Nationwide survey on the use of local antibiotics during anterior cruciate ligament reconstruction in Norway

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Abstract
Objective: The use of local antibiotics in surgical reconstruction of the anterior cruciate ligament (ACLR) in Europe and Scandinavia is increasing.

We wanted to survey the scope of this practice in Norway. In cooperation with the Norwegian cruciate ligament registry we contacted all institutions in Norway performing ACLR to find out.

Results: The results showed that the practice of local antibiotics in ACLR is not widely used in Norway.

Introduction
Antibiotic resistance is an increasing problem in Norway, and worldwide. The trend is unambiguous. Antibiotic resistance causes approximately 33 000 deaths annually in Europe [1].

In orthopedic surgery, antibiotics are important in two crucial settings. The first is the use of antibiotic prophylaxis to prevent a postoperative infection. The second is when an infection occurs; antibiotics are vital for curing the infection and preserving the implant.

Reconstruction of the anterior cruciate ligament (ACLR) of the knee with an autograft is one of the most common procedures in orthopedic surgery. Established infection prevention procedures in ACLR involve the use of preoperative intravenous antibiotics [2]. This routine significantly reduces postoperative infection rates in knee surgery and is recommended by the health authorities in Norway [3]. The Norwegian Cruciate ligament registry (NCLR) monitors primary ACLR as well as the infections following ACLR. The number of primary ACLR operations and the number of infections are based on a scheme sent by the surgeons both for the primary surgery and when patients with a postoperative infection following ACLR need reoperation. A new routine of applying local antibiotics, such as vancomycin, to prevent postoperative infection has been introduced in Scandinavia, including in Norway.

We wanted to determine the frequency of this procedure in Norway as it is not possible to document this on the scheme sent in connection with the primary surgery.

Main Text
Orthopedic surgeons need to be conscious of their use of antibiotics. The use of prophylactic
antibiotics to prevent surgical site infections (SSI) should be evidence-based. Reconstruction of the anterior cruciate ligament (ACLR) of the knee with an autograft is a common orthopedic procedure. In Norway, approximately 1800 ACLRs are performed every year. The incidence of postoperative infections following ACLR is reported to be low (approximately 0.3%) in ACLR [4]. There is a risk of underreporting from the institutions regarding this complication due to the reporting routine, but the true incidence of infection after ACLR is still supposed to be low.

A postoperative infection may have severe consequences for the patient. The effect of intravenous antibiotics before surgery on the prevention of SSI is well documented in hip arthroplasty [5]. This routine is also a national recommendation for ACLR. Despite this well-documented routine, an increasing number of surgeons have adopted a new trend, in addition to intravenous antibiotics, of applying local antibiotics to the graft perioperatively. This routine originated in Australia in 2012 [6] and has spread worldwide, including to Norway. The rationale for this routine is that the graft has been contaminated by its contact with the skin when it was harvested. This is especially believed to be true for the harvesting of hamstring grafts [7].

According to this routine, the graft is soaked in vancomycin for 15 minutes before insertion. However, the evidence for the risk-reducing effect of this routine on the incidence of SSI after ACLR has recently been questioned.

Due to this uncertainty, we performed a mail survey in cooperation with the Norwegian cruciate ligament registry with all institutions in Norway performing ACLRs. The survey contained questions on the use of local antibiotics and the type and dose of antibiotics used.

In total, 73% (42/57) of the institutions performing ACLR procedures answered. Two institutions used vancomycin, and one institution used gentamycin as a means of local prophylaxis in ACLR with autografts. We conclude that the use of local antibiotics in ACLR is rare in Norway. The limitations of this pilot study include the use of a mailed survey and the suspicion of underreporting of the incidence of SSI after ACLR.

The increasing resistance to antibiotics is a worldwide problem contributing to a rising concern regarding the increased inability to treat infectious diseases with antibiotics.
Norwegian health authorities have demanded a 30% reduction in the use of broad-spectrum antibiotics by 2025. Despite the use of systemic antibiotics perioperatively, no single factors have been shown to be of significant importance in reducing the risk of SSI. The multifactor origin of this complication supports the use of well-established infection prevention and control routines to avoid SSI rather than increasing the antibiotic load.

Vancomycin is effective when it reaches a minimum inhibitory concentration (MIC) for 12 hours when delivered intravenously [8]. Fifteen minutes of a topical application to the graft is theoretically insufficient to achieve any therapeutic effect. Hence, the vancomycin is most likely washed off the graft as soon as it is implanted. Several studies have shown the lack of an effect of local antibiotics. Two systematic reviews on the topic have been published in 2019. A German study concluded that the use of local vancomycin is based on evidence of a preventive effect [9]. This systematic review included level three and four studies as well as abstracts and is therefore not reliable. The second systematic review was more skeptical of the level of evidence regarding the use of vancomycin and concluded that more research is needed [10].

The higher infection rates in surgeries involving hamstring grafts are concerning, but we advise the use of bone-to-bone patellar grafts instead of hamstring grafts soaked in vancomycin.

A form is filled out by the surgeon in connection with the primary ACLR and sent to the Norwegian National Cruciate Ligament Registry. On this form, it is not possible to register the use of local antibiotics.

To monitor whether the use of local antibiotics as a means of prophylaxis is effective, it should be made possible to mark this on the form. In addition, measures must be taken to improve the registrations of postoperative infections.

It would be possible to administer a questionnaire to the patients in conjunction with the patient reported outcomes (PROMS) after two years if they underwent surgery or were treated with antibiotics after the primary surgery.

This is probably the only realistic method to determine whether the local application of vancomycin is effective as a means of prophylaxis in ACLR.
Limitations
A mailed survey might not reflect the true use of local antibiotics. Underreporting of the incidence of infection after ACLR is likely to exist in the registries of knee ligament surgeries.

Abbreviations
ACLR: anterior cruciate ligament reconstruction
NCLR: Norwegian cruciate ligament registry
PROMS: patient reported outcome
SSI: Surgical site infection

Declarations

Ethics approval and consent to participate
The study is approved by the regional ethical committee (2017/372). The trial will be registered on http://clinicaltrials.gov and conducted according to Good Clinical Practice (GCP) guidelines and principles of the Declaration of Helsinki. The Norwegian Cruciate ligament registry was given a concession from the Norwegian Data Protection in 2004 to process health information. The concession is valid until 2019.

An application for ‘Registration of a research project’ was sent to the research group at Akershus University Hospital and is approved.

We confirm that the manuscript has been read and approved by all named authors and that there are no other persons who satisfied the criteria for authorship but are not listed. The consent was obtained written by e-mail correspondence.

We further confirm that that the order of authors listed in the manuscript has been approved by all of us.

Availability of data and material
Availability of data and materials; the annual report from the Norwegian knee ligament registry is available on their home page; http://nrlweb.ihelse.net

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Consent for publication
Not applicable

**Competing interests**

Competing interest; none of the authors have competing interests regarding the content of the manuscript. We wish to confirm that there are no known conflicts of interest associated with this publication and there has been no significant financial support for this work that could have influenced its outcome.

**Author's contribution**

Authors contribution; MS drafted the manuscript and performed the survey. I.S reviewed the manuscript. E.S reviewed the manuscript. S.H.L reviewed the manuscript. A.Å has reviewed the manuscript. All authors approved the final manuscript.

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