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Prehabilitation for delirium prevention in elderly patients with chronic limb threatening ischemia

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Prehabilitation for delirium prevention in elderly patients with chronic limb threatening ischemia

Prehabilitation in the elderly with chronic limb threatening ischemia

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Declarations of conflict of interest: none

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ARTICLE HIGHLIGHTS

Type of research: Multicenter prospective observational cohort study

Key Findings: Prehabilitation for patients undergoing revascularization for critical limb-threatening ischemia showed a non-significant reduction in delirium (n=2/101, 2%) compared to controls (n=23/255, 9%; after adjustment for confounders OR=0.28, 95%CI 0.06-1.3, p=.097). Significant differences included shorter length of stay (2 vs 4 days; *p*=<.001) and fewer minor complications (14% vs 26%, *p*=.01) in the prehabilitation cohort.

Take home Message: Prehabilitation among elderly CLTI patients is safe and has the potential to yield multiple beneficial effects on general outcomes following revascularization, while also achieving high levels of patient satisfaction.

TABLE OF CONTENTS SUMMARY

Prehabilitation for patients undergoing revascularization for critical limb-threatening ischemia showed a non-significant reduction in delirium and significantly shorter length of stay in this observational cohort study comprising 356 patients. Prehabilitation is safe for elderly CLTI patients and may improve outcomes and patient satisfaction.

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ABSTRACT

Objective

Elderly patients with Chronic Limb Threatening Ischemia (CLTI) undergoing revascularization are prone to delirium and prolonged hospitalization. Preoperative prehabilitation may prevent delirium and reduce the length of stay. This study investigates the effect of multimodal prehabilitation on delirium incidence in elderly CLTI patients undergoing revascularization.

Methods

A comparative observational cohort study conducted in a large teaching hospital (intervention cohort n=101, retrospective control cohort n=207) and a university hospital (prospective control cohort n=48) from 2020 to 2023. Patients aged ≥ 65 years undergoing revascularization were included, with acute treatment or severe cognitive impairment as exclusion criteria. The three-week prehabilitation program included screening of general health and presence of delirium risk factors by a vascular nurse practitioner, screening and provision of personalized, home-based exercises by a physiotherapist, provision of nutritional advice by a dietician, and if indicated comprehensive geriatric assessment by a geriatrician, assessment of self-reliance and home situation by a prearranged homecare nurse, guidance and support for smoking cessation by a quit smoking coach, and anaemia treatment. Primary outcome was 30-day delirium incidence, analysed using regression models adjusting for potential confounders (age, physical impairment, history of delirium, preoperative anaemia and revascularization type). Secondary outcomes were length of stay, postoperative complications, 30-day mortality, and patient experiences.

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Results

Median age (IQR) was 76 years (71-82). Delirium incidence was lower in the prehabilitation cohort (n=2/101, 2%) compared to controls (n=23/255, 9%; OR=0.21, 95%CI 0.05-0.89, *p*=.04). Adjusted analysis showed a non-significant delirium reduction (OR=0.28, 95%CI 0.06-1.3, p=.097). The prehabilitation cohort had a significantly shorter length of stay (2 [1-5] vs 4 [2-9] days; *p*=<.001), and fewer minor complications (14% vs 26%, *p*=.01). No differences were present in major complications and 30-day mortality. Patients reported high compliance and satisfaction (median score 8/10, IQR 7-9).

Conclusions

Prehabilitation among elderly CLTI patients is safe and has the potential to yield multiple beneficial effects on general outcomes following revascularization, while also achieving high levels of patient satisfaction. Further validation and considering implementation in surgical settings is recommended.

TRIAL

This protocol is registered at the Netherlands National Trial Register (NTR) number: NL9380.

KEY WORDS

Chronic Limb Threatening Ischemia;

Vascular Surgery;

Delirium;

Length of stay (LoS);

Prevention;

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INTRODUCTION

In the face of an aging population, the prevalence of chronic limb-threatening ischemia (CLTI) among elderly persons has become a major public health concern. CLTI, a severe form of peripheral arterial disease, is characterized by atherosclerotic occlusion of the arteries supplying the lower extremities, leading to ischemic rest pain and/or tissue damage[1–3]. In addition to the risk of losing a limb, CLTI impairs overall health and quality of life (QoL). Annually, 500-1000 new cases of CLTI occur per 1 million people in Europe[4]. Revascularization is the primary treatment for CLTI. However, this does not guarantee limb salvage; up to a quarter of the CLTI patients is at risk for major amputation despite revascularization attempts[5–10]

Postoperative delirium poses a significant risk in elderly CLTI patients undergoing revascularization[11–13]. This serious neuropsychiatric disorder is characterized by an acute and fluctuating change in cognition and a disturbance of consciousness, and is associated with prolonged hospital stay, worsening of functional and cognitive performance, decreased QoL, increased mortality and significant increase in healthcare costs[14–17]. The incidence of postoperative delirium in elderly CLTI patients is high (5 to 39%), and varies with treatment strategies[12,18]. The exact aetiology of delirium remains unknown but is multifactorial, involving factors such as pre-existing cognitive and physical impairment, increased age, anaemia, and prior delirium[16,19,20]. The typical elderly CLTI patient presents with multiple comorbidities, reduced physiological reserves and increased vulnerability, which increases the risk of developing geriatric syndromes[21–23].

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Recognizing the need for a strategy to minimize the risk of developing delirium and other complications, multimodal prehabilitation has emerged as a promising preoperative approach within various types of surgery[24–28]. Prehabilitation is the all-encompassing term of preoperative optimization of the patient's functional capacity and resilience, by identifying and correcting potential risk factors for postoperative complications[29]. Interventions may include physical, cognitive and nutritional optimization.

This comprehensive approach addresses the multifactorial nature of delirium, and offers a promising strategy for improving surgical outcomes in elderly CLTI patients that are often frail. The lack of prehabilitation studies in CLTI patients may be attributed to the assumption that they require urgent revascularization upon diagnosis, eliminating the possibility of a prolonged preoperative trajectory. However, enhancing fitness of the frequently fragile CLTI patient prior to revascularization may offer multiple positive effects. The aim of this study is to investigate the effect of a three-week, multicomponent, multimodal CLTI prehabilitation program on the incidence of delirium in elderly CLTI patients after revascularization.

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METHODS

The study design and the prehabilitation program were previously published and are shortly described in the following section[30].

Design and setting

An observational cohort study was conducted between 2020 and 2023. The intervention was offered as standard care since November 2020 in a non-university, large teaching hospital in the Netherlands and was evaluated until August 2023. This hospital also provided a retrospective control cohort from December 2017 to December 2019. A second control cohort was prospectively followed from August 2022 to August 2023 in a university hospital in Belgium. The two control cohorts were combined as one control cohort for statistical analysis.

Recruitment and participants

Patients aged ≥ 65 years with a new onset of CLTI and planned for surgical or endovascular revascularization were screened for eligibility. Exclusions comprised patients undergoing conservative therapy, requiring acute hospitalization or treatment within 2 weeks post-initial presentation, or facing challenges in participating due to linguistic limitations or severe cognitive impairment.

Outcomes

Primary outcome was the incidence of delirium. Delirium was screened for using the Delirium Observation Screening (DOS) score in combination with the DSM-V criteria and the Confusion Assessment Method, as reported in previous studies[15,26,31,32]. The geriatrician was consulted in case

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of DOS-scores ≥ 3 to confirm the diagnosis of delirium. DOS scores were routinely registered for all patients during both the control and the intervention periods. Secondary outcomes included postoperative complications (minor [Clavien Dindo score I-II] or major [Clavien-Dindo score III-V]), Length of Stay (LoS), and 30 day-mortality[33,34].

Sample size calculation

The initial sample size calculation was based on a postoperative delirium rate of 18%, acutely admitted patients included[30]. However, since acutely admitted patients are excluded from this study, we adjusted the expected delirium rate for elective patients rate to 9%, based on previous research[5]. This revised rate was used for the final sample size determination. Under the assumption of decreasing the rate of delirium from 9% to 3%, with an estimated power of 80%, a predefined *p*-value of 5% and an intervention to control ratio of 1:2, the study required a sample size of 531 patients of which 177 in the intervention cohort and 354 in the control cohort. This calculation was carried out using the online statistical power analysis program 'Statulator'[35].

Standard preoperative workup

In both the intervention and control cohorts, an identical standard preoperative workup was implemented. Patients with suspected CLTI were examined by the vascular surgeon during the first outpatient clinic visit. The WiFi-(Wound, Ischemia and foot Infection) score classified the severity of the threatened limb at initial presentation[3,36]. Additional examination included Ankle-Brachial Index (ABI) or toe pressure (TP) for non-compressible vessels. Vascular imaging was done by duplex, Magnetic Resonance Angiography or Computed Tomography Angiography. Vascular pathology location and extend were scored using the Trans-Atlantic Inter-Society Consensus Document on Management of Peripheral Arterial Disease II (TASC-II) and crural outflow in 1, 2

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or 3 arteries was noted[2,37,38]. Patients were screened by the anaesthesiologist and cardiologist prior to surgery.

Prehabilitation program

A detailed overview of the program, including indications for referral to components of the program, can be found in the protocol[30]. The six major components are: 1) screening of general health and presence of delirium risk factors by a vascular nurse practitioner, 2) screening and provision of personalized, home-based exercises by a physiotherapist, and, if indicated: 3) provision of nutritional advice by a dietician, 4) comprehensive geriatric assessment (CGA) by a geriatrician, 5) assessment of self-reliance and home situation by a prearranged homecare nurse, 6) guidance and support for smoking cessation by a quit smoking coach..

The nurse practitioner evaluated baseline characteristics, including frailty indicators (Clinical Frailty Scale [CFS], ISAR-HP, Geriatric 8 [G8]), comorbidities (Vascular Possum Score, Charlson Comorbidity Index), cognitive function (MMSE), nutritional status (SNAQ-RC, MNA-SF), functional independency (KATZ-ADL), ASA score, and delirium risk factors, and collected blood samples (Supplemental Table I). Afterwards, the physiotherapist provided personalized, home-based exercise instructions targeting strength, transfer training, respiratory muscle training, and improving cardiopulmonary condition[39]. Patients recorded their activities in a daily diary.

A dietician evaluated the nutritional status and offered high protein nutrient drinks if necessary. The geriatrician performed a comprehensive geriatric assessment (CGA) to evaluate the physical, psychological and functional capabilities and limitations in order to assess frailty and the risk of developing a delirium[40,40,41]. Based on the CGA, the geriatrician developed a tailored care plan that

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addressed the specific needs of the patient, including defining preventive measures for delirium and functional decline. In case of anaemia, defined as a level of haemoglobin <8.1 mmol/L (male) and <7.4 mmol/L (female), patients received intravenously iron infusion using 1000mg ferric carboxymaltose, administered in 15 minutes. Homecare following revascularization was prearranged if required. Active smokers were referred to a 'quit smoking coach' to receive guidance in reducing nicotine abuse.

During the weekly multidisciplinary meeting comprising vascular surgeons and interventional radiologists, anatomical findings and patients' complaints were integrated to determine the most suitable approach for revascularization; surgical or endovascular. When the screening aspect during prehabilitation provided a different perspective on the patient's condition compared to the initial assessment, it could influence the treatment strategy, such as choosing endovascular over surgical revascularization, or vice versa, based on the patient's frailty.

Upon hospital admission for the intervention, biochemistry tests were repeated. Compliance was assessed through a process evaluation form completed by patients at the end of the prehabilitation period, which also gathered their feedback on the program's effectiveness and the overall experience.

Statistical analysis

A two-sided *p*-value <.05 was considered statistically significant. Results of categorical data variables were described in frequencies (percentages) and differences were tested using the Chi-square test. Continuous data were described as median (interquartile range) and Mann-Whitney U-tests (MWU) were performed to test for cohort differences. Ordinal variables were tested using MWU. Logistic regression analysis with adjustment for key prognostic factors was the primary

analysis for the delirium incidence. These predefined confounders were based on previous research and comprised age, physical impairment, history of delirium, preoperative anaemia and revascularization type.[5] Age was modelled as a continuous covariate. Categorical covariates were history of delirium (yes/no), physical impairment (KATZ-score =>1 yes/no), preoperative anaemia (yes/no) and the type of revascularization (endovascular or surgical). These analyses were repeated in the endovascular and surgical cohort. One year after initiation of the study, a preliminary analysis was conducted to verify safety, by comparing amputation rates and mortality between the prolonged prehabilitation cohort and the retrospective control cohort. Statistical analyses were performed using IBM SPSS statistical software (SPSS Inc., Chicago, Illinois, USA)[42].

Ethics committee approval and registration number

Ethical approval for this study was obtained from the MEC-U, the Netherlands, registration number W21.061 and from the Ethics Committee Research UZ/KU Leuven, Belgium, reference number S66370. This study followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guideline for cohort studies[43].

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RESULTS

Participants

A total of 123 patients was referred to the outpatient clinic for prehabilitation with 101 consenting to participate in the intervention cohort (Figure 1). In the prospective control cohort, 48 patients were included. The retrospective control cohort included 207 patients. All patients successfully completed follow-up and were included in the analysis. Despite the original sample size calculation, the study concluded with a smaller sample size due to slower than anticipated enrolment rates.

Baseline characteristics of the intervention and control cohort exhibited significant differences in age, ASA score, preoperative anaemia, renal impairment and physical impairment (Table I). Among the 356 patients, 181 (51%) were male, with a median age (IQR) of 76 years (71-82). The majority of prehabilitation patients underwent endovascular revascularization (56/101, 55%), while the control cohort mostly underwent surgical procedures (196/255, 66%, p=<.001).

Prehabilitation program

The prehabilitation program involved a median duration (IQR) of 23 days (14-34). The number of patients referred to each component is shown in Table II. The median number (IQR) of components attended was 3 (2-4) of 6. Of the 41 anaemic patients, 19 did not receive iron infusion; among them, 9 had prior treatment for chronic anaemia, 4 were referred to internal medicine for evaluation, 4 were not ordered, and 2 didn't require Ferric carboxymaltose after consulting internal medicine. Out of the 21 active smokers that were not referred to a stop smoking coach, 17 were not motivated to quit, 2 were already undergoing therapy, and 2 aimed to quit independently.

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Among the 101 patients, 92 compliance forms were received. According to 70 out of 92 forms the program was successfully completed. Reasons for non-compliance were primarily associated with painful limbs due to CLTI or a lack of motivation. However, none mentioned that the preoperative trajectory was excessively lengthy. The median (IQR) program rating, scored on a scale from 1 to 10, was 8 (7-9). Patients were appreciative of the dedicated time during which they were screened and given information about the ongoing health processes.

Primary outcome

The incidence of delirium was significantly lower in the prehabilitation cohort (2/101, 2%), compared to the control cohort (23/255, 9.1%, OR=0.21, 95%CI .05-.89, *p*=.04) (Table III). After regression analysis with adjustment for predefined confounders, the decrease of delirium incidence was non-significant (adjusted OR [aOR]=0.28, 95%CI .06-1.3, *p*=.09, Table IV). Subgroup analysis were performed for endovascular and surgical treatment. Delirium incidences were 1.8% in prehabilitation versus 4.7% in control (*p*=.37; OR=0.37 CI .04—3.4, *p*=.38; aOR= .46, CI .05-4.8, *p*=.52) and 2.2% in prehabilitation versus 11% in control (*p*=.07; OR=.18, CI .23-1.4; *p*=.09; aOR=.24, CI .03-1.9, *p*=.18) for endovascular treatment and surgical treatment respectively (Supplemental Table II and III).

Secondary outcomes

The prehabilitation cohort showed a significant shorter LoS compared to the control cohort (median [IQR], 2 [1-5] days vs 4 [2-9] days; *p*=<.001), which was also noted in the endovascular and surgical cohort separately. Significantly less minor complications occurred in the prehabilitation cohort (14/101, 14% vs 66/255, 26%, *p*=.01). No significant differences were found in major

complications (18/101, 18% in prehabilitation vs 59/255, 23% in control, p=.27) and 30-day mortality (2/101, 2% in prehabilitation vs 7/255, 3.3% in control, p=.68). No other significant differences in outcomes between the prehabilitation and control cohort were observed within the endovascular or surgical cohort.

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DISCUSSION

This study demonstrates that prehabilitation in elderly CLTI patients is safe and has the potential to yield multiple beneficial effects on general outcomes following revascularization. Although a reduced incidence of delirium was observed in the prehabilitation cohort, this difference did not reach statistical significance after adjusting for predefined confounders. The prehabilitation cohort showed a significant shortened LoS and significantly less minor complications compared to controls.

To our knowledge, this is the first study to explore multimodal multicomponent prehabilitation in elderly CLTI patients. A review by Palmer et al. revealed no randomized controlled trials on prehabilitation for lower limb surgery for peripheral arterial disease, and another review only included limited studies on delirium prevention in vascular surgery, with only a few involving CLTI patients[44,45]. The scarcity of prehabilitation studies for CLTI patients may be due to the perception that urgent revascularization is necessary upon diagnosis. However, CLTI patients are often frail, malnourished and prone to develop geriatric syndromes. They have a longer LoS, and are discharged to a higher level of care compared to non-frail patients[21–23,46,47]. This outlines the importance of preoperative optimization. Preliminary and final analyses revealed no significant differences in amputation rate and mortality in the intervention cohort compared to the control cohort, indicating the safety of preoperative prehabilitation. Recent literature also suggests that immediate revascularization isn't always essential, supporting the idea that a prehabilitation program doesn't adversely affect outcomes by delaying revascularization[6,7,10,30]

In contrast to prehabilitation in CLTI patients, prehabilitation has already been abundantly described in abdominal surgery and has gained interest in multiple other types of surgery[25,27,48–50]. A recent RCT showed the benefit of a multimodal prehabilitation program before colorectal cancer surgery as reflected by fewer severe and medical complications postoperatively and an optimized postoperative recovery compared with standard care[28]. More specific regarding delirium, Humeidan et al. reported a decreased risk for delirium after major noncardiac surgery using cognitive prehabilitation[50].

LoS was significantly shortened in the prehabilitation cohort compared to the control cohort. This finding holds crucial clinical significance within strains on healthcare resources and growing evidence supporting early mobilization and discharge. While it is anticipated that the historical cohort (forming the majority of the combined control cohort) would have a longer LoS, a significant difference was also observed between the contemporary control cohort and the prehabilitation cohort. This suggests that the notable difference cannot solely be attributed to the longer LoS in the historical cohort.

We assessed the impact of a multimodal, multicomponent prehabilitation program, which is favored over unimodal prehabilitation[51,52]. For instance, many CLTI patients are malnourished, which correlates with higher rates of major amputation and mortality[47]. This already outlines the reason why unimodal prehabilitation (exercise based without nutritional advice from a dietician) would not be the best standard of care. Additionally, the benefits of comprehensive geriatric assessments and administering Ferric carboxymaltose for anemic patients have been explored in prior studies, suggesting their potential inclusion in prehabilitation programs[53–55]. Therefore, evaluating the program as a whole, customized for each individual, is crucial rather than

analyzing each component separately. The observation that only five patients were referred to more than four components emphasizes the importance of tailoring prehabilitation instead of unnecessarily administering the entire program to all patients.

This study has limitations. To start with, the design is not a RCT. The distinction between prehabilitation and non-intervention cohorts within the same hospital is difficult, as healthcare providers involved in the prehabilitation program may inadvertently emphasize prehabilitation aspects in control patients as well, blurring the lines between the cohorts. Therefore, we opted for an observational approach, incorporating one historical control cohort from the same hospital and one contemporary control cohort from a different hospital with comparable medical care settings. After separate analysis, these control cohorts were combined into one single control cohort, as outlined in the supplementary material.

In addition, patients with severe cognitive impairment, such as dementia, to the extent that completion of questionnaires and participation in prehabilitation was impossible, were excluded. While these patients are at high risk for delirium, our center's prior research indicated a low incidence of severe cognitive impairment among CLTI patients, most of whom received conservative treatment[56]. As the aim of this study was preventing postoperative delirium after revascularization, conservatively treated patients were ineligible for this study. Immediate need for revascularization or hospitalization, hindering participation in the 3-week prehabilitation program, was also an exclusion criterion.

The study was concluded before reaching the planned sample size due to slower recruitment than initially projected. Extending the enrollment period to achieve the target sample size was deemed

impractical within the study's timeframe. This may have reduced the statistical power to detect smaller differences between groups and resulted in broader confidence intervals, introducing some uncertainty in the effect estimates. However, given the heterogeneity and complexity of this vulnerable patient population, the findings still provide valuable insights, though further research with a larger sample size would help to strengthen the conclusions.

Furthermore, in the retrospective cohort, important variables regarding the healthcare trajectory of CLTI patients were not documented. For instance, the WiFi score, a comprehensive tool for evaluating the clinical status and prognosis of CLTI patients, was not utilized, and therefore not addressed within this article. Additionally, indicators of frailty, such as the clinical frailty score, ISAR-HP, G8, and MMSE, were not documented. All of them were recorded for the prospective cohorts (Supplemental Table II). This was another reason to implement an additional prospective control cohort. It is recommended to include and evaluate these factors in future research. Since this study focused on 30-day outcomes, no long-term follow-up results are available. This could be investigated in future studies.

Finally, overall compliance was assessed by reviewing completed effect forms from participants. While monitoring homebased exercises participation may be less reliable than in-person training, mandating elderly patients to visit the physical therapist thrice weekly would pose implementation challenges[57]. Due to organizational challenges, it was not possible to objectify the physical effects of the prehabilitation program at the end of the prehabilitation period.

Despite its limitations, this study successfully explored prehabilitation within a challenging and vulnerable cohort. The study design and low number of events posed challenges in achieving

statistical significance, despite the notable decrease in delirium incidence among the prehabilitation cohort. In conclusion, multimodal prehabilitation emerges as a safe and beneficial strategy for elderly CLTI patients undergoing revascularization. It demonstrates a trend towards reduced delirium incidence, significantly shortened LoS, and significant less minor complications without increased amputation risk. Moreover, an extended preoperative period to enhance frail patients' overall fitness and resilience appears advantageous rather than harmful, as reflected in high patient satisfaction rates. These findings support the possibility for featuring prospective research studies for prehabilitation in CLTI patients.

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Declaration of interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Conflict of interest statement

All authors declare that they have no competing interests.

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TABLES

Table I: Basic characteristics

		Retrospective control (1) n=207 (58.1%)	Prospective control (2) n = 48 (13.5%)	Prehabilitation (3) n=101 (28.4%)	P-value 1 vs 3	P-value 2 vs 3
Basic characteristics						
Demographics	Age	76 (70-81)	77 (70-82)	78 (72-83)	.03	.64
	Gender (male)	95 (45.9)	29 (60)	57 (56.4)	.08	.65
Comorbidities, medical history	ASA[a] >2	154 (74.4)	46 (96)	87 (90.6)	.005	.03
	Anaemia[b]	96 (70)	26 (57)	41 (42)	.27	.08
	Cardiac disease	128 (61.8)	29 (6)	56 (55.4)	.28	.57
	COPD	99 (47.8)	8 (17)	35 (34.7)	.03	.02
	Renal impairment	90 (43.5)	23 (48)	31 (30.7)	.03	.04
	Cerebrovascular disease	59 (28.5)	9 (19)	24 (23.8)	.38	.49
	Diabetes Mellitus	79 (38.2)	25 (52)	42 (41.6)	.56	.23
	Hypertension	152 (73.4)	42 (88)	75 (74.3)	.88	.07
Intoxications	Active smoking	81 (39.1)	11 (23)	36 (35.6)	.09	.85
	Daily alcohol	54 (26.1)	7 (15)	24 (23.8)	.25	.2
Impairments	Physical impairment[c]	76 (37.1)	18 (38)	16 (15.8)	<.001	.003
	Undernourishment[d]	42 (20.7)	6 (13)	16 (15.8)	.35	.59
	Visual impairment	51 (24.6)	31 (71)	74 (73.3)	<.001	.73
	Auditory impairment	55 (26.6)	3 (9)	63 (62.4)	<.001	<.001
	History of delirium	36 (17.6)	10 (21)	14 (13.9)	.55	.28
Extent of vascular disease	Fontaine III	96 (46.4)	7 (15)	49 (48.5)	.98	<.001
	Fontaine IV	111 (53.6)	41 (85)	54 (53.5)		
Revascularisation	Endovascular	62 (30)	24 (50)	56 (55.4)	<.001	.53
	Surgical	145 (70)	24 (50)	45 (44.6)		
	Bypass[e]	105 (72.4)	10 (42)	20 (44.4)	<.001	.83
	Endarteriectomy[e]	40 (27.6)	14 (58)	25 (55.6)		

Table I: basic characteristics
Data are presented as n (%) or median (interquartile range)
[a] ASA =American Society of Anaesthesiologists classification
[b] Anaemia: Haemoglobin <8.1mmol/l (male) or <7.4 mmol/l (female)
[c] Physical impairment = KATZ-ADL (Katz index of Independence in Activities of Daily Living) score =>1
[d] Undernourishment = SNAQ-RC (Short Nutritional Assessment Questionnaire for Residential Care) score =>3
[e] % of the surgical patients

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Table II: Number of patients per prehabilitation program component

	Number of patients n (%)
Program component	
Physical therapy	101 (100)
Dietary advice	71 (70)
Nutritional drinks	11 (11)
Comprehensive geriatric assessment	74 (73)
Ferric carboxymaltose injection	22 (22)
Stop smoking program	15 (15)
Prearranged homecare	7 (7)
Total number of components per patient	
1	2 (2)
2	26 (26)
3	43 (43)
4	25 (25)
5	4 (4)
6	1 (1)

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Table III: Postsurgical outcomes of control group versus prehabilitation group in all patients (N = 356).

		Control n= 255 (71.6%)	Prehabilitation n=101 (28.4%)	P-value
Results				
Primary outcome	Incidence of delirium	23 (9.1)	2 (2)	.02
Hospital stay	Length of stay	4 (2-9)	2 (1-5)	<.001
	Readmission[a]	24 (9.4)	11 (11.1)	.67
	Re-operation nr. of patients	58 (22.7)	15 (15)	.09
Complications < 30 days	Minor complication[b]	66 (26)	14 (14)	.01
	Major complication[c]	59 (23.1)	18 (18.2)	.27
	Major amputation	8 (3.1)	4 (4.1)	.46
	Surgical complication	40 (15.7)	8 (8.1)	.06
	Cardiac complication	18 (7.1)	5 (5.1)	.49
	Pulmonal complication	11 (4.3)	3 (3)	.58
	Cerebrovascular complication	2 (0.8)	1 (1)	.84
Mortality	30-day mortality	7 (3.3)	2 (2)	.68

Table III: Results

Data are presented as n (%) or median (interquartile range).
[a] Readmission on the surgical ward
[b] Number of patients with at least one minor complication
[c] Number of patients with at least one major complication

Table IV: Odds ratios for primary outcome.

		Prehabilitation : Control			
		Unadjusted OR (95% CI)	P-value	Adjusted OR (95% CI)	P-value
Incidence of delirium	Total group	.21 (.05-.89)	.035	.28 (.06-1.3)	.097
	Endovascular subgroup	.37 (.04-3.4)	.38	.46 (.05-4.8)	.52
	Surgical subgroup	.18 (.23-1.4)	.09	.24 (.03-1.9)	.18

Table IV: (Un)adjusted odds ratios for primary outcome. Prehabilitation versus control
Covariates that are adjusted for: age (continuous), physical impairment (KATZ =>1, yes/no), history of delirium (yes/no), preoperative anaemia (yes/no), and, only in the total group: type of revascularisation (endovascular/surgical)

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FIGURE TITLES AND LEGENDS

Figure 1. CONSORT flow diagram

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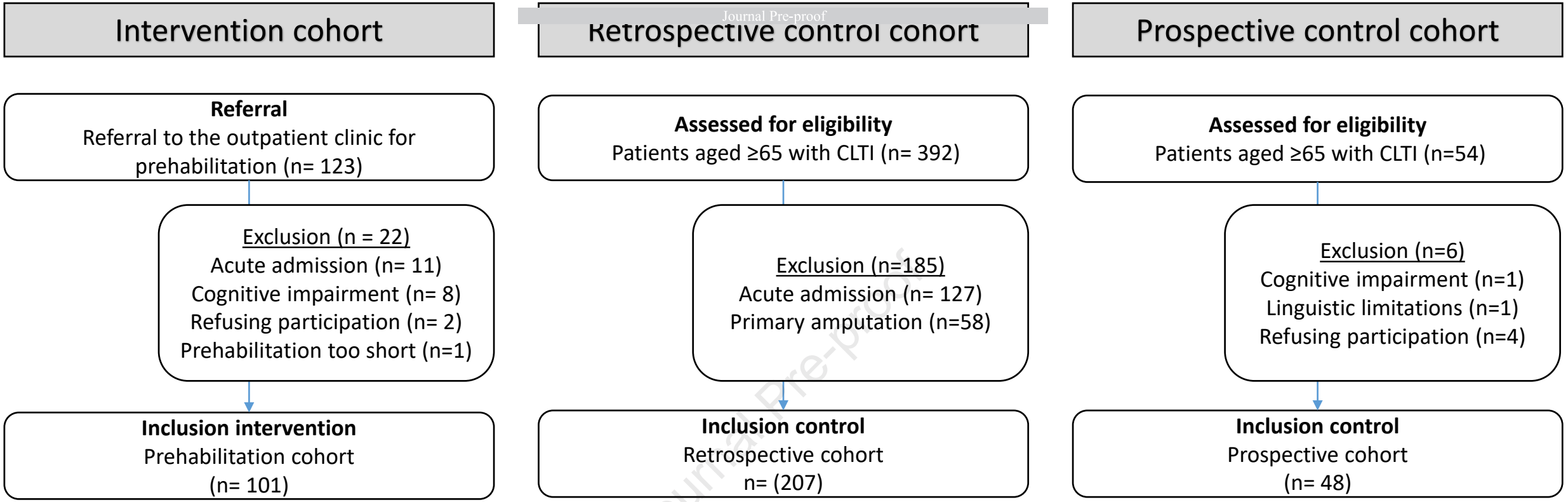

Figure 1. CONSORT Flow Diagram

Content of online only supplemental material

Supplemental Table I	Extended Table I (basic characteristics) of the total group, both individual control groups and subgroups endovascular and surgical revascularization
Supplemental Table IIa	Results of both individual control groups and subgroups endovascular and surgical revascularization
Supplemental Table IIb	Results of subgroups endovascular and surgical revascularization
Supplemental Table III	Regression analysis per subgroup (endovascular and surgical) and the total control cohort

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SUPPLEMENTAL TABLE I

Extended Table I (basic characteristics) of the total group, both individual control groups and subgroups endovascular and surgical revascularization

	Total group n = 356 (100%)						
	Retrospective control (1) n=207 (58.1%)	**Prospective control (2) n = 48 (13.5%)**	**Control 3: Total (1+2) n= 255 (71.6%)**	**Prehabilitation (3) n=101 (28.4%)**	**P-value 1 vs 3**	**P-value 2 vs 3**	**P-value 3 vs 3**
Age - y, med (IQR)	76 (70-81)	77 (70-82)	76 (69-83)	78 (72-83)	.03	.64	.04
Gender (male)	95 (45.9)	29 (60.4)	124 (48.6)	57 (56.4)	.08	.65	.18
ASA >2	154 (74.4)	46 (96)	200 (79.1)	87 (90.6)	.005	.03	.04
Anemia*	96 (70)	26 (56.8)	122 (49)	41 (42.6)	.27	.08	.17
Cardiac disease	128 (61.8)	29 (60.4)	157 (61.6)	56 (55.4)	.28	.57	.29
COPD	99 (47.8)	8 (16.7)	107 (75.4)	35 (34.7)	.03	.02	.20
Renal impairment	90 (43.5)	23 (47.9)	113 (44.3)	31 (30.7)	.03	.04	.02
Cerebrovascular disease	59 (28.5)	9 (18.8)	68 (26.7)	24 (23.8)	.38	.49	.57
Diabetes Mellitus	79 (38.2)	25 (52.1)	104 (40.8)	42 (41.6)	.56	.23	.9
Hypertension	152 (73.4)	42 (87.5)	194 (76.1)	75 (74.3)	.88	.07	.72
Charlon Comorbidity Index	n.a.	8 (5-9)	n.a.	7 (5-9)	n.a.	.87	n.a.
Vascular Possum Score	n.a.	26 (22-31)	n.a.	21 (18-25)	n.a.	<.001	n.a.
Active smoking	81 (39.1)	11 (22.9)	92 (36.1)	36 (35.6)	.09	.85	.19
Daily alcohol	54 (26.1)	7 (14.6)	61 (23.9)	24 (23.8)	.25	.2	.36
Alcohol abuse	12 (5.8)	0	12 (4.7)	7 (6.9)	.13	.06	.15
Physical impairment*	76 (37.1)	18 (37.5)	94 (37.2)	16 (15.8)	<.001	.003	<.001
Undernourishment*	42 (20.7)	6 (12.5)	48 (19.1)	16 (15.8)	.35	.59	.5
Visual impairment	51 (24.6)	31 (70.5)	82 (32.7)	74 (73.3)	<.001	.73	<.001
Auditory impairment	55 (26.6)	3 (8.6)	58 (24)	63 (62.4)	<.001	<.001	<.001
History of delirium	36 (17.6)	10 (20.8)	46 (18.2)	14 (13.9)	.55	.28	.5
Clinical frailty scale	n.a.	4 (3-5)	n.a.	4 (3-5)	n.a.	.41	n.a.
MMSE	n.a.	28 (26-30)	n.a.	28 (26-29)	n.a.	.41	n.a.
ISAR-HP	n.a.	n.a.	n.a.	3 (1-4)	n.a.	n.a.	n.a.
Geriatric 8 (G8)	n.a.	n.a.	n.a.	14 (12-15)	n.a.	n.a.	n.a.
Increased fallrisk	n.a.	34 (71)	n.a.	61 (61)	n.a.	.24	n.a.
Fontaine III	96 (46.4)	7 (14.6)	103 (40.4)	49 (48.5)	.98	<.001	.29
Fontaine IV	111 (53.6)	41 (85.4)	152 (59.6)	54 (53.5)	.98	<.001	.29
Ankle brachial index	.43 (.26-.7)	.38 (.29-.7)	.375 (.3-.7)	.34 (.2-.48)	<.01	.08	<.01
Aorto-iliac TASC: 0	102 (49.3)	16 (43.2)	118 (48.4)	44 (44.9)	<.001	.06	.003
A	38 (18.4)	9 (24.3)	47 (19.3)	35 (35.7)	"	"	"
B	20 (9.7)	8 (21.6)	28 (11.5)	12 (12.2)	"	"	"
C	19 (9.2)	4 (10.8)	23 (9.4)	2 (2)	"	"	"
D	19 (9.2)	0	19 (7.8)	5 (5.1)	"	"	"
Femoral popliteal TASC: 0	15 (7.2)	1 (2.4)	16 (6.5)	0	.015	.05	.024
A	22 (10.6)	12 (29.3)	34 (13.7)	15 (15)	"	"	"
B	67 (32.4)	13 (31.7)	80 (32.3)	24 (24)	"	"	"

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C	35 (16.9)	6 (14.6)	41 (16.5)	22 (22)	"	"	"
D	64 (30.9)	9 (22)	73 (29.4)	39 (39)	"	"	"
WIFI score amputation	n.a.	3 (2-3)	n.a.	2 (2-3)	n.a.	.1	n.a.
WIFI score revascularisation	n.a.	4 (3-4)	n.a.	3 (2-4)	n.a.	.02	n.a.
Endovascular Revasc.	62 (30)	24 (50)	86 (33.7)	56 (55.4)	<.001	.53	<.001
Surgical Revasc.	145 (70)	24 (50)	169 (66.3)	45 (44.6)	<.001	.53	<.001
Bypass*	105 (72.4)	10 (41.7)	115 (68)	20 44.4)	<.001	.83	.004
Endarteriectomy*	40 (27.6)	14 (58.3)	54 (32)	25 (55.6)	<.001	.83	.004

Continued

	Endovascular n = 142 (40% of total)						
	Retrospective control (1) n = 62 (43.6%)	**Prospective control (2) n = 24 (16.9%)**	**Control 3: Total (1+2) n = 86 (60.6%)**	**Intervention (3): Prehabilitation n = 56 (39.4%)**	**P-value 1 vs 3**	**P-value 2 vs 3**	**P-value 3 vs 3**
Age - y, med (IQR)	80.5 (76-84)	81 (67-84)	81 (67-84)	80 (76-84)	.56	.99	.64
Gender (male)	22 (35.5)	11 (46)	32 (38.6)	27 (48.2)	.16	.85	.26
ASA >2	43 (69.4)	22 (92)	62 (76.5)	45 (88.2)	.05	.1	.22
Anemia*	27 (51.9)	14 (70)	41 (57)	26 (46.4)	.57	.07	.24
Cardiac disease	43 (69.4)	12 (50)	52 (62.7)	29 (51.8)	.05	.88	.2
COPD	33 (53.2)	3 (12.5)	36 (43.3)	23 (41.1)	.19	.01	.79
Renal impairment	42 (67.7)	14 (58)	54 (65.1)	23 (41.1)	.004	.16	.005
Cerebrovascular disease	20 (32.3)	2 (8.3)	22 (26.5)	15 (26.8)	.52	.09	.97
Diabetes Mellitus	29 (46.8)	13 (54)	41 (49.4)	25 (44.6)	.82	.53	.58
Hypertension	47 (75.8)	21 (87.5)	65 (78.3)	47 (83.9)	.27	.68	.41
Charlon Comorbidity Index	n.a.	6 (7-8)	n.a.	7 (5-11)	n.a.	.93	n.a.
Vascular Possum Score	n.a.	26 (23-32)	n.a.	22 (19-25)	n.a.	.005	n.a.
Active smoking	17 (27.4)	3 (12.5)	20 (24.1)	17 (30.4)	.15	.01	.2
Daily alcohol	16 (25.8)	3 (12.5)	19 (22.9)	12 (21.4)	.32	.44	.49
Alcohol abuse	5 (8.1)	0	5 (6)	3 (5.4)	.33	.35	.49
Physical impairment*	29 (47.5)	9 (37.5)	37 (45.1)	11 (19.6)	.003	.09	.005
Undernourishment*	13 (21.3)	2 (8.3)	15 (18.3)	9 (16.1)	.47	.46	.66
Visual impairment	18 (29)	16 (70)	32 (38.6)	41 (73.2)	<.001	.62	<.001
Auditory impairment	20 (32.3)	1 (5.3)	21 (26.9)	38 (67.9)	<.001	<.001	<.001
History of delirium	8 (13.1)	4 (16.7)	12 (14.6)	7 (12.5)	.92	.62	.72
Clinical frailty scale	n.a.	4 (3-4)	n.a.	4 (3-5)	n.a.	.66	n.a.
MMSE	n.a.	28 (25-29)	n.a.	28 (25-29)	n.a.	.79	n.a.
ISAR-HP	n.a.	n.a.	n.a.	3 (1-4)	n.a.	n.a.	n.a.
Geriatric 8 (G8)	n.a.	n.a.	n.a.	14 (12-15)	n.a.	n.a.	n.a.
Increased fallrisk	n.a.	19 (81)	n.a.	39 (69)	n.a.	.24	n.a.

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Fontaine III	20 (32.3)	1 (4.2)	21 (45.7)	25 (44.6)	.17	<.001	.017
Fontaine IV	42 (67.7)	23 (96)	62 (74.7)	31 (55.4)	.17	<.001	.017
Ankle brachial index	.45 (.3-.68)	.45 (.3-.8)	.45 (.3-.8)	.39 (.22-.47)	.008	.05	.004
Aorto-iliac TASC: 0	39 (62.9)	11 (69)	49 (63.6)	29 (53.7)	.13	.44*	.11
A	8 (12.9)	2 (12.5)	10 (13)	16 (29.6)	"	"	"
B	5 (8.1)	2 (12.5)	7 (9.1)	5 (9.30	"	"	"
C	3 (4.8)	1 (6.3)	4 (5.2)	1 (1.9)	"	"	"
D	3 (4.8)	0	3 (3.9)	3 (5.6)	"	"	"
Femoral popliteal TASC: 0	6 (9.7)	0	6 (7.7)	0	<.001	.05*	<.001
A	7 (11.3)	8 (44)	15 (19.2)	11 (20)	"	"	"
B	37 (59.7)	7 (39)	43 (55.1)	15 (27.3)	"	"	"
C	7 (11.3)	1 (5.6)	8 (10.3)	12 (21.8)	"	"	"
D	4 (6.5)	2 (11)	5 (6.4)	17 (30.9)	"	"	"
WIFI score amputation	n.a.	3 (3-3)	n.a.	2 (2-3)	n.a.	.017	n.a.
WIFI score revascularisation	n.a.	4 (4-4)	n.a.	3 (2-3)	n.a.	.004	n.a.
Endovascular Revasc.	62 (30)	24 (50)	86 (33.7)	56 (55.4)	<.001	.53	<.001
Surgical Revasc.	145 (70)	24 (50)	169 (66.3)	45 (44.6)	<.001	.53	<.001
Bypass*	105 (72.4)	10 (41.7)	115 (68)	20 44.4)	<.001	.83	.004
Endarteriectomy*	40 (27.6)	14 (58.3)	54 (32)	25 (55.6)	<.001	.83	.004

Continued

	Surgical n = 214 (60% of total)						
	Retrospective control (1) n=145 (67.8%)	**Prospective control (2) n = 24 (11.2%)**	**Control 3: Total (1+2) n= 169 (79%)**	**Intervention (3): Prehabilitation n= 45 (21%)**	**P-value 1 vs 3**	**P-value 2 vs 3**	**P-value 3 vs 3**
Age - y, med (IQR)	75 (71-80)	76 (71-79)	76 (70-77)	74 (72-79)	.13	.84	.21
Gender (male)	73 (50.3)	18 (75)	92 (53.5)	30 (66.7)	.06	.47	.88
ASA >2	111 (58.4)	24 (100)	138 (80.2)	42 (93.3)	.01	.2	.037
Anemia*	69 (81.2)	12 (48)	80 (47.3)	15 (36)	.19	.34	.19
Cardiac disease	85 (58.6)	17 (70)	105 (61)	27 (60)	.87	.37	.9
COPD	66 (45.5)	5 (20)	71 (41.3)	12 (26.7)	.03	.59	.07
Renal impairment	48 (33.1)	9 (37.5)	59 (34.3)	8 (17.8)	.05	.07	.033
Cerebrovascular disease	39 (26.9)	7 (29)	46 (26.7)	9 (20)	.35	.52	.35
Diabetes Mellitus	50 (34.5)	12 (50)	63 (36.6)	17 (37.8)	.69	.25	.89
Hypertension	105 (72.4)	21 (87)	129 (75)	28 (62.2)	.19	.028	.09
Charlon Comorbidity Index	n.a.	7 95-9)	n.a.	7 (5-8)	n.a.	.77	n.a.
Vascular Possum Score	n.a.	28 (21-31)	n.a.	20 (18-24)	n.a.	.003	n.a.
Active smoking	64 (44.1)	8 (33)	72 (41.9)	19 (42.2)	.49	.47	.59
Daily alcohol	38 (26.2)	4 (17)	42 (24.4)	12 (26.7)	.62	.26	.65
Alcohol abuse	7 (4.8)	0	7 (4.1)	4 (8.9)	.24	.09	.20

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Physical impairment*	47 (32.6)	9 (37.5)	57 (33.3)	5 (11.1)	.015	.009	.011
Undernourishment*	29 (20.4)	4 (17)	33 (19.5)	7 (15.6)	.65	.91	.72
Visual impairment	33 (22.8)	15 (71)	50 (29.8)	33 (73.3)	<.001	.98	<.001
Auditory impairment	35 (24.1)	2 (12.5)	37 (22.6)	25 (55.6)	<.001	.002	<.001
History of delirium	28 (19.4)	6 (25)	34 (19.9)	7 (15.6)	.71	.34	.7
Clinical frailty scale	n.a.	4 (4-5)	n.a.	4 (3-4)	n.a.	.06	n.a.
MMSE	n.a.	29 (26-30)	n.a.	29 (26-29)	n.a.	.47	n.a.
ISAR-HP	n.a.	n.a.	n.a.	2 (1-3)	n.a.	n.a.	n.a.
Geriatric 8 (G8)	n.a.	n.a.	n.a.	13 (12-15)	n.a.	n.a.	n.a.
Increased fallrisk	n.a.	15 (60)	n.a.	22 (50)	n.a.	.42	n.a.
Fontaine III	76 (52.4)	6 (25)	82 (47.7)	22 (48.9)	.68	.04	.89
Fontaine IV	69 (47.6)	18 (75)	90 (52.3)	23 (51.1)	.68	.04	.89
Ankle brachial index	.26 (.23-.36)	.35 (.25-.5)	.35 (.25-.5)	.34 (.2-.51)	.68	.56	.021
Aorto-iliac TASC: 0	63 (43.4)	5 (24)	69 (41.3)	15 (33.3)	.02	.18	.036
A	30 (20.7)	7 (33)	37 (22.2)	19 (42.2)	"	"	"
B	15 (10.3)	6 (25)	21 (12.6)	7 (15.6)	"	"	"
C	16 (11)	3 (14)	19 (11.4)	1 (2.2)	"	"	"
D	16 (11)	0	16 (9.6)	2 (4.4)	"	"	"
Femoral popliteal TASC: 0	9 (6.2)	1 (4)	10 (5.9)	0	.49	.36	.48
A	15 (10.3)	4 (17)	19 (11.2)	4 (8.9)	"	"	"
B	30 (20.7)	6 (25)	37 (21.8)	9 (20)	"	"	"
C	28 (19.3)	5 (21)	33 (19.4)	10 (22.2)	"	"	"
D	60 (41.4)	7 (30)	68 (40)	22 (48.9)	"	"	"
WIFI score amputation	n.a.	2 (0-3)	n.a.	2 (2-3)	n.a.	.85	n.a.
WIFI score revascularisation	n.a.	3 (0-4)	n.a.	3 (2-4)	n.a.	.85	n.a.
Endovascular Revasc.	62 (30)	24 (50)	86 (33.7)	56 (55.4)	<.001	.53	<.001
Surgical Revasc.	145 (70)	24 (50)	169 (66.3)	45 (44.6)	<.001	.53	<.001
Bypass*	105 (72.4)	10 (41.7)	115 (68)	20 44.4)	<.001	.83	.004
Endarteriectomy*	40 (27.6)	14 (58.3)	54 (32)	25 (55.6)	<.001	.83	.004

Data are presented as n (%) or median (interquartile range).

* ASA = American Society of Anesthesiologists classification

* Anemia: Hemoglobin <8.1mmol/l (male) or <7.4 mmol/l (female)

* Physical impairment = KATZ-ADL (Katz index of Independence in Activities of Daily Living) score =>1

* Undernourishment = SNAQ-RC (Short Nutritional Assessment Questionnaire for Residential Care) score =>3

Wifi score amputation: Estimation of risk of amputation at 1 year.

Wifi score revascularisation: Estimate of need for/benefit of revascularization

(*) percentage of the surgical patients

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Supplemental Table IIa

Results of both individual control groups and subgroups endovascular and surgical revascularization

	Total group n = 356 (100%)						
	Retrospective control (1) n=207 (58.1%)	**Prospective control (2) n = 48 (13.5%)**	**Total control (3) n= 255 (71.6%)**	**Prehabilitation (3) n=101 (28.4%)**	**P-value 1 vs 3**	**P-value 2 vs 3**	**P-value 3 vs 3**
Incidence of delirium	19 (9.2)	4 (8.5)	23 (9.1)	2 (2)	.019	.061	.02
Minor complication	44 (21.3)	22 (45.8)	66 (26)	14 (14)	.13	<.001	.01
Major complication	49 (23.7)	10 (20.8)	59 (23)	18 (18.2)	.26	.68	.27
Major amputation	8 (3.9)	0	8 (3.1)	4 (4.1)	.7	.16	.46
Surgical complication	37 (17.9)	3 (6.4)	40 (15.7)	8 (8.1)	.02	.72	.06
Cardiac complication	13 (6.3)	5 (10.6)	18 (7.1)	5 (5.1)	.67	.21	.49
Pulmonal complication	8 (3.9)	3 (6.4)	11 (4.3)	3 (3)	.71	.34	.58
Cerebrovascular complication	2 (1)	0	2 (0.8)	1 (1)	.98	.49	.84
Length prehabilitation - d, med (IQR)	n.a.	n.a.	n.a.	23 (14-34)	n.a.	n.a.	n.a.
Length hospital stay - d, med (IQR)	7 (4-10)	4 (2-9)	4 (2-9)	2 (1-5)	<.001	<.001	<.001
Readmission	35 (16.9)	7 (23.3)	42 (16.5)	11 (11.1)	.16	.09	.18
Re-operation nr. of patients	49 (23.6)	9 (18.8)	58 (23)	15 (15)	.09	.56	.1
30-day mortality	6 (2.9)	1 (2.1)	7 (3.3)	2 (2)	.63	.97	.68

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Supplemental Table IIb

Results of subgroups endovascular and surgical revascularization

	Endovascular n = 142 (40% of total)						
	Retrospective control (1) n = 62 (43.6%)	**Control 2: Leuven n = 24 (16.9%)**	**Control 3: Total (1+2) n = 86 (60.6%)**	**Intervention (3): Prehabilitation n = 56 (39.4%)**	**P-value 1 vs 3**	**P-value 2 vs 3**	**P-value 3 vs 3**
Incidence of delirium	3 (4.8)	1 (4.2)	4 (4.7)	1 (1.8)	.36	.53	.37
Minor complication	12 (19.4)	11 (45.8)	23 (27)	7 (12.5)	.33	.001	.04
Major complication	18 (29)	4 (16.7)	22 (26)	8 (14.3)	.06	.79	.1
Major amputation	3 (4.8)	0	3 (3.5)	2 (4.3)	.9	.35	.98
Surgical complication	8 (12.9)	3 (12.5)	11 (12.8)	3 (5.4)	.16	.27	.07
Cardiac complication	4 (6.5)	1 (4.2)	7 (8.1)	4 (7.1)	.89	.61	.83
Pulmonal complication	2 (3.2)	1 (4.2)	3 (3.5)	3 (5.4)	.57	.82	.59
Cerebrovascular complication	1 (1.6)	0 (0)	1 (1.2)	0 (0)	.34	n.a.	.42
Length prehabilitation - d, med (IQR)	n.a.	n.a.	n.a.	24 (14-30)	n.a.	n.a.	n.a.
Length hospital stay - d, med (IQR)	6 (2-9)	2 (2-3)	2 (2-2)	1 (1-1)	<.001	<.001	<.001
Readmission	12 (19.4)	4 (16.7)	16 (19)	7 (12.5)	.31	.62	.96
Re-operation nr. of patients	14 (22.6)	4 (16.7)	18 (21)	7 (12.7)	.17	.62	.09
30-day mortality	3 (4.8)	1 (4.2)	4 (4.7)	2 (3.6)	.73	.9	.76

Continues

	Surgical n = 214 (60% of total)						
	Retrospective control (1) n=145 (67.8%)	**Control 2: Leuven n = 24 (11.2%)**	**Control 3: Total (1+2) n= 169 (79%)**	**Intervention (3): Prehabilitation n= 45 (21%)**	**P-value 1 vs 3**	**P-value 2 vs 3**	**P-value 3 vs 3**
Incidence of delirium	16 (11)	3 (12.5)	19 (11)	1 (2.2)	.07	.08	.065
Minor complication	32 (22.1)	11 (46)	43 (25)	7 (15.6)	.35	.006	.16
Major complication	31 (21.4)	6 (25)	37 (22)	10 (22.2)	.9	.79	.96
Major amputation	5 (3.4)	0	5 (3)	2 (5.6)	.76	.29	.62
Surgical complication	41 (28)	0	41 (24)	5 (11.6)	.09	.04	.21
Cardiac complication	11 (7.6)	4 (16)	15 (8.9)	1 (2.3)	.32	.03	.13
Pulmonal complication	6 (4.1)	2 (8)	8 (4.7)	0	.18	.05	.14
Cerebrovascular complication	1 (0.7)	0	1 (0.6)	1 (2.3)	.36	.46	.32
Length prehabilitation - d, med (IQR)	n.a.	n.a.	n.a.	20 (13.5-39.5)	n.a.	n.a.	n.a.
Length hospital stay - d, med (IQR)	7 (5-10)	6 (4-9)	6.5 (4-9)	5 (3-7)	<.001	.004	<.001
Readmission	10 (6.9)	3 (12.5)	13 (7.7)	4 (8.9)	.65	.64	.79
Re-operation nr. of patients	32 (22)	5 (21)	37 (22)	8 (17.8)	.54	.76	.55
30-day mortality	3 (2.1)	0	3 (1.8)	0	.33	1	.37

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Supplemental Table III

Regression analysis per subgroup (endovascular and surgical) and the total control cohort

	Retrospective control vs Prehabilitation		Prospective control vs Prehabilitation		Total control group vs Prehabilitation	
	OR (95% CI)	**P-value**	**OR (95% CI)**	**P-value**	**OR (95% CI)**	**P-value**
Total group						
Unadjusted OR	.2 (.05-.89)	.035	.23 (.04-1.2)	.1	.21 (.05-.89)	.035
Adjusted OR	.32 (.07-1.5)	.15	.32 (.05-2.1)	.23	.28 (.06-1.3)	.097
Subgroup: Endovascular revascularisation						
Unadjusted OR	.36 (.036-3.5)	.38	.42 (.03-6.9)	.54	.37 (.04-3.4)	.38
Adjusted OR	.36 (.03-4)	.41	.66 (.02-23)	.82	.46 (.05-4.8)	.52
Subgroup: Surgical revascularisation						
Unadjusted OR	.18 (.02-1.4)	.11	.16 (.02-1.6)	.12	.18 (.23-1.4)	.09
Adjusted OR	.25 (.-03-2.1)	.2	.22 (.02-2.5)	.22	.24 (.03-1.9)	.18

Supplemental Table III: Unadjusted and adjusted odds ratios. Prehabilitationgroup versus controlgroup

Primary outcome adjusted for: age, physical impairment (KATZ =>1), history of delirium, pre-operative anemia, and type of revascularisation (endo/surg) in the total group

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Figure 1. CONSORT flow diagram

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