The main purpose of this study was to compare the effect of the 2 minimally invasive surgical techniques for treating axillary hyperhidrosis: superficial tumescent suction curettage and curettage only. A total of 22 patients diagnosed with axillary hyperhidrosis received one type of treatment at each side, randomized. Examinations were performed pre-operatively and at 3, 6 and 12 months following treatment. Sweating was measured by gravimetry and a new skin conductance method. Subjective rating of sweating was assessed by a visual analogue scale. Skin conductance was recorded during a stress-test including acoustic, mental and physical stressors. Five patients withdrew or did not meet for any follow-up examination, giving 17 subjects in total for data analysis. Significant reduction in sweating after surgery lasting at least 12 months was found based on skin conductance, gravimetry and visual analogue scale scoring. Comparison between types of treatment revealed a significantly better effect of tumescent suction curettage than curettage only. Key words: axillary hyperhidrosis; liposuction; curettage; skin conductance.

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Primary focal hyperhidrosis is a condition that causes excessive sweating of the palms, soles and/or the axillae, with a positive familial history in 30–50% of cases suggesting genetic involvement (1). The disorder occurs in either sex, with a prevalence of up to 5.5% (2) and commonly begins in childhood or puberty. The pathophysiology of the disease is not fully understood, but may involve a complex dysfunction of the sympathetic nervous system due to an imbalance in the hypothalamus, being influenced by emotional stimuli from the limbic system and cortex (3). No quantitative or qualitative histopathological changes in the eccrine sweat glands of hyperhidrosis patients have been found (4).

Currently, botulinum toxin (BTX) is considered the treatment of choice in focal hyperhidrosis, with high efficacy, minimal side-effects and an effect lasting 6–8 months (4). Surgical excision of axillary sweat glands is associated with high complication rates (5). Minimally invasive suction curettage has been compared with excisional surgery, with similar efficacy and a lower complication rate for suction curettage (6). The minimally invasive surgical techniques have been established as the standard surgical care for axillary hyperhidrosis, with good results and minimal side-effects (7, 8). These techniques include superficial tumescent suction curettage, which involves subcutaneous infiltration of large volumes of crystalloid fluid containing low concentrations of lidocaine and epinephrine and requires equipment used for liposuction procedures, or use of different cannulas for subdermal curettage only.

In most cases the decision to treat patients is based on their description of symptoms. Diagnostic criteria for the diagnosis of primary focal hyperhidrosis have been proposed by the Multi-Speciality Working Group on Hyperhidrosis (9). No test has proved to be useful diagnostically, but gravimetry could be used as a tool for quantitative measurement of sweating. Hund et al. (10) defines axillary hyperhidrosis as a sweat rate of minimum 50–100 mg/5 min per axilla. Sweating often varies rapidly under different conditions, further impeding the evaluation of sweating, both pre- and post-treatment. Consequently, there is no consensus based on objective criteria as to when treatment should be given. Other methodologies that can be applied to measure sweating include trans-epidermal water loss (TEWL), where the water evaporation rate above an area of skin is measured by humidity sensors (11); Minor’s iodine-starch test, where an iodine-starch mixture is applied to the skin for determination of the sweat producing area (12). The ninhydrin-test is similar to the iodine-starch test, but allows for sweat production quantification via digital analysis of the image produced on paper by the chemical reaction between ninhydrin and amino acids in sweat (13). In addition, a method based on the skin alternating current (AC) conductance below a gel electrode attached to the skin has been proposed for the measurement of sweat activity (14).

The main goal of this study was to compare a tumescent suction curettage with simple curettage needing no spe-
cial equipment. A secondary goal was to evaluate the skin AC conductance method as an objective measurement for treatment evaluation, and to compare this with the traditional quantitative assessment by the filter paper method.

MATERIALS AND METHODS

Patients
All patients referred to the Department of Dermatology or Plastic Surgery, Oslo University Hospital, with the diagnosis of axillary hyperhidrosis between January 2007 and December 2009 were invited to participate. Inclusion criteria were: primary focal hyperhidrosis of the axillae not responding to conventional non-surgical treatment, and age over 18 years. Exclusion criteria were: pregnancy, breastfeeding, previous treatment with BTX, or previous surgery of the axillae. A total of 22 patients (median age 27 years, range 20–44 years, 4 males, 18 females) were included after signing written informed consent. The study was approved by the regional ethical committee and conducted according to the Declaration of Helsinki.

Surgical procedures
Each axilla was randomized to either tumescent suction curettage (treatment type A) or curettage only (treatment type B). Both procedures were performed simultaneously by 2 surgeons who treated the hair-bearing part of the axilla at the junction of dermis and subcutis.

The axilla receiving curettage only was anesthetized with a 50/50 mixture of lidocaine 1% with adrenaline and saline water, maximum volume 40 ml. Through 2 punch biopsy holes the curettage was carried out with a sharp ring curette (KAI disposable dermal curette, Selles Medical, Hull, UK) performing radial movements from the punch hole outwards. To avoid haematoma after curettage, between 4 and 6 quilting sutures were placed in the treatment area after suturing the punch biopsy holes.

The suction curettage was carried out in tumescence anaesthesia (200 ml 0.9% saline combined with 8 ml lidocaine 2% and 0.2 mg adrenalin), which was introduced with a standard tumescent cannula (Coleman/Byron system, Mentor, USA) through 2 stab incisions at the distal border of truncal and extremital part of the axilla. The suction curettage was performed with a standard 3-mm cannula with a 60 ml syringe (The Tulip Instrumentation System, Tulip Medical, San Diego, USA), and during the procedure the opening on the tip of the cannula was towards the dermis. Both stab incisions were sutured.

The treatment on both sites was stopped when skin lividity was observed and the treated areas were covered with compression bandage.

Both treatments included curettage to destroy the eccrine glandular tissue with subcutaneous access. The curettage-only method utilized an easily accessible, disposable curette, whereas suction curettage included a specialized suction curette under negative pressure to remove glandular tissue. All patients were evaluated one week after the treatment procedure, and infection, haematoma and postoperative pain were recorded.

Subjective outcome measures: questionnaires
At each visit preoperatively and at 3, 6 and 12 months after surgery, the patients were asked to complete the Dermatological Life Quality Index (DLQI) form (5) for the impact of sweating on the quality of life, in addition to the subjective scoring of the degree of sweating, and the total quality of life, all on visual analogue scales (VAS) ranging from 0 to 10.

Objective outcome measures: gravimetry and skin alternating current conductance
The patients were examined by the following protocol preoperatively and at 3, 6 and 12 months following surgery. They were instructed to shave their armpits 2 days before the examination in order to avoid influence from razor cuts on the measurements. Sweating was first measured by the gravimetric filter paper method (10). Circular filter paper 90 mm in diameter (Schleicher & Schuell, Dassel, Germany) was weighed by a Mettler Toledo AT200 precision weight. While the patient was resting in bed with hands behind the neck, the preweighed paper was attached to both axillae with a plastic film taped over it to avoid evaporation. A stocking filled with cotton was carefully knotted around the axillae to apply gentle pressure to the paper against the skin. After 5 min, the paper was removed and reweighed immediately. The difference in weight after 5 min of attachment to the skin was used as the gravimetric sweat production parameter.

With the aim of also measuring sweating in reaction to different types of stress, a test protocol was designed as shown in Fig. 1.

For the acoustic stimulus at 7 min, a 2.5 s sound sample of a breaking glass was played by a set of speakers hidden below the bed at an intensity measured to be 82 dB 1 m away. At 14 min, mental stress was provoked by asking the patient to subtract given numbers continuously, starting from 1,000 and lasting for 2 min. The difficulty was adjusted according to the speed of correct answering in order to equalize the effect of the provocation among the subjects. At 23 min, provocation by physical activation was induced by asking the patient to raise the upper body as far as possible while keeping the back straight and the hands behind the head, and then relaxing after reaching the maximal level. Seven min of relaxation without talking was given before and after each provocation to allow sweating to return to baseline, giving a total of 30 min for the skin conductance (SC) recording. To avoid habituation to the test over the repeated examinations, the protocol was gone through with the patients before each session.

Sweating was measured continuously during the test by changes in skin AC conductance (14) using a Sudologger system (BioGauge AS, Oslo, Norway). Sensor electrodes of the Arbo Kittycat™ solid gel type, as recommended in (15), were attached to the apex of both axillae, the hypothenar area of the right hand and at the T9 dermatome above the navel. The 2 latter sites were kept at 23 °C and reweighed immediately. The difference in weight after 5 min of attachment to the skin was used as the gravimetric sweat production parameter.

Data analysis
On several occasions, patients were not able to attend some of the scheduled post-operative examinations. In total, there were 216 C. Tronstad et al.

Fig. 1. Time-line of the stress-test protocol for recording sweating responses to different types of stimuli. The recording starts with 7 min of relaxation until a sudden loud sound is played. After a further 7 min of relaxation, the subject performs a subtraction task for 2 min. At 23 min, after a further 7 min of relaxation, the subject is asked to raise the upper body as far as possible. The recording is completed with 7 min of relaxation.
5 patients who either withdrew from the study or did not meet for any of the follow-up examinations and were excluded from the analysis. This resulted in a total data-set of 17 pre-operative measurements, 10 at 3 months, 12 at 6 months, and 12 at 12 months post-operative examinations.

The SC recordings were parameterized into one value (Sum SC) representing each examination, calculated as the sum of the baseline level and the responses to each of the stimuli during the stress-test (see Table S1). The Sum SC was used for statistical evaluation of the treatment outcome along with the gravimetric measurements. The frequency of palmar SC responses is known to increase with mental stress (16, 17), and the number of SC responses (NSCR) in the hypothenar time-series was calculated to enable correction for stress habituation as the examinations were repeated.

The VAS sweating question was not specific to each side at the preoperative visit; hence the total value was used for both sides for the preoperative data in the analysis. The DQLI and the quality of life VAS scores were not included in the analysis, as they were not specific to the sides of the body and the treatment type post-operatively. (Table SII gives a complete list of all the parameters used for the statistical analysis).

In order to evaluate the outcome of the surgery over time, the pre-operative and all post-operative measurements were included in a linear mixed effects (LME) model, with winter and type of surgery as fixed effects and subject as a random effect. Pairwise comparisons of estimated marginal means were carried out with Bonferroni adjustment.

To evaluate the difference between treatment outcomes post-operatively, the 3 months to 12 months data was analysed with a LME model with time and treatment as fixed effects and subject as a random effect. Pairwise comparisons of means were carried out post-hoc with Bonferroni adjustment. Treatment × time was initially added as a fixed effect, but excluded after confirming no significant interaction for any of the treatment-dependent variables.

The tests on the objective measurements of SC and gravimetry were also run with hypothenar NSCR as a random effect covariate to correct for changes in stress levels. In order to correct for possible influences of seasonal variations in outdoor temperature, the heat-rank of the season in which the measurement was performed was also included as a fixed effect covariate, with winter given value 1, spring or autumn 2 and summer 3. For the comparison between types of treatment, the pre-operative measurements were added as random effects covariates to adjust for any possible initial differences between the 2 randomized groups of axilla assigned for each treatment.

The gravimetric measurements had a very skewed distribution and log-transformed values were used for the LME analysis. Correlation analysis by Spearman’s rank order was applied between all combinations of Sum SC, gravimetry and the VAS sweating score.

RESULTS

Effect of surgery on sweating

As shown in Fig. 2, there was a significantly lower ($p<0.001$) Sum SC during the stress-test at all post-operative examinations compared with before treatment. There was no significant difference in Sum SC between any of the 3 follow-up examinations. Adjusting for hypothenar NSCR stress-levels and season produced the same result.

The gravimetric measurements were significantly lower at 6 ($p<0.05$) and 12 months ($p<0.01$) compared with before treatment, but there was no significant improvement at 3 months or any significant difference between the post-operative measurements. Adjusting for covariates made the 6 months improvement non-significant ($p=0.098$).

The same result applied for the subjective VAS scoring of sweating as for the Sum SC, with a significant reduction ($p<0.01$) in self-assessed sweating at all post-operative visits compared with the first visit. There was also no significant difference between the VAS sweating score at any of the follow-up visits.

Comparison between types of treatment

For the post-operative stress-test measurements, the type B treated axilla had a higher Sum SC than type A (mean difference 4.26, $p=0.011$). There was no significant effect of time from 3 to 12 month examinations ($p=0.72$). Adjusting for covariates produced the same result, with mean difference 3.33, $p=0.029$, and no significant effect of time ($p=0.53$).

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Fig. 2. Box-plots showing the change in sweating assessed by skin conductance (SC) (a), gravimetry, (b) and visual analogue scale (VAS) (c) from pre-operative to 3, 6 and 12 months after surgery with treatment type A (black boxes) and B (grey boxes). Significant improvements (reduction from the pre-operative measurements assessed by the linear mixed effects (LME) analysis) are indicated by *$p<0.05$, **$p<0.01$ and ***$p<0.001$. Outliers are presented according to the Tukey method.
The LME test on the gravimetric post-operative data also resulted in significantly lower values for the type A treated axilla than for type B \( (p = 0.028) \), with no significant effect over time \( (p = 0.26) \). Adjusting for the covariates produced the same result, with \( p = 0.021 \) and no significant effect of time \( (p = 0.39) \).

There was a significantly better result from type A than type B surgery also for the subjective VAS scoring of sweating \( (p < 0.01) \), with a mean difference of 1.6. There was also no significant effect of time for this parameter \( (p = 0.35) \).

**Correlations between parameters**

Although the stress test with the SC measurements revealed changes that the gravimetric measurements did not, there was a significant correlation between the 2 objective parameters, as shown in Fig. 3a and b, with \( \text{rho} = 0.66, p < 0.001 \). Shown in Fig. 3c and d, the subjective rating of sweating correlated significantly with both objective measurements, and was in better agreement with the SC measurement \( (\text{rho} = 0.54, p < 0.01) \) than the gravimetric measurement \( (\text{rho} = 0.38, p < 0.01) \).

**Sweating reactions according to stimulus type and skin site**

There was a variation in the magnitude of the sweating response according to type of stimulus and also between the different measuring sites. As seen in Fig. 4, the arithmetic stimulus produced the highest response amplitudes in the skin conductance. Among skin sites, the hypothenar site had the largest sweating responses for all of the stimulus types. Responses were often completely absent at the abdomen site.

**Side-effects**

No infections that required systemic antibiotics or haematoma were registered at follow-up after one week. Scarring was not observed at any treatment site during the follow-up period. One patient receiving suction with curettage experienced postoperative neuropathic pain, lasting through the observational period.

**DISCUSSION**

Both the subjective and objective assessments indicate that the surgery reduced the axillary sweating, and that the effect of treatment lasted at least 12 months. Tumescent suction curettage seemed to be superior to curettage alone. The SC measurements correlated with gravimetry, and were in better agreement with the subjective scores of sweating than the gravimetry.

The diagnosis of primary focal hyperhidrosis is based on criteria according to Hornberger et al. (9), and a patient history and clinical examination is sufficient for diagnosis. All patients in this study were evaluated before inclusion by one investigator (ALK) and the patients fulfilled the diagnostic criteria of primary focal hyperhidrosis. However, few of these patients fulfilled the requirement for axillary hyperhidrosis as proposed by Hund et al. (10) based on gravimetry. The reason for this discrepancy between clinical criteria and objective measurements is difficult to determine, but all patients underwent gravimetry in calm surroundings, with a stable temperature between 22 and 24°C in well-ventilated rooms. However, the results from this study may not be valid in people who sweat heavily. Tumescent suction curettage has, in several studies, been shown to be effective in focal axillary hyperhidrosis, but the

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*Fig. 3.* Scatter-plots of the correlation between the different parameters used to assess sweating. (a) Correlation between skin conductance (SC) and gravimetry, also shown in (b) on logarithmic scales. (c, d) Correlation between the visual analogue scale (VAS) sweating scores and SC and gravimetry, respectively.
procedure requires special equipment. Our aim was to investigate whether a simple curettage was equally effective, making minimal surgery for focal axillary hyperhidrosis more available to patients. Tumescent suction curettage seemed more effective than curettage in our patients judged by the objective measurements of SC and gravimetry and also the subjective VAS scores of perceived sweating.

There are several factors that are important in relation to the differences found between the 2 methods. Basically, the curettage procedure has to be performed equally on both sides in order to compare the 2 techniques. This was clarified in advance; equal areas were treated and the procedure was performed at the same skin level. When it comes to the difference between the 2 techniques, there are 2 significant differences. The first is that there is a negative pressure when using suction curettage that allows the dermis to be carved into the hole in the cannula, which may lead to a more radical removal of both glandular tissue and nerve endings. In addition, the suction curettage removes the cutreted tissue. This tissue also contains fat cells, which include mesenchymal stem cells (MSC). It is shown that these cells may have regenerative effects (18, 19). On the side where only curettage was performed it is possible that more MSC have been triggered, which affects the regenerative capacity of the sweat glands and neural outgrowth, and thereby prevents a permanent result as obtained postoperatively. Our results demonstrated a trend towards best effect at 6 months after both surgical procedures. This is consistent with 2 small studies that showed a mean relapse time of between 6 and 12 months (20, 21). This also correlates with the mean time it takes to regenerate the sweat glands and neural outgrowth in the treated area, independent of the effect of the MSC. However, in the same studies relapse times varied between 6 weeks to >1 year, showing that the relapse time is not only dependent on the general regenerative potential, but also other factors, such as the primary result after treatment and patient-related conditions.

The stress test with the SC measurement revealed more significant effects of surgery than with the gravimetric measurement, although there was a significant correlation between the 2 measurements. Inspecting the relationship between the 2 types of measurement shown in Fig. 3, it is clear that there is a relatively large variation in SC values, while many gravimetric values are close to zero. In these low gravimetric measurements, only one small, or no, drops of sweat were visible on the filter paper after removal from the axilla. This indicates that the gravimetric measuring method may have insufficient sensitivity for estimation of sweat production at the lower end of the scale. The opposite relationship seems to occur at the higher end of the scale, with a relatively large variation in the gravimetric values, while the SC values are close to 40. This was caused by a saturation in the SC measurement among the most extreme sweaters, and should not be regarded as a limitation of the SC method, as this was due to equipment settings that did not meet the unexpected extreme values. In the most extreme case, as seen by the outlier in Fig. 2b, 2 filter papers had to be attached at each axilla to avoid saturation of sweat absorption in the paper. Hence, the stress-test with the SC measurement may be better suited to diagnose and evaluate treatment effect when sweat production is low during the measurement, but the traditional gravimetric method could be better when sweat production is very high. As seen in Figs 2a and b, there were some substantial outliers post-operatively. This indicates that there were a few extreme sweaters, who, even after treatment, still had a sweat rate substantially higher than the rest of the study population.

Another advantage of the SC method is the ability to examine sweating responses to certain stimuli by the high temporal resolution of the method, which is not possible with the gravimetric measurement. As shown in Fig. 4, there was a large difference in response magnitudes between the different types of stimuli. However, the 2-min duration of the arithmetic stimulus could explain the higher amplitudes for this type compared with the short acoustic and physical stimuli. The large difference between the magnitudes of hypothenar and abdomen responses is probably a combination of sweat gland density and dermatome innervation. There were also large differences between subjects in the way that the same stimulus could produce a strong sweating reaction in one subject, but little to no reaction in another. While the arithmetic stimulus produced the strongest reaction in most subjects, in 4 subjects the strongest reaction was to the acoustic or physical stimuli. This indicates that the method could help the physician to pin-point the specific symptom-inducing stressor in the patient. This could be a reason for the higher correlation between the SC measurements from the stress test and the VAS scoring, as the subjective score concerns...
the typical individual sweating level, which is better approached with a stress-test including several factors related to the daily life than the point measurement of the gravimetric method.

The stress-test protocol was developed by the authors specifically for this study, and could probably be improved either by expanding to include more typical stressors or by narrowing to the few most relevant stressors for the patients. The 30 min test in the clinic could still be a very different situation from the daily lives of the patients. Many patients had low objective sweating scores during the examination, while reporting excessive sweating under normal circumstances, indicating that the setting was different or that the protocol failed to provoke the correct symptom triggers. Ideally, the measurement should be done with an ambulatory patient equipped with sensors recording the sweat activity during a typical 24 h session. This is possible with the Sudologger system, but the size of the device and the sensor cabling would be cumbersome to most patients for long-term wear. The technology is, however, very possible to miniaturize with current electronic solutions.

Figs 3c and d show that there is a large interindividual difference in how each subject rates their symptoms. There are VAS scores over the whole range, while the measurements are at the lower end. It seems, however, that when the Sum SC score is above 15 or the gravimetry is above 100, most patients rate their sweating at the higher end of the scale, indicating that this level is associated with a general self-perception of excessive sweating.

Based on the agreement between the SC method and gravimetry, the improved sensitivity to detect positive treatment results, the higher agreement with the subjective symptom scores than for the gravimetry, the ability to continuously measure quick sweating responses to different types of stimuli, the SC method is proposed as an assisting clinical tool in diagnostic or treatment evaluation. Due to the small size of the equipment (a pocket-size box with wireless data transmission with electrodes and wires), the technology is easy to use in the clinic.

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Disclosure: SG and CT played main parts in the development of the Sudologger system, which was used in this study. The Sudologger is currently marketed by BioGauge AS, in which SG has commercial interest.

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