

# Can perioperative vitamin C supplementation reduce the risk of arthrofibrosis after total knee arthroplasty?

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<b>Registration date</b> 08/02/2018	<b>Overall study status</b> Completed	<input type="checkbox"/> Protocol
<b>Last Edited</b> 02/07/2018	<b>Condition category</b> Musculoskeletal Diseases	<input type="checkbox"/> Statistical analysis plan
		<input checked="" type="checkbox"/> Results
		<input type="checkbox"/> Individual participant data

## Plain English summary of protocol

### Background and study aims

Arthrofibrosis is one of the most common complications after knee replacement surgery and occurs in up to 16% of patients. It is defined as painful limitation in knee range of motion. An extended scar tissue layer caused by chronic inflammation can be observed within the joint. An accumulation of free radicals may lead to this excessive tissue formation. Vitamin C is a reducing agent that eliminates free radicals. The aim of this study is to find out whether vitamin C supplementation can prevent arthrofibrosis after knee replacement.

### Who can participate?

Patients aged 18 and over with advanced osteoarthritis of the knee undergoing knee replacement surgery

### What does the study involve?

Participants are randomly allocated to take either vitamin C or a placebo (dummy) supplement every day starting on the day before their operation and continuing for a total of 50 days. Knee joint range of motion is measured before the operation and at 8 weeks and 12 months after the operation.

### What are the possible benefits and risks of participating?

If the study shows that vitamin C improves range of motion, it could provide valuable information about a possible new treatment. Prolonged courses of painful rehabilitation or even further surgery could be avoided. By reducing the need for further treatment and hospital stay healthcare costs could be lowered. Besides the risks of vitamin C overdose which are well documented and described in the product information, no further risks are expected.

### Where is the study run from?

Cantonal Hospital St Gallen (Switzerland)

### When is the study starting and how long is it expected to run for?

February 2010 to July 2016

Who is funding the study?  
Cantonal Hospital St Gallen (Switzerland)

Who is the main contact?  
Dr Henrik Behrend

## Contact information

**Type(s)**  
Public

**Contact name**  
Dr Henrik Behrend

**Contact details**  
Cantonal Hospital St Gallen  
Rorschacherstreet 95  
St Gallen  
Switzerland  
9007

## Additional identifiers

**EudraCT/CTIS number**

**IRAS number**

**ClinicalTrials.gov number**

**Secondary identifying numbers**  
CTU 10/050

## Study information

**Scientific Title**  
Perioperative Vitamin C supplementation following total knee arthroplasty: a double-blind placebo-controlled randomized study

**Study objectives**  
Arthrofibrosis (AF) is a debilitating complication after total knee arthroplasty (TKA) with a reported incidence of up to 16%. It is considered a clinical diagnosis defined as limited range of motion (ROM) in flexion and/or extension as a result of post-operative soft-tissue fibrosis.

The primary objective of the study is to investigate whether the administration of vitamin C improves the range of motion (ROM) in patients undergoing TKA. It is hypothesized that vitamin C improves the joint mobility, avoids intra articular tissue damages by eliminating free radicals and reduces thereby the risk for arthrofibrosis in patients undergoing TKA.

**Ethics approval required**  
Old ethics approval format

**Ethics approval(s)**

Ethics Committee of the Cantonal Hospital St Gallen, 27/10/2010, ref: EKSG 10/098

**Study design**

Single-center randomized double-blind placebo-controlled two-arm Phase IV study

**Primary study design**

Interventional

**Secondary study design**

Randomised controlled trial

**Study setting(s)**

Hospital

**Study type(s)**

Prevention

**Participant information sheet**

Not available in web format, please use contact details to request a participant information sheet

**Health condition(s) or problem(s) studied**

Arthrofibrosis

**Interventions**

Registered patients were randomized to either VC at a daily dose of 1000 mg (two 500 mg tablets) or to matching placebo starting on the preoperative day and continuing for a total of 50 days. Randomization of patients was performed by the Clinical Trials Unit (CTU) using R statistical software version 2.9.2. VC and matching placebo was kindly provided by Burgerstein /Antistress AG (Rapperswil-Jona, Switzerland). Treatment compliance was assessed using a drug diary at 8 weeks ( $\pm$  2 weeks) postoperatively.

**Intervention Type**

Supplement

**Primary outcome measure**

Knee joint ROM measured with a goniometer by a trained study nurse who was blinded to the research history, assessed preoperatively, at 8 weeks and 12 months postoperatively

**Secondary outcome measures**

1. Incidence of arthrofibrosis (AF), defined as extension deficit  $>5^\circ$  and/or  $\leq 100^\circ$  flexion of the knee, measured at 8 weeks and 12 months postoperatively
2. Vitamin C plasma concentrations measured in  $\mu\text{mol/l}$  before surgery and 4 and 7 days after surgery
3. The Western Ontario and McMaster Universities Arthritis Index (WOMAC) measured at 8 weeks and 12 months postoperatively
4. The Forgotten Joint Score-12 (FJS-12) measured at 8 weeks and 12 months postoperatively

**Overall study start date**

10/02/2010

**Completion date**

12/07/2016

## Eligibility

**Key inclusion criteria**

1. Patients with primary osteoarthritis of knee joint undergoing TKA presenting with grade 3 or 4 osteoarthritis (Kellgren-Lawrence score)
2. Age  $\geq$ 18 years
3. Written informed consent, including written consent to participate in the local prosthesis registry of the hospital

**Participant type(s)**

Patient

**Age group**

Adult

**Lower age limit**

18 Years

**Sex**

Both

**Target number of participants**

With a two-sided significance level of 5%, and a total of 240 patients (including a dropout rate of 20%), the study had a power of 80% to detect a mean difference of 5 degrees in ROM at 8 weeks and 12 months postoperatively.

**Key exclusion criteria**

1. History of nephrolithiasis, hemochromatosis, uremia, beta-thalassemia
2. Known intolerance to vitamin C or any of the excipients
3. Dietary vitamin C intake <3 days before intervention
4. CRP values >10mg/l

**Date of first enrolment**

01/07/2011

**Date of final enrolment**

01/04/2015

## Locations

**Countries of recruitment**

Switzerland

**Study participating centre**  
**Kantonsspital St Gallen**  
Rorschacherstreet 95  
St Gallen  
Switzerland  
9007

## **Sponsor information**

### **Organisation**

Cantonal Hospital St Gallen

### **Sponsor details**

Rorschacherstreet 95  
St Gallen  
Switzerland  
9007

### **Sponsor type**

Hospital/treatment centre

### **ROR**

<https://ror.org/00gpmb873>

## **Funder(s)**

### **Funder type**

Hospital/treatment centre

### **Funder Name**

Cantonal Hospital St Gallen

## **Results and Publications**

### **Publication and dissemination plan**

The trialists are planning to publish a manuscript with the title: "Perioperative Vitamin C Supplementation following Total Knee Arthroplasty: A double-blind placebo-controlled randomized study" in an orthopaedic Journal in March 2018.

### **Intention to publish date**

10/03/2018

## Individual participant data (IPD) sharing plan

The datasets generated during and/or analysed during the current study are not expected to be made available as consent was not obtained from the participants.

## IPD sharing plan summary

Not expected to be made available

## Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">Results article</a>	results	01/04/2019		Yes	No