–3 mm umieszczano w 5-milimetrowych łaźniach i rozciągano między dwoma haczykami. Równocześnie badano segment proksymalny i dystalny RA pochodzącej od danego pacjenta. Krążki naczyniowe po stabilizacji przez okres 60–80 min i pasywnym naprężaniu do napięcia podstawowego 20 mN kilkakrotnie przykurczano przez jednakowe stężenia KCl (60 mM), a po uzyskaniu stabilnych odpowiedzi na KCl podawano kumulatywne wzrastające dawki fenylefryny (PE) (10^{-9}–10^{-2} M) i kolejno angiotensyny II (AT-II) (10^{-12}–10^{-6} M), prostaglandyny F2α (PGF2α) (10^{-9}–10^{-5} M), endoteliny 3 (ET-3) (10^{-9}–10^{-7} M). Kurcz wyrażano jako wartość bezwzględną w mN (po odjęciu napięcia podstawowego).

Wyniki: Zaobserwowano znamienny kurcz naczyń zarówno odcinka proksymalnego, jak i dystalnego w odpowiedzi na KCl, PE, AT-II, PGF2α oraz ET-3. Stwierdzono, iż proksymalne odcinki tętnicy promieniowej wykazują znamiennie większą odpowiedź kurczową na działający nieswoiście KCl, a także odpowiedź mediowaną stymulacją odpowiednich receptorów za pomocą PE oraz AT-II. Co ciekawe, reakcja obu odcinków na wzrastające stężenia PGF2α i ET-3 była podobna. Również maksymalna reakcja skurczowa badanych naczyń w odpowiedzi na podanie do łaźni narządowej wzrastających dawek PE oraz AT-II była znamiennie większa w segmentach proksymalnych w porównaniu z dystalnymi, a takiej różnicy nie zaobserwowano po podaniu wzrastających dawek PGF2α ani ET-3. Natomiast porównanie w badanych segmentach wartości EC_{50}, czyli takiej dawki substancji, która wywołuje 50% maksymalnej odpowiedzi, nie wykazało znamiennych różnic po podaniu AT-II, ET-3 i PGF2α.

Wnioski: Bardziej podatny na czynniki naczyniokurczące, a w szczególności na KCl, PE i AT-II, jest odcinek proksymalny RA, co powinno być brane pod uwagę w klinicznym planowaniu zabiegów rewaskularyzacji z zastosowaniem RA. Co ciekawe, nie wszystkie z badanych substancji (PGF2α oraz ET-3) wykazywały znamienną różnicę w działaniu na segment proksymalny i dystalny RA. Większa podatność na kurcz fragmentu proksymalnego RA najprawdopodobniej wynikała z większej ilości mięśniówki gładkiej w obrębie błony środkowej, a także ze znaczącego i modyfikującego wpływu licznych ogólnoustrojowych czynników patofizjologicznych i farmakologicznych. Odpowiedź kurczowa segmentów RA jest zatem regulowana nie tylko ilością mięśniówki gładkiej, ale również liczbą, typem i aktywnością receptorów oraz funkcją śródbłonka.

Słowa kluczowe: tętnica promieniowa, część proksymalna, część dystalna, spazm naczyniowy

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