Eur J Vasc Endovasc Surg (2019) 57, 868–875

The Effect of Remote Ischaemic Preconditioning on Arterial Stiffness in Patients Undergoing Vascular Surgery: A Randomised Clinical Trial

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WHAT THIS PAPER ADDS

The current study is the first clinical study to examine the effect of remote ischaemic preconditioning (RIPC) on arterial stiffness in patients undergoing vascular surgery. Although this study failed to demonstrate a significant effect of RIPC on the arterial stiffness parameters, there was marked improvement in arterial stiffness parameters after surgery in both the interventional and the non-interventional (sham) groups. The finding that surgery itself may have an influence on arterial stiffness has some clinical impact.

Objectives: The main aim of this study was to evaluate the effect of remote ischaemic preconditioning (RIPC) on arterial stiffness in patients undergoing vascular surgery.

Methods: This was a randomised, sham controlled, double blind, single centre study. Patients undergoing open abdominal aortic aneurysm repair, surgical lower limb revascularisation surgery or carotid endarterectomy were recruited. A RIPC or a sham procedure was performed, using a blood pressure cuff, along with preparation for anaesthesia. The RIPC protocol consisting of four cycles of 5 min of ischaemia, followed by 5 min of reperfusion was applied. Arterial stiffness and haemodynamic parameters were measured pre-operatively and 20–28 h after surgery. Two primary outcomes were selected: augmentation index and pulse wave velocity.

Results: Ninety-eight patients were randomised. After dropouts 44 and 46 patients were included in the RIPC and sham groups, respectively. Both groups were comparable. There were no statistically significant differences in augmentation index ($p = .8$), augmentation index corrected for heart rate of 75 beats per minute ($p = .8$), pulse wave velocity ($p = .7$), large artery elasticity indices ($p = .8$), small artery elasticity indices ($p = .6$), or mean arterial pressure ($p = .7$) changes between the RIPC and sham groups. There occurred statistically significant ($p \leq .01$) improvement in augmentation index (−5.8% vs. −5.5%), augmentation index corrected for a heart rate of 75 beats per minute (−2.5% vs. −2%), small artery elasticity indices (0.7 mL/mmHg × 100 vs. 0.9 mL/mmHg × 100), and mean arterial pressure post-operatively in both the RIPC and the sham groups (change median values in RIPC and sham groups, respectively).

Conclusions: RIPC had no significant effect on arterial stiffness, but there was significant improvement in arterial stiffness after surgery in both groups. Arterial stiffness and haemodynamics may be influenced by surgery or anaesthesia or oxidative stress or all factors combined. Further studies are needed to clarify these findings.

ClinicalTrials.gov: NCT02689414

Keywords: Ischaemic preconditioning, Vascular surgical procedures, Vascular stiffness, Arteriosclerosis, Pulse wave analysis

Article history: Received 15 August 2018, Accepted 1 December 2018, Available online 22 June 2019

INTRODUCTION

Remote ischaemic preconditioning (RIPC) is a phenomenon that is believed to reduce ischaemia reperfusion damage through repeated brief cycles of non-lethal ischaemia of distant tissues. Remote ischaemia is generally achieved non-invasively by placing a tourniquet/cuff around a limb,

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1078-5884/

https://doi.org/10.1016/j.ejvs.2018.12.002

although any tissue can be used for the induction of ischaemia. Although the exact mechanisms of RIPC are unknown, it is believed that neuro-humoral pathways are induced that trigger a cascade of intrinsic effects.[1] Several studies have confirmed the protective effects of RIPC on the heart, kidneys, brain, and other tissues in animals, and from 2006, in humans in clinical circumstances.[2]

No optimal RIPC protocol has been established. Usually, a protocol consisting of three or four cycles of 5 min ischaemia is used, both with positive and negative outcomes. Some studies with longer or shorter episodes or with a different number of cycles have also had positive outcomes. A meta-analysis concluded that an ischaemia episode should last at least 5 min.[3] According to a study designed to compare RIPC protocols, four to six RIPC cycles yielded significant cardioprotection.[4]

Patients undergoing vascular surgery usually have multiple comorbidities resulting from systemic atherosclerosis. Coexisting diseases combined with major tissue trauma increase the peri-operative risk, mainly in terms of cardiovascular events. Consequently, there arises a need for an effective risk reduction strategy. During the past two decades aortic stiffness or arteriosclerosis has been proved to have a great prognostic value in predicting cardiovascular morbidity and mortality in many subgroups. The present study group also showed a relationship between decreased arterial elasticity and all cause and cardiovascular mortality in patients suffering from symptomatic peripheral artery disease.[5] It is still unknown how RIPC affects arterial stiffness during vascular surgery. It was hypothesised that RIPC reduces arterial stiffness, which may result in a better post-operative clinical outcome for patients undergoing vascular surgery. Hence a randomised controlled trial was performed on patients undergoing major vascular surgery to evaluate the effects of RIPC on arterial stiffness.

METHODS

Study group and eligibility

This randomised double blind sham controlled clinical trial took place from January 1, 2016 to February 8, 2018 at Tartu University Hospital. Patients who were undergoing open abdominal infrarenal aortic aneurysm (AAA) repair or surgical lower limb revascularisation (for claudication or critical limb ischaemia) or carotid endarterectomy (for symptomatic or asymptomatic carotid stenosis) and who gave their full informed consent for participation were recruited. The study was approved by the Research Ethics Committee of the University of Tartu, and was registered in the ClinicalTrials.gov database (NCT02689414).

The exclusion criteria were age $<$18 years, pregnancy, known malignancy in the previous five years, permanent atrial fibrillation or flutter, symptomatic upper limb atherosclerosis, the need for oxygen therapy at home, estimated pre-operative glomerular filtration rate (eGFR) $<$ 30 mL/min/1.73 m^2, myocardial infarction in the previous month, previous history of upper limb vein thrombosis or vascular surgery in the axillary region, and inability to follow the study regimen.

Randomisation

Assignment to the sham or RIPC groups was done in parallel with equal allocation. Stratified randomisation, using a block design, was applied. The stratification factors were type of surgery (aneurysm repair or other), age (under or over 65 years) and American Society of Anesthesiologists (ASA) physical status classes 2, 3, or 4. Allocation was concealed using opaque sealed envelopes. Randomisation and concealment were carried out by a third party, who was not involved in any other aspects of the study. The envelopes were opened when the patients arrived at the operating theatre and intervention was started thereafter.

Intervention

For remote ischaemic preconditioning, four 5 min episodes of ischaemia were induced. Between all the episodes there was a 5 min period of reperfusion. Ischaemia in the RIPC group was achieved, using a blood pressure cuff on an arm, by raising cuff pressure to 200 mmHg or, when the patient's blood pressure exceeded 180 mmHg, to a value that was 20 mmHg higher than the systolic blood pressure value. Intervention started simultaneously with preparation for anaesthesia, or a few minutes earlier. In the sham group there were four 5 min episodes during which pressure in the cuff was equal to venous pressure. Venous pressure was achieved, using a blood pressure cuff on an arm, by raising cuff pressure to 10—20 mmHg. As in the RIPC group, there was a 5 min pause between each episode and the sham procedure started simultaneously with the preparation for anaesthesia. Anaesthesia and peri-operative use of medications were carried out at the anaesthetist's discretion with no restrictions.

Blinding

The patient, patient's physician, surgeon, anaesthetist, and everyone else in the surgical team were blinded to study intervention. Blinding was attained with the manometer's scale covered. The second arterial stiffness measurement was carried out by a study member who was not aware of the patient's group allocation.

Primary outcomes

Two primary outcomes were selected: aortic pulse wave velocity (PWV) and augmentation index (AIx). Both were measured with Sphygmocor XCEL PWA and PWV (AtCor Medical, Sydney, Australia) pre-operatively and 20—28 h after surgery. The measurements were performed in the resting state with the patient having fasted and not having smoked for at least three preceding hours.

For AIx assessment, the brachial waveform was captured by inflating the cuff partially. The central aortic waveform, followed by pulse wave analysis, was generated by SphygmoCor Brachial GTF. AIx, AIx corrected for a heart rate of 75 beats per minute (AIx@75), central blood pressure, pulse pressure, and mean arterial pressure were provided.

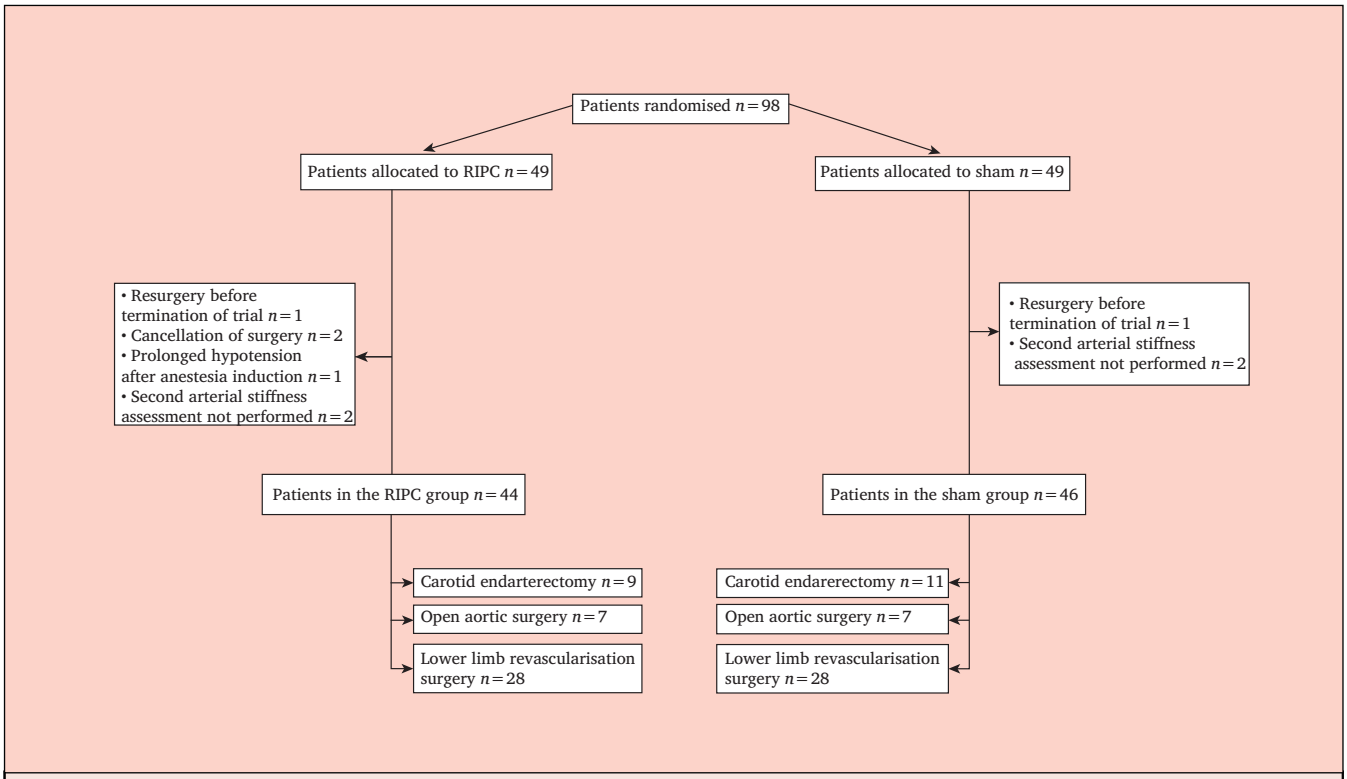

Figure 1. Flowchart of patients randomised for remote ischaemic preconditioning (RIPC) or for sham procedure before carotid, open aortic or lower limb revascularization surgery to study arterial stiffness.

For PWV assessment, femoral and carotid pulse waves were recorded simultaneously. The femoral waveform was captured by inflating the cuff partially over the thigh. The carotid waveform was captured by means of applanation tonometry. At least two quality PWV measurements were obtained.

Secondary outcomes

The elasticity indices of large (C1) and small (C2) arteries were obtained non-invasively using the HDI/PulseWave CR-2000 research CardioVascular Profiling System (Hypertension Diagnostics, Inc., MN, USA). At least two quality measurements were required.

The elasticity indices were measured along with PWI and AIx pre-operatively and 20—28 h after surgery. Data on the type of anaesthesia, administration of propofol, and placement of an epidural catheter were obtained from the surgery protocol. As the sham procedure presumably does not alter arterial stiffness, change in arterial stiffness parameters can be attributed to surgery, anaesthesia, and the medications used.

Statistical analysis

Continuous variables were compared using the Student *t* test, the two sample t-test, the Wilcoxon signed rank, or the Wilcoxon rank sum test as appropriate. Categorical variables were compared with the chi-square test. A p value $< .05$ was considered to be significant.

As no previous studies had evaluated the effect of RIPC on vascular elasticity parameters, data required for calculation of sample size were not available. Hence, sample size was calculated based on the data of the first 30 participants. Also, as the *a priori* prediction was directional, one tailed Welch's *t* test was used for calculation of sample size. The desired study power was set at 80% and the magnitude of the effect to be obtained was 5% of the difference in AIx@75 between the study group and the sham group. The calculated sample size was 44 for each group.

RESULTS

Characteristics of the study groups

Enrolment in the study was terminated in both the sham and RIPC groups when there were at least 44 individuals whose arterial stiffness was assessed twice. Ninety-eight patients were randomised into the study groups. After dropouts, there were 44 patients in the RIPC group and 46 patients in the sham group, whose arterial stiffness parameters were assessed twice. The reason for not measuring arterial stiffness twice was the patient's stay on the intensive care unit. Fig. 1 is a flowchart of patients. There were no statistically significant differences between the groups regarding the baseline characteristics (Table 1). Propofol was used in 25 patients (54%) in the sham group and in 19 patients (43%) in the RIPC group ($p = .396$). Epidural analgesia was used in 30 patients (65%) in the sham group and in 35 patients (80%) in the RIPC group ($p = .200$). The mean time from the end of intervention to the beginning of surgery was 36 min in the RIPC group and 29 min in the sham group ($p = .069$). No adverse events as a result of RIPC were reported.

Table 1. Baseline characteristics of patients randomised for remote ischaemic preconditioning (RIPC) or for sham procedure before carotid, open aortic or lower limb revascularization surgery to study arterial stiffness

Variable	RIPC (n = 44)	Sham (n = 46)	p value
Age, years (SD)	67 (±9)	66 (±10)	.526
Male	36 (82)	30 (65)	.123
Body mass index, kg/m^2 (SD)	26.1 (±6.4)	26.3 (±6.8)	.847
ASA physical status score			
ASA 2	18 (41)	19 (41)	1
ASA 3	19 (43)	22 (48)	.818
ASA 4	7 (16)	5 (11)	.694
Administration of contrast medium 7 days pre-operatively	21 (48)	22 (48)	1
Preoperative medication			
ACEI or ARB	20 (45)	29 (63)	.143
Calcium channel blockers	9 (20)	17 (37)	.135
Beta blockers	10 (23)	19 (41)	.097
Statins	13 (30)	13 (28)	1
Diabetes	5 (11)	8 (17)	.608
Myocardial infarction	8 (18)	3 (6)	.172
Stroke	10 (23)	10 (22)	1
Smoker (current or ex-smoker)	39 (89)	40 (87)	1
Peripheral systolic BP (PSBP), mmHg (SD)	143 (±18)	141 (±16)	.545
Peripheral diastolic BP (PDBP), mmHg (SD)	78 (±11)	79 (±11)	.762
Central systolic BP (CSBP), mmHg (SD)	131 (±15)	129 (±14)	.589
Central diastolic BP (CDBP), mmHg (SD)	79 (±11)	80 (±11)	.636
Mean arterial pressure (MAP), mmHg (SD)	99 (±12)	99 (±11)	.777
Heart rate, beats per minute (SD)	66 (±9)	67 (±11)	.774
Large artery elasticity index (C1), mL/mmHg × 10 (IQR)	11.6 (9.1–14.0)	11.1 (7.9–15.0)	.601
Small artery elasticity index (C2), mL/mmHg × 100 (IQR)	2.6 (2–3.6)	2.7 (2.1–3.5)	.949
Augmentation index (Alx), % (SD)	36 (±11)	34 (±13)	.455
AIx@75, % (SD)	31 (±11)	30 (±13)	.542
Pulse wave velocity (PWV), m/s (IQR)	9.4 (8.1–10.4)	9.0 (7.9–9.8)	.257

Data are given as n (%) unless otherwise indicated. ACEI = angiotensin converting enzyme inhibitor; ARB = angiotensin II receptor antagonist; ASA = American Society of Anesthesiologists; AIx@75 = augmentation index corrected for heart rate of 75 beats per minute (%); BP = blood pressure; IQR = interquartile range; RIPC = remote ischaemic preconditioning; SD = standard definition.

Comparison between the groups: effects of RIPC

There were no statistically significant differences between the RIPC and sham groups in AIx (p = .828), AIx@75 (p = .837), PWV (p = .701), C1 (p = .785), C2 (p = .635), or mean arterial pressure (MAP, p = .676) when the pre-operative values were compared with those acquired 20–28 h post-operatively

Post-operative changes

There were statistically significant improvements 20–28 h post-operatively in AIx, AIx@75, and C2 in both groups, but changes in PWV and C1 were not significant (Fig. 2).

In the RIPC group changes in the arterial stiffness parameters were as follows: PWV mean change −0.26 m/s, (SD 1.68); AIx median change −5.75%, (IQR -15–0); AIx@75 median change −2.5%, (IQR -9.75–0.5); C1 median change 0.52 mL/mmHg × 100, (IQR -1.55–3.68; C2 median change 0.72 mL/mmHg × 100, (IQR -0.02–3.4). In the sham group changes in the arterial stiffness parameters were the following: PWV mean change −0.4 m/s, (SD 1.38); AIx median change −5.5%, (IQR -13.5–0.5); AIx@75 median change −2%, (IQR -10–1); C1 median change 0.1 mL/mmHg × 10, (IQR -1.7–2.45); C2 median change 0.85 mL/

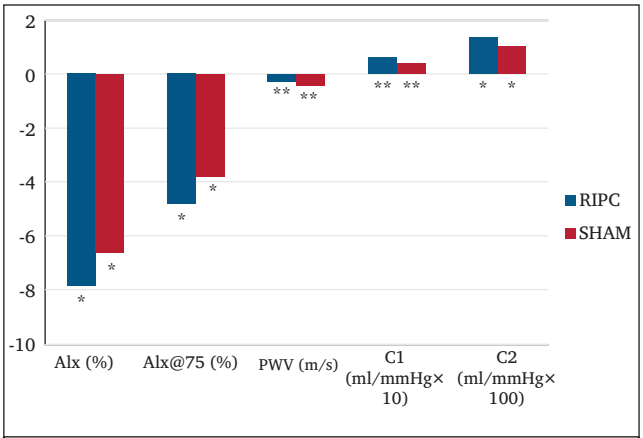

Figure 2. Changes in the arterial stiffness parameters in the study groups. AIx – augmentation index (%); AIx@75 – augmentation index corrected for heart rate of 75 beats per minute (%); PWV – pulse wave velocity (m/s); C1 – large artery elasticity index; C2 – small artery elasticity index; *p < 0.05; **p > 0.05.

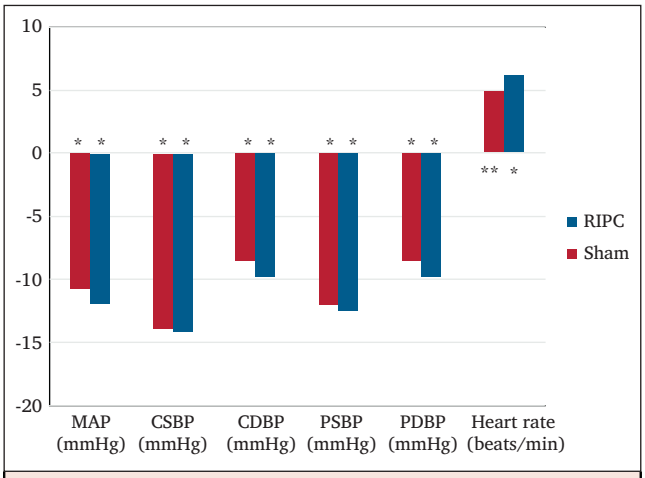

Figure 3. Changes in the postoperative haemodynamic parameters in comparison to the preoperative values in patients randomised for remote ischaemic preconditioning (RIPC) or for sham procedure before carotid, open aortic or lower limb revascularization surgery to study arterial stiffness. CDBP = central diastolic blood pressure; CSBP = central systolic blood pressure; MAP = mean arterial pressure; PDBP = peripheral diastolic blood pressure; PSBP = peripheral systolic blood pressure. *$p < .001$; **$p = .013$.

mmHg × 100, (IQR 0–2.15). All haemodynamic changes were statistically significant in both groups (Fig. 3)

Subgroup analysis

Changes in AIx, AIx@75, PWV, C1, C2, and MAP in the RIPC subgroups are presented in Table 2. In the RIPC group, there was a significant decrease in MAP in patients treated with epidural analgesia and significant differences in changes in MAP depending on the type of surgery. Patients who underwent open AAA repair or aortobifemoral bypass had the greatest decrease in MAP. There was a correlation between PWV and decrease in MAP (in the sham group cor = 0.5, $p = .001$; in the RIPC group cor = 0.4, $p = .009$) and between increase in C1 and decrease in MAP in the sham group (cor = −0.4, $p = .007$), but not in the RIPC group ($p = .125$). There was no correlation between decrease in AIx ($p = .126$), AIx@75 ($p = .065$), or C2 ($p = .092$) and MAP.

DISCUSSION

The present study shows for the first time that RIPC has no significant effect on arterial stiffness parameters in patients undergoing vascular surgery. However, marked improvements occurred in AIx, AIx@75, and C2 irrespective of the decrease in MAP in the intervention (RIPC) group and non-intervention (sham) groups post-operatively. Only PWV, a relatively

Table 2. Changes in the selected postoperative arterial stiffness and haemodynamic parameters in comparison to the preoperative values in patients randomised for remote ischaemic preconditioning (RIPC) in different subgroups

Confounder	AIx (%)	*p*	AIx@75 (%)	*p*	PWV (m/s)	*p*	C1 (mL/mmHg × 10)	*p*	C2 (mL/mmHg × 100)	*p*	MAP (mmHg)	*p*
Use of propofol												
Propofol (SD) $n = 19$	−6.6 (±8.8)	.472	−1 (−11.5–2)[a]	.473	0.2 (±1.2)	.220	0.3 (−1.4–2.4)[a]	.751	1.8 (−0.5–4.6)	.361	−10 (±13)	.821
No propofol (SD) $n = 25$	−8.9 (±12.1)		−3 (−9.5–0)[a]		−0.5 (±1.9)		1.3 (−1.8–4.6)[a]		0.6 (0–2)		−11 (±13)	
Use of epidural analgesia												
Epidural analgesia (SD) $n = 35$	−6 (−16–0)[a]	.633	−3 (−10–0)[a]	.395	−0.4 (±1.7)	.310	1.1 (±5.4)	.088	0.6 (−0.1–3.3)[a]	.573	−13 (±13)	.009
No epidural analgesia (SD) $n = 9$	−4 (−14–(−2))[a]		0 (−9–2)[a]		0.3 (±1.4)		−1.0 (±2.2)		1.75 (0.4–3.6)[a]		−1 (±9)	
Type of surgery												
Carotid endarterectomy (SD) $n = 9$	−5.8 (±10.9)	.327	−2.5 (±9.6)	.804	0.3 (±1.4)	.621	−1 (±2.2)	.134	1.9 (±2.0	.024	−1 (±9)	.002
Open aortic aneurysm repair (SD) $n = 7$	−11.4 (±9.6)		−5.6 (±6.1)		−0.6 (±1.0)		2.4 (±6.4)		3.2 (±2.2)		−22 (±8)	
Aortobifemoral bypass (SD) $n = 6$	−13.8 (±13.1)		−6.9 (±10.9)		−1.3 (±1.9)		−2.7 (±2.1)		2.1 (±3.4)		−19 (±16)	
Lower limb revascularisation (excl. aortobifemoral bypass) (SD) $n = 22$	−6.1 (±10.3)		−5.0 (±8.9)		−0.3 (±2.0)		1.7 (±4.1)		0.4 (±1.8)		−8 (±11)	

AIx = augmentation index; AIx@75 = augmentation index corrected for a heart rate of 75 beats per minute; C1 = large artery elasticity index; C2 = small artery elasticity index; MAP = mean arterial pressure; PWV = pulse wave velocity; SD = standard deviation.
[a] Median value (first quartile–third quartile).

constant aortic stiffness parameter, remained unaffected. As the sham procedure presumably has no influence, the above changes must have resulted mainly from surgery combined with anaesthesia and from peri-operative medications.

To the authors' knowledge, only one study has focused on the effects of RIPC on arterial stiffness parameters. Zagidullin *et al*.[6] found that RIPC reduced MAP, AIx, and systolic blood pressure in patients with stable angina pectoris. Multiple factors have been found to contribute to the mechanisms of RIPC, with some being directly connected to endothelial function. It was recently shown that the protective effect of remote ischaemic post-conditioning against ischaemia reperfusion injury in primary percutaneous coronary intervention is mediated via nitric oxide (NO).[7] Earlier, several studies demonstrated the role of NO in the mechanisms of RIPC in non-clinical settings.[8,9] Moreover, in a systematic review RIPC was found to promote endothelial function and to have an effect on lowering systolic and diastolic pressures and MAP in the longer term.[10] In addition, ischaemic preconditioning has been shown to increase endothelial progenitor cells and vascular endothelial growth factor expression,[11] as well as to activate the parasympathetic nervous system,[12] which is also beneficial for arterial compliance.

As RIPC seems to have a strong impact on endothelial function, and as endothelial dysfunction leads to arterial stiffening, there might be a connection between arterial stiffness and the effect of RIPC. Moreover, the effect of RIPC on lowering AIx and peripheral and central systolic blood pressures, as well as pulse pressure in patients with angina pectoris, has been described by Zagidullin *et al*., who also linked the effect to improvement in endothelial function.[6] Taking the above data into account, the chance of seeing the effect of RIPC on arterial stiffness in other populations, such as patients undergoing vascular surgery, is realistic.

Only a few studies have been published about the effect of remote ischaemic preconditioning in vascular surgery and their results have been controversial.[13–22] Neutral effects of RIPC are frequently associated with the study population's heterogeneity, underpowered trials, and confounders capable of reducing the effect of RIPC, as animal studies have shown sequential positive outcomes. The main disease that is believed to attenuate or even abolish the RIPC effect is diabetes.[23] The most widely discussed and potentially removable confounder in human studies believed to lessen the effect of RIPC, is propofol. It was recently shown that propofol abolishes the cardioprotective effect of RIPC in rats.[24] Up to now, trials assessing the effect of RIPC in vascular surgery have used either propofol anaesthesia,[16–22] or there has been no information about the anaesthesia provided.[13–15] However, in the present trial, there were no differences in the arterial stiffness parameters following RIPC between the patients who received propofol and those who did not. Yet the subgroups are small and no definitive conclusions can be made. In addition, the arterial stiffness parameters did not differ among the patients of the RIPC group who were treated with propofol, but there were differences in the changes in MAP depending on the surgery, and analgesia. In open AAA repair and aortobifemoral bypass surgery, epidural analgesia and general anaesthesia are commonly used, which is why both of these factors produce more pronounced changes in MAP compared with the other types of surgery. During carotid endarterectomy under general anaesthesia there is no need for epidural analgesia, hence the changes in MAP were less. As general anaesthesia and, especially epidural analgesia, tend to have an impact on haemodynamics, it is clear why the decrease in MAP between the different surgery types is distinct.

In the present study the effect of RIPC may also have been modified by the heterogeneity of the study population. The fact that patients with claudication evidently experience the effect of chronic remote ischaemic preconditioning during walking may have influenced the effect of pre-operative conditioning. It should be noted, too, that none of the three studies that recruited patients undergoing lower limb revascularisation surgery in addition to patients undergoing other types of vascular surgery, found an effect of RIPC.[13,14,19] Furthermore, in lower limb occlusive disease, the effect of clamping and reperfusion is weaker than it is during aortic aneurysm repair in which arteries are unobstructed. Thus a more systemic haemodynamic effect may result from clamping in the case of aortic aneurysm. Also, the material of the graft itself may influence arterial stiffness parameters, especially PWV. Still, it is unclear how much and in what direction graft replacement impacts these parameters.

Surgery induces a systemic stress response, which is reduced by epidural analgesia[25] and is influenced also by anaesthesia. Accordingly, surgery and medication use have a great potential impact on haemodynamics and arterial stiffness through modulation of the stress response. This could be one of the reasons why in the present trial most arterial stiffness and haemodynamic parameters improved significantly post-operatively. RIPC is believed to display its effect in two "windows", the first lasting a few hours after conditioning and the second appearing 24 h after conditioning.[26] The target of the present study was mainly the second "window" where the immediate effects of surgery and anaesthesia on arterial stiffness were abolished, but might still have been detectable.

The present finding that surgery and anaesthesia with medication may affect arterial stiffness and haemodynamics, has some clinical impact. Peri-operative monitoring of arterial stiffness, an independent predictor of cardiovascular events and mortality, may facilitate better guided treatment and prevention of the cardiovascular risks of vascular surgery patients. Peri-operative increase of central haemodynamics and arterial stiffness may result in elevated cardiac afterload and reduced coronary perfusion, which presumably leads to a greater risk of cardiovascular events (myocardial infarction, heart failure, stroke, etc.).[27] RIPC has also been found to modulate the inflammatory response.[28] Yet there was no effect of RIPC seen on inflammatory mediators either in propofol anaesthetised[29] or sevoflurane anaesthetised cardiac surgery patients.[30]

There are several limitations to the present study. First, the study group was heterogeneous, which may have impacted the possible effect of RIPC. In diabetic patients the effect of RIPC may be attenuated. Although, there were not many

diabetics in the present study, the outcome may still have been biased. In addition, different type of grafts could have influenced the pulse wave. Also, whether or not the patient had obstructive or aneurysmal arterial disease may have played a role. Finally, the fact that patients with claudication are believed to have chronic ischaemic conditioning may have reduced the effect of intervention. However, RIPC might exert some effect on arterial stiffness in the same cohort if evaluated before surgery, thereby eliminating any impact caused by it.

Taken together, the effect of RIPC on arterial stiffness in the present trial may have been overshadowed by multiple confounders, which is inevitable in vascular surgery. Despite no effect of RIPC on arterial stiffness parameters being revealed from this study, it cannot be concluded that RIPC has no impact on arterial stiffness. Further studies with a more homogenous cohort and fewer confounders are needed to evaluate the effect of RIPC on arterial stiffness.

ACKNOWLEDGEMENTS

The authors are indebted to Ms. E. Jaigma for the linguistic revision of the text.

FUNDING

This study was supported by grants from the Estonian Research Council (PUT No. 1169, IUT No. 20—42, IUT No. 2—7, PRG435), and by the European Union through the European Regional Development Fund (Project No. 2014—2020.4.01.15—0012).

CONFLICT OF INTEREST

None.

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COUP D'OEIL

Iliocaval Fistula After Microdiscectomy

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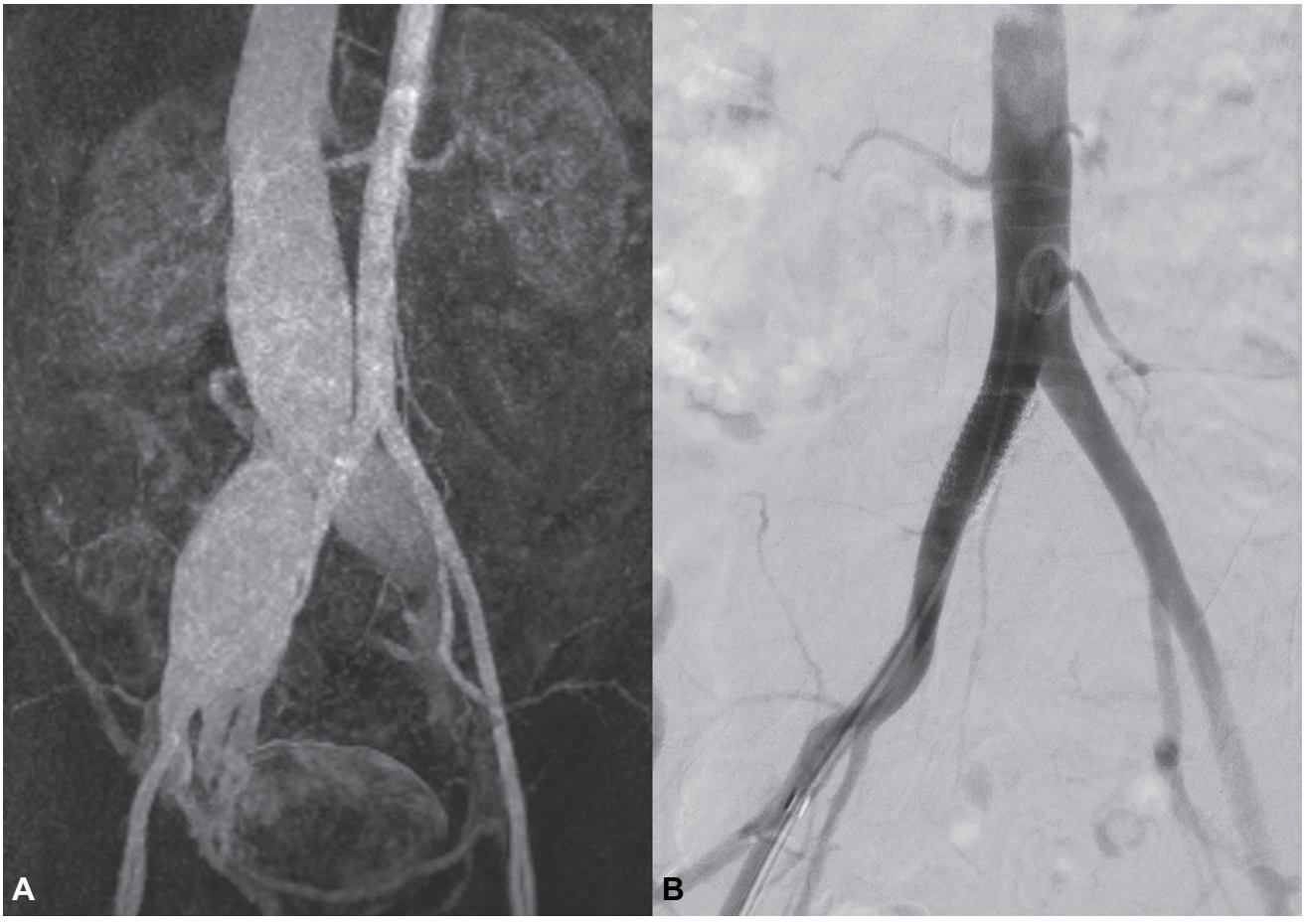

A 23 year old woman presented with lower back pain and breathlessness two years after an L4/L5 microdiscectomy. Magnetic resonance imaging (MRI, A) revealed dilatation of the inferior vena cava (IVC) and a fistula between the proximal right common iliac artery and the distal IVC. Echocardiography showed a right ventricular systolic pressure of 58 mmHg (normal 8–20 mmHg). An endovascular approach via the right common femoral artery enabled exclusion of the fistula with a 10 mm × 38 mm Advanta V12 stent (Maquet, Rastatt, Germany, B). At clinical and radiological follow up, the pain and breathlessness had resolved and echocardiography normalised. MRI confirmed exclusion of the fistula.

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https://doi.org/10.1016/j.ejvs.2019.02.014