Journal of Diabetes and Obesity

OMMEGA Publishers
Answering Intelligence

ISSN:2376-0494
OPEN ACCESS

Research Article

DOI: 10.15436/2376-0949.21.3311

Surgical Removal of Mandibular Third Molars with or without the Use of Cryotherapy; a Single-Blinded Randomized Controlled Trial

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Abstract

Purpose: The aim was to test the null-hypothesis of no difference in pain, trismus, swelling and quality of life following surgical removal of mandibular third molar (SRM3) with 30 minutes of immediate cryotherapy compared with no cryotherapy using clinical assessment, visual analogue scale (VAS), questionnaires and three-dimensional imaging.

Methods: Thirty-one patients (14 men and 17 female) were randomly allocated to cryotherapy (test) or no cryotherapy (control) in a split-mouth study design. Preoperative measurements included VAS score of pain, maximum mouth opening, delineation of facial morphology using three-dimensional imaging and oral health impact profile-14. Pain, trismus, swelling and quality of life were assessed after one day, three days, seven days and one month, respectively. Swelling was analysed using superimposition of three-dimensional facial surfaces andtemplate matching technique. Descriptive and generalised estimating equation analyses were made. Level of significance was 0.05.

Results: Thirty minutes of immediate cryotherapy following SRM3 revealed no statistically significant differences in pain, trismus, swelling or quality of life compared with no cryotherapy. Females disclosed significant less pain after one month compared with males ($P < 0.05$). Trismus was significantly associated with increased length of surgery ($P < 0.05$).

Conclusion: The therapeutic efficiency of cryotherapy following SRM3 seems to be negligible. However, further randomised controlled trials assessing longer use of cryotherapy or intermittent application are needed before definite conclusions can be provided about the beneficial use of cryotherapy following SRM3.

Keywords: Cryotherapy; Dentistry; Mandible; Pain; Third molar; Trismus

Introduction

Pain, restricted mouth opening and facial swelling are common sequelae following surgical removal of mandibular third molars (SRM3)[1]. Various prophylactic measures have been proposed to prevent or diminish postoperative morbidity including analgesics, antibiotics, corticosteroids, cryotherapy and compression[2-5]. Intermittent or continuous cryotherapy with ice packs, gel packs or Hilotherm face mask reduces the skin temperature causing reduced tissue metabolism, vasoconstriction and lessens the excitability of peripheral nerve fibers, which is assumed to diminish the inflammatory response following SRM3[6-9]. However, the therapeutic efficacy of cryotherapy following SRM3 has previously been assessed in systematic review and meta-analyses with conflicting results[10,11].

Pain is considered the worst sequelae following SRM3 and usually most pronounced the first day[12,13]. Visual analogue scale (VAS), self-administrated question-

Received date: March 24, 2021
Accepted date: April 22, 2021
Published date: April 26, 2021

Citation: Larsen, M.K., et al. Surgical Removal of Mandibular Third Molars with or without the Use of Cryotherapy; A Single-Blinded Randomized Controlled Trial. (2021) J Dent Oral Care 7(1): 1-9.

naire, numeric or verbal rating scaleand consumption of analgesics are the most commonly used methods of pain assessment revealing improved therapeutic efficacy of intermittent and continuous cryotherapy on pain, as documented in recent published systematic reviews and meta-analyses[10,14,15].

Restricted mouth opening and facial swelling are generally considered secondary outcomes[13]. Linear measurements of interincisal maximal mouth opening with a ruler or caliper are often used for assessment of restricted mouth opening demonstratinglessened trismus with intermittent cryotherapy following SRM3[16]. Two-dimensional (2D) measurements between reference points or anatomic landmarks are frequently used for assessment of facial swelling disclosingdiminished swelling with prolonged intermittent cryotherapy[16,17]. However, facial swelling is characterised by a localised volumetric enlargement of the cheek due to accumulation of fluid. Two-dimensional measurements of a three-dimensional (3D) volumetric enlargement is therefore associated with vagueness due to in accurate facial depth and shape measurements[18,19]. Volumetric assessment using 3D optical scanning technique following SRM3 have demonstrated significantly diminish facial swelling and VAS score of pain with 45 minutes of immediate Hilotherm cryotherapy compared with conventional cooling compresses[20]. However, evaluation of facial swelling with the use of 3D imaging technique following SRM3 with or without cryotherapy has never been conducted. Thus, the objective of the present study was to test the null-hypothesis of no difference in pain, restricted mouth opening, facial swelling and quality of life following SRM3 with 30 minutes of immediate cryotherapy compared with no cryotherapy using clinical assessment, VAS score of pain, self-administrated questionnaires and 3D imaging.

Material and Methods

Study design

Arandomised single-blinded controlled trial using a split-mouth study design was conducted at the Departments of Oral and Maxillofacial Surgery, Copenhagen University Hospital, Rigs hospital, and Aalborg University Hospital, Denmark. The study was performed in accordance with the Declaration of Helsinki II and the Consolidated Standards of Reporting Trials (CONSORT) statement[21] and approved by Research Ethics Committee and the Danish Data Protection Agency (Approval no.: N-20170016).

Panoramic radiograph of patients scheduled for SRM3 prior to orthognathic surgery were screened. Candidates with bilateral and comparable impacted third molars according to Pell and Gregory classification were invited to participate and received written information of the study[22]. Those patients who met the inclusion criteria received additional verbal information about the study protocol and signed an informed consent form before initiating the study. Included patients were informed that it was voluntary and free of charge to participate and they could at any given time withdraw from the study.

Sample size calculation and study population

Sample size calculation was conducted using Clincalc.com (http://clincalc.com/stats/samplesize.aspx, accessed 9th March 2017). Based on sample size calculation and assuming a 10% dropout rate, it was planned to enrol 31 patients for each treatment group, in order to detect a 20 mm difference VAS-score of pain on the first postoperative day between the two treatment modalities, with a power of 0.8 and a significance level equal to 0.05.

Position of the mandibular third molarson panoramic radiographs were classified using Pell & Gregory system and Winter's classification[22].

Inclusion criteria were:

- Bilateral symmetrical impacted third molars
- Indication for removal of third molars
- Age between 18 and 40 years

Exclusion criteria were:

- Acute infection in the oral cavity at the time of surgery
- Previous maxillofacial trauma
- Craniofacial clefts or syndromes
- Systemic bone disease (i.e. arthritis) or diabetes mellitus
- Psychological disease
- Pregnancy and breastfeeding
- Failure to attend follow-up

Randomisation and blinding

A computer-aided block randomisation was used to fabricate a randomisation sheet with a serial number from 1 to 31 allocating the mandibular third molar to 30 minutes of immediate postoperative cryotherapy (test side) or no cryotherapy (control side) (http://www.randomization.com, Randomization.com, date: 26th December 2018). Sealed envelopes were used to store the numbers. Each patient opened an envelope with a number, which was passed to the assistant nurse, who combined the number with the randomisation sheet to allocate the third molar to test or control group. The randomisation sheet was kept by the assistant nurse until the study was unblinded.

The surgeon and assessor were blinded in relation to test or control group, since the assistant nurse placed the cold gel pack on the patient´s cheek after the surgeon had left the room and was also responsible for removing the gel pack after 30 minutes.

Surgical procedure

Included patients underwent SRM3 in local anaesthesia by the same trained surgeon (MKL) using a standard technique. Each patient had only one third molar removed at each time. All patients received prophylactic analgesic including 400 mg ibuprofen (Ipren®, Takeda Pharma, Denmark) and 1,000 mg paracetamol (Pinex®, Actavis A/S, Denmark), one hour prior to surgery.

The inferior alveolar nerve and the lingual nerve were anesthetised with 20 mg/mL mepivacaine hydrochloride and 5µg/mL adrenaline (Carbocain-Adrenalin®, AstraZeneca, Denmark). An incision from the anterior border of the ascending mandibular ramus to the distal part of the lower first molar was performed. The mucosal flap was elevated, and bone removal was performed with a round burr under irrigation with 0.9% saline solution. If necessary, the third molar was sectioned witha fissure bur before the tooth was elevated out. The extraction socket and surrounding bone was irrigated with 0.9% saline

solution, and the surgical site was sutured (4-0 VicrylRapide®, Ethicon, Johnson and Johnson, Germany).

A freezable cold gel pack (Soft Stretch Jaw Wrap with Cold Packs, Cool Jaw, USA) was applied on the cheek immediately after SRM3 for 30 minutes, if the third molar was allocated for cryotherapy.

Regardless of the randomisation groups, all patients received standard postoperative instructions and pain medication including mouth rinse with 0.12% chlorhexidine three times a day (KlorhexidinMundskyl 0,12%®, Faaborg Pharma, Denmark), 400 mg of ibuprofen three times a day (Ipren®, Takeda Pharma, Denmark) and 1.000mg paracetamol four times a day (Pinex®, Actavis A/S, Denmark).

Data collection

Data was collected by the same assessor (MKL). Assessments were performed preoperatively (T0), one day (T1), three days (T2), seven days (T3), and one month (T4) following SRM3, respectively.

Patient perception of pain was evaluated by a 100-mm VAS-score obtained preoperatively (T0), one day (T1), three days (T2), seven days (T3) and one month (T4) following SRM3, respectively. Instructions for using VAS was explained in details and patients had to mark on the line the point that they felt represented their pain. Zero indicated no pain, and 100 indicated worst imaginable pain. The VAS score was measured to the nearest millimetres with a ruler.

Mouth opening was measured as the maximum distance between the upper and lower incisal edges in millimetres with a ruler preoperatively (T0), three days (T2), seven days (T3) and one month (T4) following SRM3, respectively.

The facial morphology was delineated using 3D optical scan (David SLS-3 3D scanner, DAVID Vision Systems, Germany) obtained preoperatively (T0), three days (T2) and seven days (T3) following SRM3, respectively. Patients were positioned one meter from the 3D optical scanner in an upright chair with closed mouth, relaxed facial expression and adequate head support. The position of the 3D optical scanner and the chair was secured in a uniform position valid for all scans. Straight laser lighters were used to standardise the location of the head in a uniform and reproducible position. The laser line followed the frankfurter horizontal plane. DAVID-4-PRO software (DAVID Vision Systems, Germany) was used to capture the 3D optical scans and convert the scans to STL-files, which were transferred to Landmarker (Software, Landmarker 2.0.6, Denmark) [23]. The volumetric difference in the facial morphology between T0 was compared with T2 and T3 using Landmarker and template matching technique[24-26]. A recent contribution applying a similar philosophy to calculate facial volume has recently been applied[27].

The volume V_s of facial swelling was defined as the volume (in cm^3) of the 3D space located between two face surfaces within a swelling region s. The region of facial swelling was defined as a user-defined region of interest (ROI) in the face where V_s was to be calculated. The method was devised in such a way that V_s could be monitored in the same swelling region over time and in every subject. A swelling region on an artificially created 3D template face was drawn and the template was subsequently deformed to the shape of each scan, thereby transferring the swelling region to each scan (Figure 1). This process assured that a portion of a subject scan corresponding to the swelling region would have detailed point correspondence with the swelling region of all other subject scans.

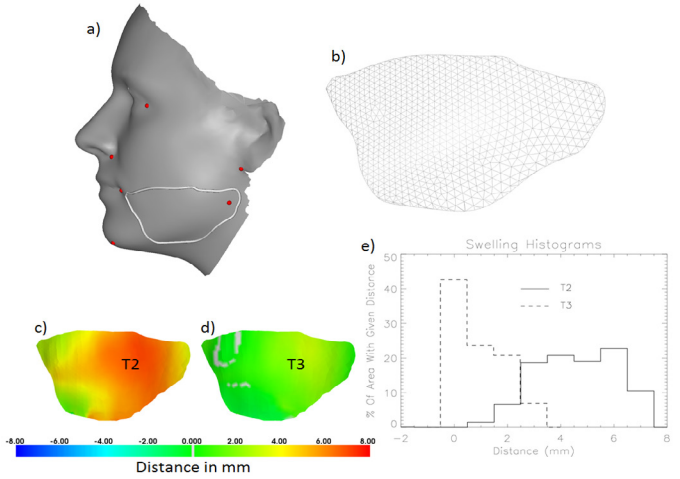

Figure 1: Illustration of the measurement process of facial swelling.a) The template face scan with the swelling region (white outline) and six alignment landmarks (red spheres). b) Swelling region shown as wire-frame. c) Swelling region in an example subject, color coded according to distance in mm between surface at T0 and T2. d) Swelling region in the same example subject, color coded according to distance in mm between surface at T0 and T3. e) Histograms of the distances displayed in figures c) and d). Solid curve: T2, Dashed curve: T3.

An outline of the swelling region was drawn on the template face surface (Figure.1a-b), and six anatomical landmarks (Figure.1a) visible on both the template face surface and the T_0 surface were selected and pointed out by the operator on both the template and the T_0 surface. A sub-region $T_{0,sub}$ of the T_0 surface, which was not expected to be affected by the treatment (a region where only minimal change would occur over time) was selected at the forehead and bridge of nose. The Iterated Closest Point algorithm (ICP)[28] was used to spatially align all subsequent scans in the same subject, T_i, to $T_{0,sub}$. A similarity transform was applied using the six landmarks obtained to bring the swelling region $s_{template}$ in the template to the general location of the swelling regions s_i in the T_0 scan and all subsequent scans (T_i). The $s_{template}$ was further deformed to each of the s_i regions by moving each point in $s_{template}$ to the closest surface location on s_i. This last step established detailed point correspondence between all the s_i scans. For each triangle in s_i, the distance to the corresponding triangle in s_0 was calculated. A sign was added to the distance depending on whether s_0 was inside (positive sign, swelling) or outside (negative sign, shrinkage) of s_0. The result was a number of m distance maps (an example is shown in Figure.1c-e). For each triangle in s_0, a polyhedron (pentahedron, skew triangular prism) with five faces was created by connecting each of its three vertices with the corresponding vertices in s_i, forming a small volume element, and its volume v was calculated (Figure.1c-d). The volume of the swelling region was the sum of all the volume elements: V_{si}=sum(v_j) where j counted the triangles in s. Thereby, the volumetric changes in facial morphology were measured.

The accuracy and precision of the 3D scanner was assessed before the described study was initiated in pilot studies. A total of 40 scans of a mannequin head were compared to a

reference scan of the same mannequin head, which was based on averaging 30 scans of a mannequin head using a 3dMDhead.u (3dMD.com, Atlanta, GA, USA) full head scanner. The distance between the reference and each of the 40 scans was calculated at each surface point after each of the 40 scans had been spatially aligned with the reference using the ICP algorithm[28]. Histograms of the distances were created and corresponding mean and standard deviation of the distances were reported as a measure of accuracy and precision of the David SLS-3 3D scanner. Moreover, 3D scans of eight artificial swellings were compared to reference scans of the same swellings. In order to validate the method of swelling volume calculation, artificial swellings were created by applying silicone material (Coltène President Putty, Coltène Whaledent AG, Switzerland) to the mannequin head. The silicone material was applied in realistic swelling shapes on the mannequin head and scanned in the David SLS-3 3D scanner as well as in a cone beam computed tomography scanner (Planmeca ProMax 3D Max, Planmeca OY, Finland) with voxel resolution 0.4, 0.4, 0.4 mm. The silicone material had a different computed tomography value than the mannequin head and could thus be segmented by intensity thresholding. Eight different artificial swellings were created and scanned in both devices and volumes were calculated and compared. In order to determine the threshold parameter for the cone beam computed tomography segmentation, an object of known dimensions (a Lego Duplo brick, The Lego Group, Denmark) was covered in silicone material and scanned in the cone beam computed tomography scanner. The silicone material was segmented in the resulting images using different intensity thresholds, each time measuring the inside width of the silicone shape corresponding exactly to the width of the Duplo brick. The optimal threshold was determined by linear regression in a plot of threshold versus measured width.

Quality of life was evaluated by oral health impact profile-14 (OHIP-14) questionnaire. OHIP-14 is organised into seven conceptual dimensions including functional limitation, physical discomfort, psychological discomfort, physical disability, psychological disability, social disability and handicap. Two items are used to measure each dimension and consequently the questionnaire consists of 14 items. Response format of OHIP-14 was as follows: Very often = 4; Fairly often or many times = 3; Occasionally = 2; Hardly ever or nearly never = 1; Never/I do not know = 0. The OHIP-14 scale ranged from 0 to 56 and dimension score ranged from 0 to 8. The values of the 14 items and each dimension were summed to calculate the OHIP-14 severity score with higher scores indicating poorer quality of life. Patients were carefully instructed in the OHIP-14 questionnaire and completed the questionnaires by themselves. The OHIP-14 questionnaire was filled out preoperatively (T0) and compared with OHIP-14 questionnaire after seven days (T3) and one month (T4) following SRM3.

Intra- and postoperative complications including bleeding, infection, mucosal dehiscence, dry socket, and neurosensory disturbance of the inferior alveolar nerve were registered after three days (T2), seven days (T3) and one month (T4) following SRM3, respectively.

Statistical analysis

Anatomical position was presented as counts and percentage on each treatment group. The time of surgery was presented with mean, standard deviation, minimum and maximum. Mean difference in pain, restricted mouth opening, facial swelling and quality of life were analysed with a generalised estimating equation analysis, GEE analysis for repeated observations. Missing observations in outcome variables were assumed to be missing randomly. The estimated mean value for pain, restricted mouth opening, facial swelling and quality of life were expressed with a 95% confidence interval (CI). Statistical significance of the P-value was set at 0.05. The analyses were descriptive and adjusted for age, sex, smoking and time of surgery.

Data management and statistical analysis was performed with Excel (version 2013, Microsoft, Redmond, Washington) and R (version 3.6.1, Missouri, USA).

Results

Study population

Thirty-one patients (14 men and 17 female) with a mean age of 22.7 years (± 4.6) were included. One patient dropped out due to loss of follow-up. To obtain equal distribution between groups, one patient was included additionally. Mean length of surgery was 7.0 minutes (± 3.7) with no statistically significant difference between test and control group (P = 0.186) (Table 1). The contralateral third molar was removed after 21 days (range: 10-39 days).

Table 1: Anatomical position of mandibular third molars and time of surgery in the two groups and total.

Variable	Level	No cryotherapy (n=31)	Cryotherapy (n=31)	Total (n=62)
Anatomical position (Winter), n (%)	1	20 (64.5)	13 (41.9)	33 (53.2)
	2	5 (16.1)	4 (12.9)	9 (14.5)
	3	4 (12.9)	8 (25.8)	12 (19.4)
	4	2 (6.5)	6 (19.4)	8 (12.9)
Anatomical position (P&G transversal), n (%)	1	0 (0.0)	0 (0.0)	0 (0.0)
	2	29 (93.5)	29 (93.5)	58 (93.5)
	3	2 (6.5)	2 (6.5)	4 (6.5)
Anatomical position (P&G vertical), n (%)	1	10 (32.3)	9 (29.0)	19 (30.6)
	2	13 (41.9)	14 (45.2)	27 (43.5)
	3	8 (25.8)	8 (25.8)	16 (25.8)
Time of surgery (minutes)	mean (sd)	7.39 (4.28)	6.68 (3.05)	7.03 (3.70)
	min	3	4	3
	max	20	15	20

P&G, Pell & Gregory;n, number of wisdom teeth;Q1, first quartile; Q3, third quartile; sd, standard deviation

Postoperative instructions were followed by all patients. Infection involving either fever, chills, sore lymph nodes and pus occurred following removal of six third molars, which were treated sufficiently with antibiotics involving phenoxymethyl penicillin 800 mg (Primcillin®, Meda, Denmark) four times a day and metronidazole 500 mg (Metronidazol "DAK", Takeda Pharma, Denmark) two times a day for seven days. However, one patient presented with a long-lasting infection involving pus, bone sequestration and continuous facial swelling, which

were treated sufficiently with phenoxymethylpenicillin 800mg (Primcillin®, Meda, Denmark) four times a day for a month. Further complications were not observed.

The David SLS-3 3D scanner was highly accurate and precise during scanning of a static object and highly reliable, when comparing the difference between volumes. The mean and standard deviation of the mean distance histogram was 0.000 ± 0.037. The mean and maximum of the differences between volume measurements carried out using the two modalities (Vcone beam computer tomography – Vsurface) were -0.20 cm^3 and 0.73 cm^3, (n = 8), (P = 0.63), respectively, while the correlation between them was 0.98 (95% confidence interval [0.92;1.00]).

Pain

Mean VAS score of pain with or without cryotherapy was 8.47 ± 16.17 (T0), 59.42 ± 24.01 (T1), 37.48 ± 25.42 (T2), 20.70 ± 21.07 (T3) and 3.36 ± 11.62 (T4).There was no statistically significant difference between the two treatment modalitiesat any time point (Table 2). However, a tendency to lower VAS score of pain was observed after three days (T2), seven days (T3) and one month (T4) with cryotherapy compared with no cryotherapy (Figure.2).

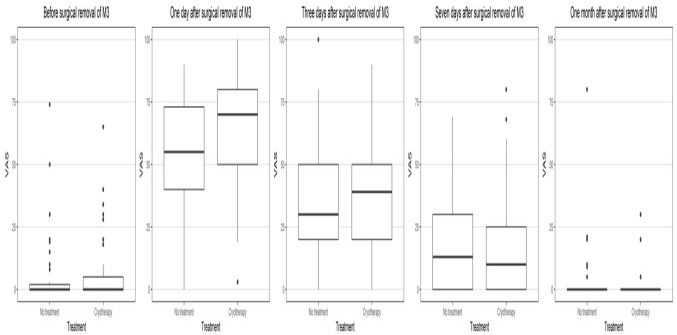

Figure 2: Boxplot illustrating the variability of VAS score between cryotherapy and no cryotherapy

There was no statistically significant difference in VAS score of pain between the two treatment modalities at any time points, when the groups were adjusted for age, smoking and length of surgery. However, VAS score of pain was 9.47 mm lower in females compared with males after one month (T4), which was statistically significant (P< 0.05).

Mouth opening

Mean maximum mouth opening with or without cryotherapy was 47.26 ± 6.55 (T0), 34.30 ± 9.71 (T2), 40.28 ± 9.89 (T3) and 44.27 ± 8.70 (T4). There was no statistically significant difference between the two treatment modalities at any time point (Table 2 and Figure. 3). However, a tendency to lessened restricted mouth opening was observed with cryotherapy compared with no cryotherapy at all time point.

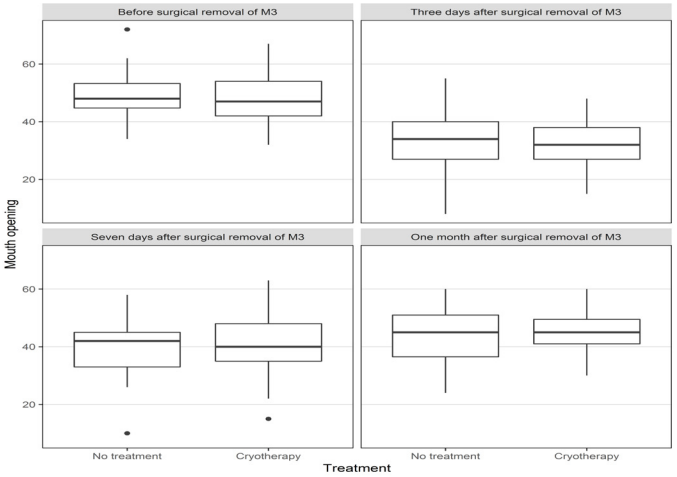

Figure 3: Boxplot illustrating the variability of mouth opening between cryotherapy and no cryotherapy.

There was no statistically significant difference in maximum mouth opening between the two treatment modalities at any time points, when groups were adjusted for age, sex and

Table 2: Results before removal of M3 (T0) compared with one day (T1), three days (T2), seven days (T3) and one month (T4).

Time		T1-T0				T2-T0				T3-T0				T4-T0			
Cryotherapy		Esti	95% CI	se	P	Esti	95% CI	se	P	Esti	95% CI	se	P	Esti	95% CI	se	
Swelling	÷					Ref.				Ref.							
	+					0.54	[-2.99; 4.06]	1.797	0.765	0.05	[-1.86; 1.95]	0.972	0.96				
Pain	÷	Ref.				Ref.				Ref.				Ref.			
	+	1.65	[-9.39; 12.68]	5.632	0.77	-1.84	[-15.08; 11.40]	6.754	0.785	-1.07	[-15.62; 13.48]	7.424	0.885	-7.12	[-16.59; 2.36]	4.834	0.141
Trismus	÷					Ref.				Ref.				Ref.			
	+					1.74	[-2.79; 6.28]	2.315	0.451	0.33	[-4.24; 4.90]	2.333	0.887	1.09	[-5.20; 7.38]	3.209	0.734
QoL	÷									Ref.				Ref.			
	+									1.1	[-5.14; 7.34]	3.184	0.73	0.46	[-4.08; 5.00]	2.315	0.843

CI, confidence interval; Esti, estimate; M3, mandibular third molar; QoL, quality of life; se, standard error; Ref.: reference; VAS, visual analog scale.
Third molars allocated to no cryotherapy were used as reference for the group with cryotherapy.
Swelling: Assessed by superimposition of three-dimensional scans. Estimated value reveals differences in cubic millimetres with cryotherapy compared to no cryotherapy.
Pain: Assessed by VAS. Estimated value reveals differences in VAS score of pain in millimetres with cryotherapy compared with no cryotherapy.
Trismus: Assessed by a ruler. Estimated value shows how many mm the incisal distance has increased or decreased compared to no cryotherapy.
Quality of life: Assessed by OHIP-14 score. Estimated value reveals differences in immediate quality of life with cryotherapy compared to no cryotherapy

smoking. However, maximum mouth opening was statistically significant restricted after three days (T2) and seven days (T3) with increasing length of surgery ($P < 0.05$). Maximum mouth opening continuously decreased by 1.2 mm after three days (T2) and 1.1 mm after seven days (T3), when length of surgery increased by one minute.

Facial swelling

Mean facial swelling with or without cryotherapy was 8.2 ± 6.3 mm^3 (T2) and 2.6 ± 3.6 mm^3 (T3) compared with (T0). There were no statistically significant differences between the two treatment modalities at any time point (Table 2). However, a tendency to lessened facial swelling was observed with no cryotherapy compared to cryotherapy.

Quality of life

Mean OHIP-14 score with or without cryotherapy was 14.05 ± 12.74 (T0), 19.67 ± 13.28 (T3) and 6.03 ± 8.52 (T4). There was no statistically significant difference between the two treatment modalities at any time point (Table 2 and Figure. 4).

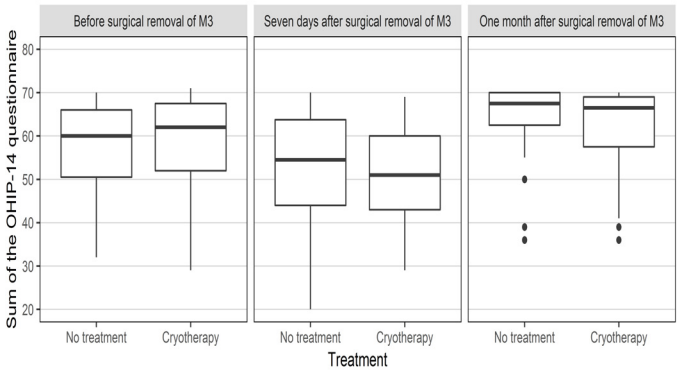

Figure 4: Boxplot illustrating the variability of OHIP-14 score between cryotherapy and no cryotherapy.

There was no statistically significant difference in OHIP-14 score between the two treatment modalities, when groups were adjusted for age, smoking and length of surgery. However, OHIP-14 score was 7.63 higher in females compared with males after one month (T4), indicating reduced short-term quality of life in females after one month. The difference was statistically significant ($P < 0.05$).

Discussion

The objective of the present study was to test the null-hypothesis of no difference in pain, restricted mouth opening, facial swelling and quality of life following SRM3 with 30 minutes of immediate cryotherapy compared with no cryotherapy. The null-hypothesis could not be rejected due to absence of statistically significant difference between the two treatment modalities, although a tendency to lower VAS score of pain and trismus was observed with the use of cryotherapy. However, the present study is characterised by certain limitations including small patient sample, collecting data at predetermined time intervals, quality of life assessment by one self-administrated questionnaire and inconsistent consumption of analgesics following SRM3. Furthermore, the temperature of the skin and subcutaneous tissue was not registered. Moreover, association between educational background, socioeconomic status, income, physical and mental health was not examined. Conclusions drawn from the results of this study should therefore be interpreted with caution and further randomised controlled trials assessing a longer time period of continuous cryotherapy or intermittent application are needed before definite conclusions can be provided about the beneficial use of cryotherapy to diminish postoperative sequelae following SRM3.

Pain is generally considered the worst nuisance following SRM3 causing mild to severe physical discomfort and commonly interfere with a person's quality of life and general functioning[12,13]. The therapeutic efficacy of cryotherapy on pain relief following SRM3 has previously been assessed in systematic reviews concluding negligible effect of short-term continuous cryotherapy, which is in accordance with the results of the present study[10,11,29]. However, a significant reduction in pain has been reported with continuous cryotherapy for 45 minutes or intermittent cryotherapy for 30 minutes every hour during the 24 hours or every hour and a half during 48 hours[16,17,30]. Consequently, the therapeutic efficiency of intermittent or continuous cryotherapy on pain relief following SRM3 is inconclusive based on the current knowledge.

Patient´s perception of pain following SRM3 is influenced by several demographic factors including age, gender, anxiety, culture, ethnicity, socioeconomic status and psychological factors as well as expectations and actual pain experiences[13,31–33]. Considerable inter individual variation in pain perception and consumption of analgesics are not uncommon and young age, pre-existing pain and female sex have previously been identified as predictive factors for severe postoperative pain regardless of the type of surgical procedure[34]. In the present study, VAS score of pain was significant lower in females compared with males after one month, which is in accordance with a newly published study assessing different doses of methylprednisolone following SRM3[35]. However, these results are in contrast to previous studies reporting higher perception of pain in females compared with males following SRM3[32,36]. Consequently, association between demographic factors and predictors for pain should be included in further studies assessing perception of pain following SRM3.

Temporary restricted mouth opening is common following SRM3[37]. The therapeutic efficacy of cryotherapy on restricted mouth opening has previously been assessed in systematic reviews disclosing insignificant effect of short-term continuous cryotherapy, which is in accordance with the results of the present study[10,11,29]. However, a significant reduction in temporary restricted mouth opening has been reported with intermittent cryotherapy for 30 minutes every hour during the first day[16]. Predictive factors of restricted mouth opening following SRM3 include preoperative index of surgical difficulty, length of surgery and surgical trauma[38]. In the present study, demographic parameters and index of surgical difficulty did not differ significantly, but increased length of surgery led to pronounced restricted mouth opening, which is in accordance with previous studies[35,38,39]. Consequently, temporary restricted mouth opening following SRM3 are mainly originated by the length of surgery as well as surgical trauma, while the efficiency of cryotherapy seems negligible.

The therapeutic efficacy of cryotherapy on facial swell-

ing following SRM3 has previously been assessed in systematic reviews disclosing insignificant effect of short-term continuous cryotherapy, which is in accordance with the results of the present study[10,11,29]. However, 30 minutes of intermittent cryotherapy for 24 or 48 hours have demonstrated a significant decrease in facial swelling compared with no cryotherapy, as evaluated by 2D measurements[16,17]. Quantitative analysis of changes in facial volume by 2D measurements is associated with considerable inaccuracies and non-ionising 3D facial scans provides a novel method for measuring and comparing volumetric changes of the faces[20,40]. High degree of reliability, accuracy and reproducibility in quantifying volumetric changes in the facial morphology using 3D facial scan technology have been reported in experimental and clinical studies, respectively[27,40]. Assessment of facial volume changes following SRM3 with the use of 3D optical scanner technique and Slim3D computer software have previously been conducted disclosing significant diminished facial swelling with 45 minutes of immediate Hilotherm cryotherapy compared with conventional cooling compresses after two and ten days[20]. In the present study, no significant difference in facial swelling was observed with 30 minutes of immediate continuous cryotherapy compared with no cryotherapy as evaluated by 3D facial surfaces and template matching technique after three and seven days. Modern concepts of 3D scanning technology seem to be a cheap, valid and reliable tool for quantitative analysis of facial morphology as well as assessment of volumetric facial changes over time[41-43]. However, the reliability, accuracy and reproducibility of 3D scanning technology for assessment of changes in the facial morphology at different time points are influenced by alignment errors by the observer as well as variations in facial expression or posture of the subjects scanned[40]. Moreover, superimposition and measurements of volumetric changes are associated with some inaccuracy due to changes in facial expression or head posture. In the present study, patients were positioned in an identical distance from the 3D optical scanner in an upright chair with closed mouth, relaxed facial expression and adequate head support. Uniform and reproducible natural head position was secured with laser lights to improve the accuracy, reproducibility and reliability of the method. In addition, two minor experiments were made to determine the accuracy and precision of the David SLS-3 3D scanner. The experiments showed that the David SLS-3 3D scanner was highly accurate, precise and reliable. Template matching techniqueis a simple tool for superimposition of 3D scans and has previously been used for identifying odontological differences of molars and volumetric changes after facial surgery[27,44]. The 3D template can subsequently be deformed to the shape of each scan and thereby transferring the ROI, so the 3D template can be used and fit to each 3D scan.

Deteriorated quality of life following SRM3 is frequently reported, as documented in systematic reviews[45,46]. Assessment of quality of life usually includes a subjective evaluation of the individual's oral health, functional well-being, emotional well-being, expectations and satisfaction with treatment as well as self-esteem. Moreover, length of surgery, severity of intra- and postoperative complications as well as intensity of pain adversely affect patient's perception of quality of life[47]. Previous studies have demonstrated that continuous and intermittent cryotherapy improve quality of life following SRM3, as evaluated by self-administrated questionnaire[16,30,48]. In the present study, OHIP-14 questionnaire revealed no significant differences in quality of life between the two treatment modalities at any time points even after the groups were adjusted for age, smoking and length of surgery.OHIP-14 questionnaire is a simple, validated and reliable method for assessment of the adverse impact caused by oral conditions on well-being and quality of life[49]. However, OHIP-14 declares the patient´s overall oral impairment and does not focus on a specific surgical intervention. Consequently, further studies assessing quality of life following SRM3 should include additional self-administrated questionnaires focusing on patient´s perception of the surgical intervention as well as association between outcomes and demographic factors, socioeconomic status as well as educational background.

The null-hypothesis could not be rejected due to absence of statistically significant difference in pain, trismus, facial swelling, and quality of life following SRM3 with 30 minutes immediate cryotherapy compared with no cryotherapy. However, the present study includes limitations and methodological confounding variables, which may have affected the outcome. Further randomised controlled trials assessing longer use of cryotherapy or intermittent application are therefore needed before definite conclusions can be provided about the beneficial use of cryotherapy to diminish postoperative sequelae following SRM3.

Acknowledgements: A special thanks to secretary Tanja Møller Andersen, Department of Oral and Maxillofacial Surgery, Rigshospitalet, Copenhagen University Hospital, Denmark for planning and booking of patients.

Funding: The 3D-scanner (David SLS-3 3D scanner, DAVID Vision Systems, Germany) was supported by the Danish Dental Association, Denmark.

Competing interests: None declared.

Ethical approval: The study protocol was approved by the Research Ethics Committee and the Danish Data Protection Agency.

Patient consent: Not required.

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