Title of the study: Third generation cryotherapy reduces time to surgery and local complication in patients with ankle fractures: a prospective randomized controlled trial.

Type of the Paper: Randomized Controlled Trial.

NCT number: not available

Article ID: cryotherapy012021.n01

Date of the document: 24/04/2024

This is a RCT about the preoperatory use of third generation cryotherapy in patients hospitalized for ankle fracture. The aim of this study is to assess the effects of third generation cryotherapy on time to surgery, pain, opioids intake, and local skin complications. Although the use of cryotherapy is traditionally believed to reduce pain, swelling, local skin complications and the need of analgesia, the results on ankle surgery are not well reported and still contradictory. The working hypothesis is that third generation cryotherapy is a safe, reduces time to surgery and is useful in the surgical management of ankle fractures

We confirm that each author of this article meets the journal's criteria for authorship. We confirm that the manuscript has not been submitted or is not simultaneously being submitted elsewhere, and that no portion of the data has been or will be published in proceedings or transactions of meetings or symposium volumes.

Fiximed Italia, Rome, Italy, funded the APC, but the company had no role in the design of the study, in the collection, analyses, or interpretation of data, in the writing of the manuscript, and or in the decision to publish the results.

The authors declare no external funding or other benefits from commercial sources for the work reported on in the manuscript, nor any other financial interests which could create a potential conflict of interest.

Thank you

Kind regards

Third generation cryotherapy reduces time to surgery and local complication in patients with ankle fractures: a prospective randomized controlled trial.

Study protocol and statistical analysis

We analyzed the prospectively collected data of 169 patients with ankle fracture, treated with open reduction and internal fixation (ORIF). Patients were randomized in two groups at the time of the diagnosis in the emergency department. The treatment group (T: 89 patients) were treated with a third-generation cryotherapy device (Z- One®, Zamar) which was applied daily for 2 hours two times a day up to the day of surgery. The leg was immobilized in a walking boot which was removed when the cryotherapy device was applied. The control group (C: 80 patients) did not use cryotherapy before surgery, the leg was immobilized into a half cats and elevation of the injured limb was indicated. Patients were collected in two different hospitals (Azienda Ospedaliera San Camillo Forlanini -Roma and Ospedale San Paolo – Civitavecchia) between 2021 and 2023. All patients had signed a written consent, and the study was approved by the local ethic committee.

Inclusion and exclusion criteria

Patients admitted to the emergency department with an ankle fracture were included in the current study. Exclusion criteria were open fractures, fracture-dislocations which required external fixation, patients with one or more associated fractures, and patients with a diagnose of major trauma. Patients who were not able to complain with the pre and post-surgical indications were also excluded.

Patients' assessment

A detailed physical examination was conducted in all patients, who were examined in the emergency department by local orthopedic surgeons. All patients underwent standard radiographs to diagnose the fracture, and computed tomography for the preoperatory planning if indicated. After the diagnosis was made and surgical treatment was indicated, the patient was hospitalized in the department of orthopedic and trauma surgery. Patients of group T were immobilized in a walking boot to allow the use of the cryotherapy device. Patients belong to group C were immobilized in a half cast. Pain was evaluated according to the Visual Analogue Scale (VAS) and the analgesic drug demand (including morphine or acetaminophen). The Body Mass Index (BMI), number of cigarettes smoked, presence of preoperative skin complications were assessed on a daily basis.

Surgical technique

Under loco-regional anesthesia, the patient was positioned supine with a little rise under the buttock, or in prone decubitus if posterolateral surgical approach was indicated to reduce the posterior malleolus. A tourniquet was applied at the tight, and the lower limb was prepared and draped in the usual sterile fashion. Lateral malleolus was approached first, reduced and fixed with a plate and screws. Then, surgical technique varied depending on the pattern of fracture, distal tibiofibular syndesmosis injury or associated soft tissue injury, as deltoid ligament rupture.

All patients received intraoperative antibiotic treatment, intravenous controlled analgesia for 24–48h after surgery, and standard thromboembolic prophylaxis with low molecular weight heparin (LMWE) for up to complete weight bearing. Passive motion of the ankle was encouraged from the first post-operative day.

Statistical analysis

A power analysis was performed to evaluate the sample size necessary to guarantee a power of at least 0.9 with a significance level of 0.05 using preliminary data on time to surgery.

Univariate descriptive analysis of the variables under study was carried out by calculating the centrality and variability indices for the quantitative variables and frequency tables for the variables. The homogeneity of the control group and the treatment group for the variables sex, age, type of fracture, diabetes, hypercholesterolemia, venous insufficiency, and BMI class were checked. Depending on the nature of the variables, a t-test or a chi-square test was used.

Any significant differences between the treatment and control groups were assessed using independent samples t-tests for quantitative variables and chi-square tests for qualitative variables. Where the sample size is not sufficient, the non-parametric Mann-Whitney test for independent samples was used.

An alpha significance level of 0.05 was used in all analyses mentioned. For the statistical analysis of data, IBM SPSS Statistics software version 28 was used.

CONSORT 2010 Flow Diagram

Enrollment

Assessed for eligibility (n=351)

Excluded (n=182)
- ♦ Not meeting inclusion criteria (n=161)
- ♦ Declined to participate (n=0)
- ♦ Other reasons (n= 21)

Randomized (n=169)

Allocation

Allocated to third generation cryotherapy (n=89)
- ♦ Received allocated intervention (n=89)
- ♦ Did not receive allocated intervention (give reasons) (n=0)

Allocated to control group (n=80)
- ♦ Received allocated immobilization and elevation (n=80)
- ♦ Did not receive allocated intervention (give reasons) (n=0)

Follow-Up

Lost to follow-up (give reasons) (n=0)
Discontinued intervention (give reasons) (n=0)

Lost to follow-up (give reasons) (n=0)
Discontinued intervention (give reasons) (n=0)

Analysis

Analysed (n=89)
- ♦ Excluded from analysis (give reasons) (n=0)

Analysed (n=80)
- ♦ Excluded from analysis (give reasons) (n=0)